RGUHS · MODEL ANSWER BANK

The questions RGUHS repeats — fully answered

RGUHS MS Obstetrics & Gynaecology — 2016-2026

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RECURRING-QUESTION ANSWER BANK

2006–2026

671 recurring topics · textbook-verified · guideline-current (ACOG · RCOG · FOGSI · FIGO · NICE) · cited Recent Advances

GROUNDED IN:

Williams Obstetrics 26e — obstetrics spine text
Berek & Novak's Gynecology 16e — gynaecology spine text
Speroff's Clinical Gynecologic Endocrinology & Infertility 9e — reproductive endocrinology & infertility
Te Linde's Operative Gynecology 13e — operative gynaecology
DC Dutta's Obstetrics 9e & Gynaecology 7e — Indian standard texts
Current guidelines: ACOG · RCOG (Green-top) · FOGSI · FIGO · NICE
Cited Recent Advances: PubMed + landmark obstetric & gynaecological trials
Arias' High-Risk Pregnancy 5e — obstetric high-risk spine
Munro Kerr's Operative Obstetrics 13e — operative obstetrics spine
Jeffcoate's Principles of Gynaecology 9e (2019) — gynaecology spine (clean HELINET text)

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Contents

Paper I — Applied Basic Sciences

Applied basic sciences (reproduction)

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A 25-year-old with 6 weeks pregnancy diagnosed to have acquired chicken pox infection. Outline the steps in the management

Asked in: Paper I 12-Nov-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — Chickenpox is primary infection with **varicella-zoster virus** (VZV), a DNA herpesvirus, in a non-immune gravida. At 6 weeks' gestation (first trimester), management has two simultaneous goals: treat the mother — who is more prone to VZV pneumonia than a non-pregnant adult — and assess/counsel for **congenital varicella syndrome** (CVS), since infection has occurred in the first half of pregnancy.

Step 1 — Confirm diagnosis and assess maternal severity

Assessment	Finding / test
Clinical diagnosis	Crops of pruritic vesicles on an erythematous base, at different stages (papule → vesicle → crust); usually sufficient, confirmed by history of contact
Confirmatory test (if doubtful)	PCR of vesicular fluid or a lifted skin crust
Screen for pneumonitis	Fever, tachypnoea, dry cough, dyspnoea, pleuritic chest pain — typically appear 3–5 days into the illness; get a chest X-ray if any respiratory symptom (VZV pneumonia may be present with few symptoms)
Risk stratify	Uncomplicated cutaneous disease (majority) vs pneumonia/systemic illness needing admission (≈2.5% of infected gravidas develop VZV pneumonia)

Step 2 — Isolate and give supportive care

- **Isolate** from other pregnant women, neonates, and immunocompromised contacts until all lesions have crusted (infectious from ~48 hours before the rash to crusting).
- **Antipyretic/analgesic:** paracetamol. Avoid **aspirin** (Reye syndrome risk) and avoid **NSAIDs** (associated with severe secondary bacterial/soft-tissue infection in varicella).
- **Local care:** calamine lotion/antihistamines for pruritus, keep lesions clean and dry to prevent secondary bacterial infection.

- **Admit** if pneumonitis, dehydration, or any systemic compromise; give intravenous fluids as needed.

Step 3 — Start antiviral therapy

Clinical scenario	Regimen
Uncomplicated primary varicella, outpatient (best started within 24 h of rash onset)	Oral **acyclovir 800 mg five times daily for 7 days**
Hospitalised — varicella pneumonia/systemic illness	**IV acyclovir 10–15 mg/kg every 8 hours until afebrile**, then oral acyclovir 800 mg five times daily to complete 7 days and until all lesions have crusted

- **Varicella-zoster immune globulin (VariZIG) has no role now.** VariZIG (intramuscular, 125 units/10 kg body weight, maximum 625 units/5 vials) is *post-exposure prophylaxis* for a seronegative, exposed but not-yet-infected woman — best within 96 hours of exposure, though of benefit up to 10 days. Once the rash has erupted, as in this patient, VariZIG will not prevent or attenuate the disease and is not indicated.

Step 4 — Assess and counsel on fetal risk (congenital varicella syndrome)

Gestational age at maternal rash	Risk of CVS in the fetus
Before 13 weeks (this patient, 6 weeks)	~0.4%
13–20 weeks (highest-risk window)	~2%
After 20 weeks	No clinical CVS reported; third-trimester infection rarely causes isolated CNS/skin findings

Features of CVS (numbered, counselling checklist):

- Cicatricial (zig-zag) skin scarring in a dermatomal distribution with underlying limb hypoplasia
- Chorioretinitis, microphthalmia, cataracts
- Cerebral cortical atrophy, microcephaly, psychomotor retardation
- Fetal growth restriction, hydronephrosis

Counsel the couple that at 6 weeks the quoted risk (~0.4%) is low but not zero, and that most (>97%) exposed fetuses are unaffected.

Step 5 — Plan fetal surveillance

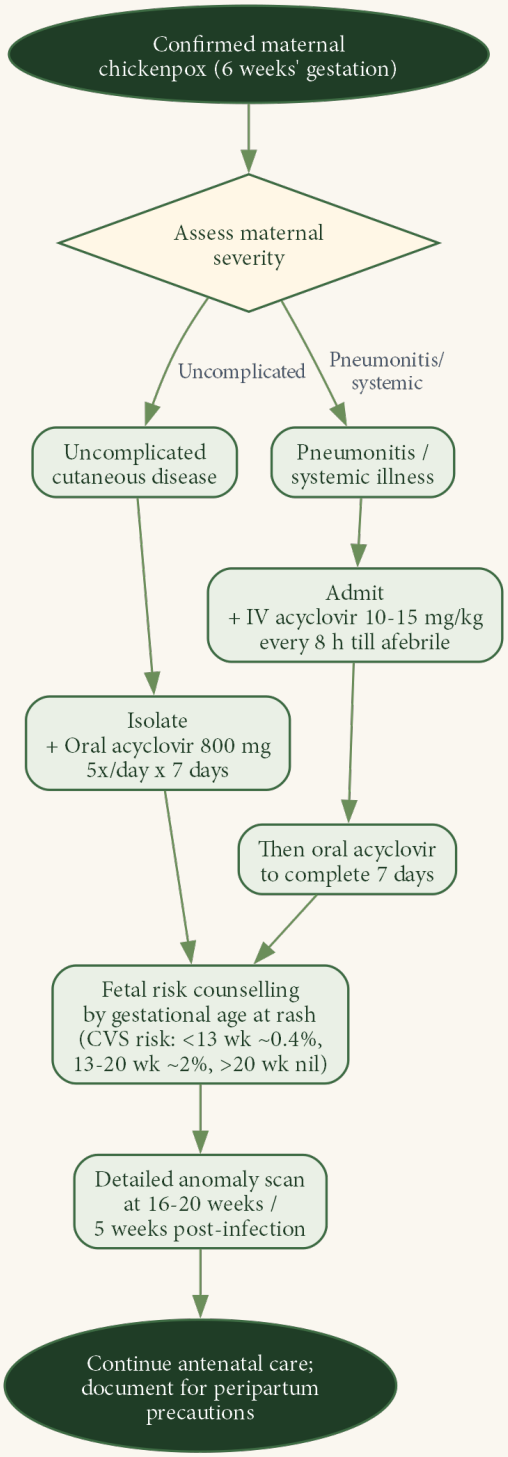
- **Refer to a fetal medicine unit** for a detailed targeted sonographic anomaly scan at 16–20 weeks' gestation, or ~5 weeks after the maternal infection (whichever is later) — look specifically for limb deformity, hydrops, echogenic bowel/liver foci, ventriculomegaly and growth restriction (scan sensitivity for CVS is low, so a normal scan does not fully exclude it).

- **Amniocentesis for VZV PCR** on amniotic fluid may be offered after informed counselling, but a positive result correlates poorly with the fetus actually developing CVS — it is not offered routinely on this basis alone.
- **Serial growth scans** through the remaining pregnancy given the growth-restriction risk.

Step 6 — Continue antenatal care

- Document the episode and immune status in the antenatal record; **do not give varicella vaccine during this pregnancy** (live-attenuated).
- Continue routine antenatal visits; reassure the woman that outcome is favourable in the great majority of cases.
- **Forward planning for later in pregnancy:** if maternal rash were to occur from 5 days before to 2 days after delivery, the neonate is at high risk of severe neonatal varicella (attack rate 25–50%, mortality ~30%) and needs neonatal VariZIG — not applicable at the present 6-week gestation, but worth noting in ongoing counselling.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Decision tree from maternal severity assessment through antiviral therapy to fetal-risk counselling and surveillance.

High-yield exam pointers

- VariZIG dose: **125 U/10 kg IM, max 625 U (5 vials)**; best <96 h, effective up to 10 days of *exposure* — **not useful once the rash has appeared**.
- Acyclovir: outpatient **800 mg 5×/day × 7 days**; hospitalised **10–15 mg/kg IV 8-hourly till afebrile**, then oral to complete 7 days.
- CVS risk by gestation: **<13 wk ≈ 0.4%, 13–20 wk ≈ 2% (peak), >20 wk ≈ nil.**
- CVS tetrad to recall: **limb hypoplasia + cicatricial skin scars + eye defects (chorioretinitis/microphthalmia) + CNS defects (cortical atrophy/microcephaly).**
- Avoid **aspirin/NSAIDs**; use paracetamol.
- Neonatal risk window: maternal rash **5 days before to 2 days after delivery** → severe neonatal varicella (attack rate 25–50%, mortality ~30%) → neonate needs VariZIG.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> The RCOG Green-top Guideline No. 13 on chickenpox in pregnancy is widely followed in practice alongside the ACOG Practice Bulletin on viral infections in pregnancy, but only the ACOG-referenced and CDC-referenced dosing above was verifiable against the corpus available; figures are drawn from Williams Obstetrics 26e as the grounded source.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; American College of Obstetricians and Gynecologists Practice Bulletin (Cytomegalovirus, Parvovirus B19, Varicella-Zoster, and Toxoplasmosis in Pregnancy); Centers for Disease Control and Prevention (2013) VariZIG guidance.

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Anticonvulsants in pregnancy

Asked in: Paper I 29-Jul-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — Anticonvulsants (antiepileptic drugs, AEDs) are agents used to control seizure disorders (epilepsy) in pregnant women with pre-existing epilepsy. Their use in pregnancy requires balancing maternal seizure control — seizures themselves cause hypoxia, trauma and a ten-fold higher maternal

mortality — against a definite, drug-specific risk of fetal teratogenicity and altered maternal pharmacokinetics.

Bidirectional effect of pregnancy and epilepsy

Direction	Effect
Pregnancy on epilepsy	Seizure frequency is classically unchanged in ~50%, increased in ~45%, decreased in ~5%; women seizure-free for ≥9 months before conception usually remain so
Epilepsy/AEDs on mother	Increased miscarriage, hyperemesis, hypertensive disorders/pre-eclampsia, placental abruption, preterm birth, postpartum depression; status epilepticus is a medical emergency
Epilepsy/AEDs on fetus/neonate	Drug-specific major malformations, fetal growth restriction, neonatal hemorrhage (vitamin-K-dependent factor depletion), neonatal drowsiness; offspring risk of developing epilepsy is 5–10%

Classification of AEDs by teratogenic risk

Drug	Malformation pattern	Monotherapy risk	First-line?
Valproate	Neural tube defects, clefts, cardiac anomalies; lower cognitive performance/ADHD	7–10% (dose-dependent; higher with polytherapy)	**Avoid** — most teratogenic AED
Phenytoin	Fetal hydantoin syndrome (craniofacial anomalies, nail hypoplasia, growth deficiency)	5–11%	No
Carbamazepine/oxcarbazepine	Hydantoin-syndrome-like features, spina bifida	2–5%	Yes (acceptable first-line)
Phenobarbital	Clefts, cardiac, urinary-tract anomalies	6–20%	No
Lamotrigine	Clefts (registry data)	Up to 2%	**Preferred first-line**
Topiramate	Clefts	2–3%	No
Levetiracetam	Theoretical skeletal effects	1–3%	**Preferred first-line**

Lamotrigine, levetiracetam or carbamazepine are the drugs of first choice on current teratogenicity data; polytherapy carries a cumulative risk with each additional drug.

Why free/serum anticonvulsant levels fall in pregnancy

- Nausea, vomiting and delayed gastric emptying reduce absorption
- Plasma volume expansion dilutes the drug
- Altered protein binding changes the free fraction
- Induction of hepatic (cytochrome) and placental drug-metabolising enzymes increases clearance
- Increased glomerular filtration rate hastens renal excretion

Preconception and antenatal management

- Counsel before conception; consider tapering if seizure-free ≥2 years; otherwise optimise to **monotherapy at the lowest effective dose**
- **Folic acid** 0.4 mg/day from ≥1 month pre-conception, **increased to 4 mg/day** once pregnant on an AED (continued through the first trimester)
- Switch away from valproate to lamotrigine, levetiracetam or carbamazepine where feasible — but do **not** destabilise a seizure-free regimen once organogenesis is underway
- Routine serum AED monitoring does not itself improve seizure control; check levels selectively after a breakthrough seizure or if non-compliance is suspected
- Prenatal screening: serum α-fetoprotein at 16 weeks + detailed anomaly scan with fetal echocardiography at 18–20/22 weeks (targeted, not routine fetal surveillance, for otherwise uncomplicated epilepsy)
- Vitamin D supplementation (deficiency is common in women on enzyme-inducing AEDs)
- Continue the same AED through labour; give parenterally if the patient is nil-by-mouth

Management of an acute seizure/status epilepticus in pregnancy

- Airway, oxygen, left-lateral position; protect from injury
- First-line: IV benzodiazepine — **lorazepam 4 mg IV slow** (repeat once after 10–15 min) or diazepam 10–20 mg slow IV
- If seizures continue (benzodiazepine-refractory/status epilepticus): **IV phenytoin, slow loading dose 15–20 mg/kg**; fosphenytoin, levetiracetam or valproate are comparably effective alternatives
- **Magnesium sulfate is not an anticonvulsant for epilepsy** — it is reserved specifically for eclamptic convulsions; an epileptic fit in pregnancy is distinguished from eclampsia by the absence of hypertension/proteinuria and a known seizure history

Postpartum, lactation and contraception

Aspect	Point
Neonatal vitamin K	1 mg IM at birth to all neonates (prevents hemorrhagic disease of the newborn from AED-induced vitamin-K-dependent factor depletion)
Neonate	May be drowsy/hypotonic if the mother is on sedating AEDs
Maternal dose	Re-adjust/taper the antenatal dose escalation back to the pre-pregnancy level by 3–4 weeks postpartum
Breastfeeding	Not contraindicated
Contraception	Copper IUCD or levonorgestrel IUD is the method of choice; combined oral contraceptives are less reliable with enzyme-inducing AEDs (and conversely lower lamotrigine efficacy), so are best avoided

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 34.3 — Gestational age and teratogenicity (DC Dutta's Obstetrics 9e, p.502)*

High-yield exam pointers

- Folic acid: **0.4 mg** pre-conception → **4 mg/day** once pregnant on an AED
- Valproate = highest teratogenic risk (7–10%, dose-dependent); lamotrigine/levetiracetam/carbamazepine = first-line choices
- Phenytoin status-epilepticus loading dose: **15–20 mg/kg IV slow**
- Neonatal vitamin K **1 mg IM** at birth — universal, not optional
- Offspring risk of epilepsy: 5–10%
- MgSO4 treats eclampsia, **not** epilepsy — do not confuse the two in an exam DDx
- Contraception of choice in epilepsy: copper IUCD/LNG-IUD (COC is enzyme-induction-unreliable)

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older texts (DC Dutta) additionally recommend maternal oral vitamin K 10 mg/day in the last two weeks for women on enzyme-inducing AEDs; current evidence for this maternal step is weak, and neonatal IM vitamin K at birth remains the definitive, universally recommended measure. Since 2018 the MHRA/EMA valproate Pregnancy Prevention Programme restricts valproate in women/girls of childbearing potential to cases with no effective alternative, given both the malformation risk above and a 30–40% neurodevelopmental-disorder risk in exposed children — a regulatory point not covered in the older textbook editions.

SOURCE & COVERAGE

Williams Obstetrics 26e (Chapter 63, Seizure Disorders, pp.1128–1130, including American Academy of Neurology/American Epilepsy Society practice guidance); DC Dutta's Textbook of Obstetrics 9e (Epilepsy in Pregnancy, pp.272–273).

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Antiphospholipid syndrome

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — Antiphospholipid syndrome (APS) is an acquired autoimmune thrombophilia in which persistently positive antiphospholipid antibodies (aPLs) — lupus anticoagulant (LA), anticardiolipin antibody (aCL), or anti-β2-glycoprotein-I antibody — cause recurrent vascular thrombosis and/or characteristic pregnancy morbidity through placental vasculopathy and thrombosis. It occurs as **primary APS** or **secondary APS** associated with an underlying connective tissue disease, most often systemic lupus erythematosus (SLE).

Classification of antibodies & diagnostic criteria

Antibody	Test used
Lupus anticoagulant (LA)	Phospholipid-dependent clotting assay (activated partial thromboplastin time [aPTT] or dilute Russell viper venom time [dRVVT]) prolonged; **not corrected** by 1:1 mixing with normal plasma; **corrected** by adding excess phospholipid — confirms LA per International Society on Thrombosis and Haemostasis (ISTH) guidelines
Anticardiolipin antibody (aCL), IgG/IgM	ELISA; medium-to-high titre (>40 GPL/MPL units, or >99th percentile)
Anti-β2-glycoprotein-I antibody, IgG/IgM	ELISA; titre >99th percentile

Diagnosis needs the **revised Sapporo (Sydney) classification criteria** (Miyakis et al., 2006) — **at least one clinical AND one laboratory criterion**, with laboratory tests positive on **two or more occasions ≥12 weeks apart**:

Clinical criteria (any one)	Laboratory criteria (any one, ×2 ≥12 weeks apart)
Vascular thrombosis — one or more episodes of arterial, venous, or small-vessel thrombosis in any tissue/organ, confirmed by imaging or histopathology	**LA** present (ISTH guidelines)
Pregnancy morbidity — (a) ≥1 unexplained death of a morphologically normal fetus ≥10 weeks' gestation, or (b) ≥1 premature birth of a morphologically normal neonate before 34 weeks due to eclampsia/severe pre-eclampsia or recognised placental insufficiency, or (c) ≥3 unexplained consecutive spontaneous miscarriages <10 weeks' gestation with maternal anatomic/hormonal and parental chromosomal causes excluded	**aCL** IgG/IgM, medium-high titre, by standardised ELISA
	Anti-β2-glycoprotein-I IgG/IgM >99th percentile, by standardised ELISA

Pathogenesis

- aPLs bind **β2-glycoprotein-I** on platelet, endothelial, and trophoblast phospholipid membranes, activating endothelium and platelets, raising tissue factor and thromboxane A2, and lowering prostacyclin and annexin V's protective shielding of these surfaces.
- Complement activation (C3, C5a) and tissue-factor pathway activation drive thrombosis and local inflammation at the decidual–trophoblast interface — placental damage is not from thrombosis alone.
- Placental bed changes: failure of physiological transformation of the spiral arterioles, intimal thickening, acute atherosis, fibrinoid necrosis, intervillous and spiral-artery thrombosis, and placental infarction — producing uteroplacental insufficiency.
- Net effect is a prothrombotic, antifibrinolytic, proinflammatory state causing both maternal vascular thrombosis and placenta-mediated pregnancy complications.

Clinical features

System	Features
Venous thrombosis	Deep vein thrombosis, pulmonary embolism, superficial thrombophlebitis (commonest event type)

System	Features
Arterial thrombosis	Stroke, transient ischaemic attack, Libman-Sacks cardiac vegetations, myocardial infarction, distal limb/visceral thrombosis and gangrene
Haematological	Thrombocytopenia, autoimmune haemolytic anaemia
Other	Livedo reticularis, migraine, epilepsy, thrombotic microangiopathy/glomerular thrombosis (renal)
Obstetric	Recurrent early pregnancy loss (<10 weeks), unexplained fetal death (≥10 weeks), early-onset severe pre-eclampsia/HELLP syndrome (occurs in ~30% of APS pregnancies), fetal growth restriction and preterm birth (in about one-third of APS pregnancies), placental abruption

Catastrophic APS (CAPS/Asherson syndrome): a rare, rapidly progressive thrombotic disorder simultaneously affecting **≥3 organs/tissues** with histological microthrombosis; renal involvement in ~80% (30% needing dialysis), plus acute respiratory distress syndrome, disseminated intravascular coagulation, myocardial and CNS microthrombi. Triggers include infection, surgery, stopping anticoagulation, and oestrogen-containing contraceptives; mortality is roughly 50%.

Investigations

Test	Purpose
LA (aPTT/dRVVT + mixing study), aCL ELISA, anti-β2-glycoprotein-I ELISA	Confirm diagnostic laboratory criterion (each repeated ≥12 weeks apart)
Antinuclear antibody, anti-dsDNA, complement levels	Screen for underlying SLE (secondary APS)
Complete blood count	Thrombocytopenia, haemolytic anaemia
Serial growth ultrasound with umbilical artery Doppler	Detect fetal growth restriction/placental insufficiency
Antepartum fetal surveillance (non-stress test, biophysical profile) from 30–32 weeks	Monitor placental function in the third trimester

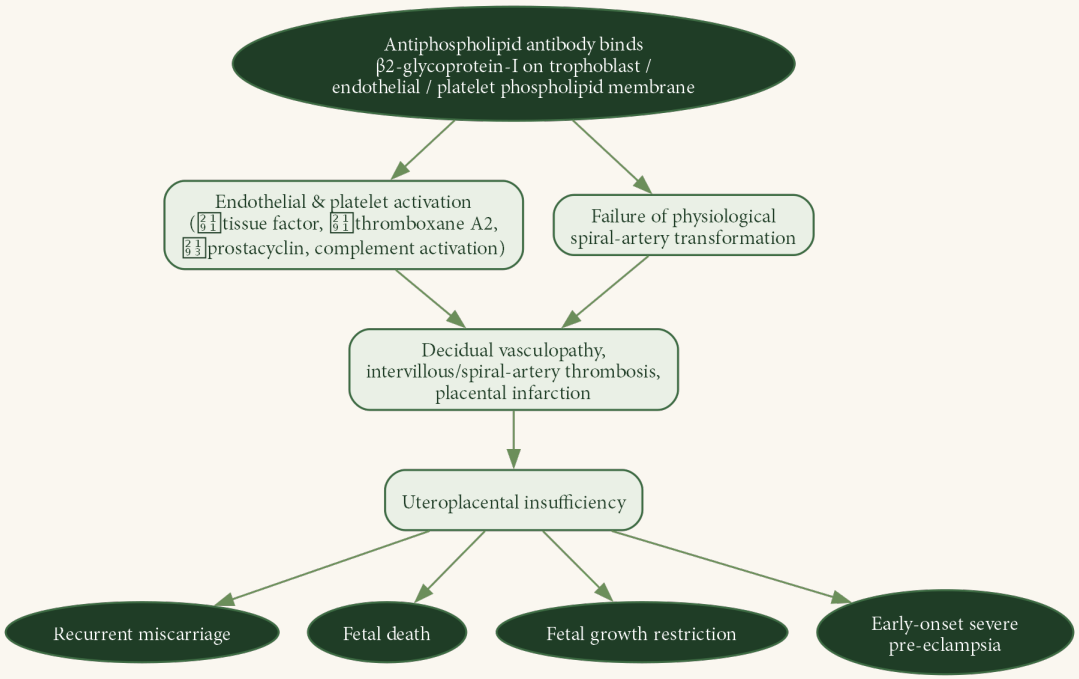
Management

- **Pre-pregnancy/early pregnancy:** counsel on maternal thrombotic and obstetric risk; confirm an intrauterine pregnancy early by transvaginal sonography; start treatment once fetal cardiac activity is seen; avoid oestrogen-containing contraceptives in women with APS.
- **Antenatal anticoagulation, risk-stratified:**

Clinical scenario	Regimen
Recurrent early miscarriage, **no prior thrombosis**	Low-dose aspirin (LDA) + unfractionated heparin (UFH) 5000–7500 U SC every 12 hours, or low-molecular-weight heparin (LMWH; enoxaparin 40 mg once daily or dalteparin 5000 U once daily)
Prior fetal death (≥10 weeks) or delivery <34 weeks for severe pre-eclampsia/placental insufficiency, **no prior thrombosis**	LDA + UFH 7500–10,000 U SC every 12 hours in the first trimester, increasing to 10,000 U every 12 hours in the second/third trimesters (or dose adjusted to keep mid-interval aPTT 1.5× control); or LMWH (enoxaparin 30 mg or dalteparin 5000 U every 12 hours)
Prior thrombosis	Therapeutic-dose UFH adjusted to aPTT/anti-Xa level, or weight-adjusted therapeutic LMWH (e.g., enoxaparin 1 mg/kg every 12 hours) with anti-Xa monitoring, continued throughout pregnancy

- **Monitoring:** antenatal visits every 2 weeks till 24 weeks then weekly, watching for pre-eclampsia and thrombosis; serial growth scans with Doppler every 3 weeks; fetal surveillance from 30–32 weeks.
- **Postpartum:** continue anticoagulation for at least **6 weeks** (switch to warfarin once thromboprophylaxis is required, especially with prior thrombosis or pre-eclampsia); women on lupus anticoagulant are monitored by anti-Xa activity rather than aPTT.
- **Adjuncts:** hydroxychloroquine may be added, particularly with coexisting SLE; corticosteroids are **not used for primary APS** (reserved for secondary APS with active SLE, at the lowest effective dose); **intravenous immunoglobulin (IVIG) is not routinely recommended** — it has not improved live-birth rates and is reserved for refractory disease or catastrophic APS.
- **Catastrophic APS:** intensive-care management — full-dose anticoagulation, high-dose corticosteroids, plasma exchange and/or IVIG, treatment of the precipitating trigger, and early delivery if the patient is pregnant.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Pathogenesis pathway: antibody binding drives two parallel injuries (cell activation + failed spiral-artery remodelling) that converge on placental thrombosis/infarction, causing uteroplacental insufficiency and its downstream obstetric outcomes.

High-yield exam pointers

- APS = LA / aCL / anti-β2-glycoprotein-I antibody + **thrombosis OR defined pregnancy morbidity**.
- Diagnosis needs the **revised Sapporo (Sydney) criteria (Miyakis, 2006)**: ≥1 clinical + ≥1 laboratory criterion; labs repeated **≥12 weeks apart**.
- Obstetric clinical criterion numbers to write exactly: **≥3** losses **<10 weeks**, OR **≥1** fetal death **≥10 weeks**, OR **≥1** preterm birth **<34 weeks** for eclampsia/severe pre-eclampsia or placental insufficiency.
- Treatment triad: **low-dose aspirin + heparin (UFH or LMWH)**, dose escalated by clinical severity (see regimen table); continue **6 weeks postpartum**.
- **Catastrophic APS (Asherson syndrome)** = ≥3 organs, renal involvement ~80%, mortality ~50%.
- Corticosteroids only for **secondary** APS with SLE; **IVIG not routinely recommended**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older Indian texts (DC Dutta's Obstetrics 9e) cite low-dose aspirin **50 mg/day**; the current ACOG/RCOG standard used with heparin is **75–100 mg/day** (commonly 81 mg in US practice) — this answer follows the current standard.

SOURCE & COVERAGE

Arias' High-Risk Pregnancy & Delivery 5e; Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Asherman's syndrome

Asked in: Paper I May 2018 · Paper III Oct 2010 · Paper I Sep 2007 (3×) — RGUHS MS Obstetrics & Gynaecology

Definition — Asherman's syndrome is partial or complete obliteration of the uterine cavity and/or cervical canal by intrauterine adhesions (synechiae) that form after destruction of the full thickness of the endometrium, including the basal (zona basalis) layer — most often following curettage of a gravid or recently-gravid uterus. First described by Joseph Asherman in 1948 as "amenorrhoea traumatica," it presents with hypomenorrhea/amenorrhea, infertility, or recurrent pregnancy loss, with ovarian function otherwise intact.

Aetiology

Category	Causes
Pregnancy-related curettage (~90% of cases)	Curettage for postpartum haemorrhage, incomplete/missed abortion or retained products of conception, elective termination of pregnancy, evacuation of hydatidiform mole
Non-pregnancy uterine surgery	Abdominal or hysteroscopic myomectomy, septum resection/metroplasty, caesarean section, uterine artery embolisation, D&C for a non-gravid uterus
Iatrogenic/intentional	Endometrial ablation (electrocautery, laser, thermal or cryoablation) for menorrhagia
Infective	Genital tuberculosis (an important cause of Asherman's syndrome in India and other developing countries), schistosomiasis, chronic non-tubercular endometritis

Category	Causes
Risk amplifiers	Curettage performed 2–4 weeks postpartum (endometrium thin and inactive), repeated curettage procedures, pre-existing endometritis

Pathogenesis

- An insult severe enough to strip the functional layer and injure the basal layer prevents normal endometrial regeneration.
- Denuded, apposed anterior and posterior uterine walls fuse; fibrosis bridges the cavity as filmy (mucosal), fibromuscular, or dense connective-tissue bands.
- Adhesions may be central (columns/bridges dividing the cavity) or marginal (half-drawn "curtains" at the cornua, which can obscure the tubal ostia).
- Depending on location and extent, adhesions partially or completely obliterate the uterine cavity, the internal os, or the cervical canal — producing amenorrhea (cavity involved) or cryptomenorrhea/haematometra (functioning upper cavity trapped behind a lower obstruction).

Clinical features

- **Menstrual abnormality** — hypomenorrhea or amenorrhea is commonest; cyclic pelvic pain without bleeding (cryptomenorrhea) if a functioning cavity is trapped behind an obstructing adhesion.
- **Infertility** (implantation failure/reduced functional endometrial area).
- **Recurrent pregnancy loss** — the classic obstetric presentation; a temporal relationship to a preceding curettage/pregnancy event is characteristic.
- **Dysmenorrhea** in cases with partial obstruction.
- **Normal secondary sexual characters and normal hormonal cyclicity** — ovarian/hypothalamo-pituitary axis is intact, which helps distinguish it from other causes of secondary amenorrhea.
- Occasionally **asymptomatic**, discovered incidentally during infertility work-up.

Diagnosis / investigations

Test	Finding / purpose
History	High index of suspicion — amenorrhea/hypomenorrhea/pregnancy loss following curettage, caesarean, or myomectomy
Estrogen–progestin (withdrawal) challenge	Sequential conjugated equine oestrogen 1.25 mg daily for 21 days + medroxyprogesterone acetate 10 mg daily for the last 5–7 days of oestrogen — **no withdrawal bleeding** supports end-organ (endometrial) failure

Test	Finding / purpose
Transvaginal ultrasound	Thin, hyperechoic, irregular endometrial echo; haematometra is an occasional but less common finding
Hysterosalpingography (HSG)	Irregular filling defects/"honeycomb" pattern, partial or complete cavity obliteration; ~80% sensitivity/specificity versus hysteroscopy
Saline infusion sonography (sonohysterography)	Equally sensitive to HSG for detecting and mapping adhesions; avoids radiation
Hysteroscopy	**Gold standard and definitive diagnostic test** — directly visualises adhesion type (filmy/mucosal vs fibromuscular/dense) and location; required to plan surgery
Endometrial biopsy, ESR, Mantoux, chest X-ray	When genital tuberculosis is suspected as the underlying cause

Practical hysteroscopic grading (several classification schemes have been proposed — none is universally validated):

Grade	Hysteroscopic appearance	Typical menstrual pattern
Mild	Thin, filmy, avascular adhesions; easily lysed with the tip of the hysteroscope	Normal to hypomenorrhea
Moderate	Fibromuscular adhesions, bleed on division; partial cavity involvement	Hypomenorrhea
Severe	Dense connective-tissue bands, cornual occlusion, near-total or total cavity obliteration	Amenorrhea

Management

- **Hysteroscopic adhesiolysis is the treatment of choice** — safer and more effective than blind curettage. Cold scissors are generally preferred over electrosurgery/laser (lower risk of further endometrial injury); simultaneous laparoscopy or transabdominal ultrasound guidance is used in severe/obliterated cavities to reduce the risk of perforation.
- **Cervical priming (optional):** vaginal misoprostol 200–400 µg before operative hysteroscopy reduces the need for mechanical dilatation.
- **Prevent adhesion reformation after lysis** — an intrauterine balloon catheter or an unmedicated IUD (e.g., Lippes loop, no copper/progestin) is left in the cavity for **7–10 days**; semisolid hyaluronic-acid gel is an alternative/adjunct barrier.

- **Antibiotic cover** while the barrier is in place: doxycycline 100 mg twice daily, or amoxicillin-clavulanate (Augmentin) 500 mg twice daily; an NSAID is added for cramping.
- **Post-operative high-dose oestrogen** to promote re-epithelialisation: conjugated equine oestrogen 2.5 mg two to three times daily (or estradiol 2–6 mg daily) for about 4 weeks, adding medroxyprogesterone acetate 10 mg daily during the final week to produce withdrawal bleeding and confirm a functional response.
- **Second-look hysteroscopy** after the next menses to lyse any early, still-filmy recurrent adhesions; severe disease often needs more than one procedure.
- **Tuberculous Asherman's syndrome** — antitubercular therapy plus hysteroscopic adhesiolysis and IUCD insertion; prognosis for fertility restoration is poor even after treatment.
- **Refractory cases (recent advance)** — regeneration of the endometrial stem-cell niche using autologous bone-marrow-derived stem cells (systemic GCSF mobilisation or intrauterine/intravascular bone-marrow aspirate infusion) is under investigation, with promising but as yet unvalidated results.
- Surgical success is confirmed by HSG or saline sonohysterography after the next menses.

Complications

- **Recurrence of adhesions** — reported in 20% to over 60% of severe cases despite adjuncts.
- **Uterine perforation** during hysteroscopic lysis, especially in a densely obliterated cavity.
- **Adverse obstetric outcomes after successful treatment** — increased risk of preterm labour, placenta accreta, placenta praevia, and postpartum haemorrhage; uterine rupture is a rare late complication.
- **Persistent infertility or recurrent pregnancy loss** if lysis is incomplete or adhesions reform.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
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> ☐ *Fig 38.75 — Hysterosalpingogram showing irregular filling of radio-opaque dye. Diagnosis: Uterine synechiae (Asherman's syndrome) (DC Dutta's Gynaecology 7e, p.571)*

High-yield exam pointers

- Asherman = **Joseph Asherman, 1948**, "amenorrhoea traumatica"; injury must reach the **zona basalis** to scar.
- **~90% follow pregnancy-related curettage**; genital **tuberculosis** is a key cause in India.
- Withdrawal-bleed test doses to recall: CEE **1.25 mg × 21 days** + MPA **10 mg** for the last 5–7 days — no bleed suggests Asherman's.
- **Hysteroscopy = gold standard** (diagnostic *and* therapeutic); HSG/sonohysterography are ~80% sensitive screening tests.

- Post-lysis triad: **balloon/IUD × 7–10 days** + antibiotic (doxycycline/Augmentin) + **high-dose oestrogen × 4 weeks** (± progestin last week).
- Recurrence 20–60% in severe disease; tuberculous cases have the worst prognosis.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

No hysteroscopic classification of intrauterine adhesions has been universally validated for prognosis (Speroff 9e; Te Linde 13e); the mild/moderate/severe grading above is the commonly taught practical scheme, not a single named, versioned staging system like FIGO.

SOURCE & COVERAGE

Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Te Linde's Operative Gynecology 13e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e.

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Autologous blood transfusion in obstetrics and gynecology

Asked in: Paper I May 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — Autologous blood transfusion (ABT) is the collection, processing/storage, and reinfusion of a patient's **own blood** — either predeposited before surgery or salvaged during/after surgery — to meet her transfusion needs instead of using **allogeneic (donor) blood**. It eliminates the risks of transfusion-transmitted infection, alloimmunisation, and ABO-incompatibility haemolytic reactions inherent to donor blood, and is valuable in obstetric/gynaecological procedures with anticipated major haemorrhage or in women who decline donor blood.

Methods of autologous blood transfusion

Method	Principle	Typical use
Preoperative autologous donation (PAD) / predeposit	1 unit phlebotomised and stored (as banked blood) 3–5 weeks before elective surgery, with iron supplementation; reinfused if needed	Elective gynaecological surgery in a woman with a rare blood group or multiple red-cell alloantibodies
Acute normovolaemic haemodilution (ANH)	Immediately after induction, 1–2 units of whole blood are withdrawn and the volume replaced with crystalloid/colloid to maintain normovolaemia; the withdrawn blood is reinfused once surgical bleeding is controlled	Major elective surgery with anticipated significant blood loss, especially when donor blood is declined

Method	Principle	Typical use
Intraoperative cell salvage ("cell saver")	Blood shed into the operative field is suctioned, anticoagulated, filtered, washed, and centrifuged to a haematocrit of ~50%, then reinfused	Caesarean delivery with anticipated major haemorrhage (placenta praevia/accreta), major myomectomy
Autotransfusion of haemoperitoneum	Fresh blood from a ruptured ectopic pregnancy is strained through 4–5 layers of sterile gauze into a bottle of 3.8% citrate solution in a 5:1 (blood:citrate) ratio, then reinfused	Ruptured ectopic pregnancy when cross-matched donor blood is unavailable; routine use is **not advocated** because of adverse reactions
Postoperative/drain salvage	Blood draining from surgical drains is collected, filtered, and reinfused	Uncommon in obstetrics/gynaecology

Indications in obstetrics and gynaecology

- Anticipated major obstetric haemorrhage — **placenta praevia**, **placenta accreta spectrum**, planned caesarean hysterectomy.
- Ruptured ectopic pregnancy with substantial haemoperitoneum when donor blood is not immediately available.
- Major myomectomy (large uterine size) with anticipated significant intraoperative blood loss.
- Cytoreductive/debulking surgery in gynaecological oncology with anticipated major blood loss.
- A woman with a **rare blood group** or **multiple red-cell alloantibodies** in whom cross-matched donor blood is difficult to procure.
- Women who **decline allogeneic blood transfusion** on religious grounds (e.g., Jehovah's Witnesses) — cell salvage, ANH, and meticulous surgical haemostasis are combined with iron/erythropoietin optimisation and topical haemostatic agents.

Technique of intraoperative cell salvage

- Blood shed into the operative field is aspirated through a double-lumen suction device with a concurrent infusion of heparinised or citrated anticoagulant, preventing clotting in the tubing.
- Anticoagulated shed blood collects in a reservoir; an in-line filter removes gross debris and clots.
- In **obstetric** use, a dedicated **leucocyte-depletion filter** is added before reinfusion to remove fetal squames, trophoblastic debris, and amniotic fluid contaminants, reducing the theoretical risk of amniotic fluid embolism.
- The collected blood is washed with saline and centrifuged within the cell-saver bowl, concentrating red cells to a haematocrit of **approximately 50%** while discarding plasma, free haemoglobin, anticoagulant, and debris.

- The washed, packed autologous red cells are transferred to a reinfusion bag and returned to the patient intravenously through a fresh blood-administration set.
- In an **RhD-negative** woman who receives salvaged blood contaminated with fetal cells, a **Kleihauer-Betke test** should be performed and additional **anti-D immunoglobulin** given as indicated.

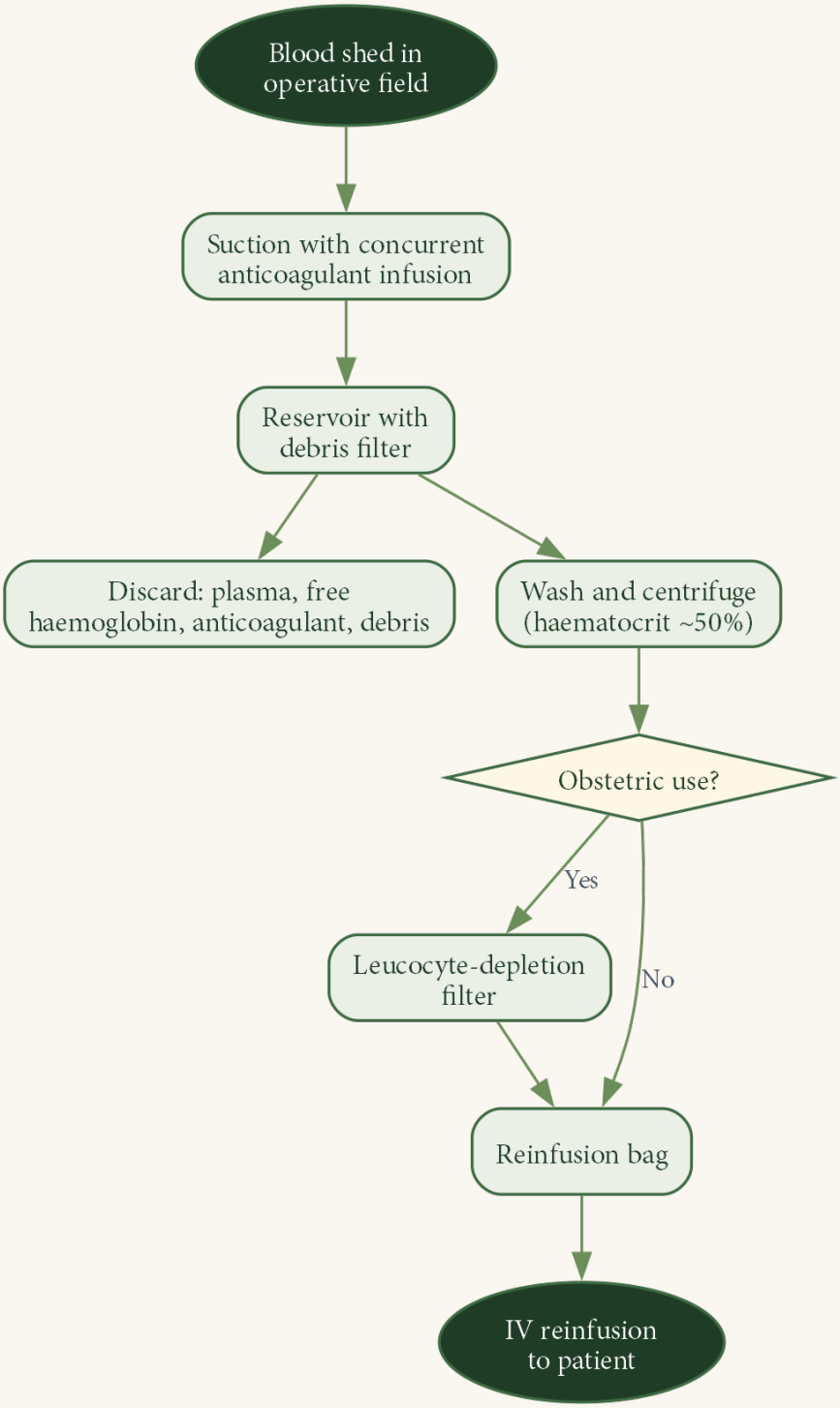
Advantages and disadvantages

Advantages	Disadvantages / limitations
Eliminates transfusion-transmitted infection (HIV, hepatitis B/C)	Salvaged blood lacks clotting factors and platelets — **does not correct coagulopathy**
No alloimmunisation and no ABO-incompatibility haemolytic reaction	PAD causes iatrogenic anaemia and wastage/cost if the unit is unused
Oxygen-carrying capacity and red-cell survival of salvaged cells are equal to or better than stored allogeneic red cells	Cell-saver equipment/disposables are costly and need trained personnel
Acceptable to women declining donor blood on religious grounds	Theoretical risk of amniotic fluid contamination/embolism with obstetric cell salvage (not substantiated in trials)
Immediately available in an emergency — avoids the delay of cross-matching	Preoperative autologous donation is poorly cost-effective when the likelihood of transfusion is low

Evidence base and current guideline recommendations

- The **SALVO trial** (Khan et al., 2017, *PLoS Medicine* 14(12):e1002471) — a pragmatic multicentre randomised controlled trial of **3028 women at risk of haemorrhage undergoing caesarean delivery** — found intraoperative cell salvage did **not significantly reduce donor (allogeneic) blood transfusion** compared with routine care (**2.5% vs 3.5%**); **no case of amniotic fluid embolism** occurred in either arm.
- **RCOG Green-top Guideline No. 47, "Blood Transfusions in Obstetrics"** recommends that **intraoperative cell salvage be considered** for caesarean delivery, particularly where major haemorrhage is anticipated (placenta praevia/accreta) and in women declining donor blood.
- The **National Heart, Lung, and Blood Institute (NHLBI) Expert Panel** does not recommend preoperative autologous donation for procedures with a **less than 10% likelihood of transfusion**, such as uncomplicated abdominal or vaginal hysterectomy.
- **Acute normovolaemic haemodilution** and controlled hypotensive/hypothermic anaesthesia are additional blood-conservation strategies used alongside cell salvage, especially when donor blood is declined or a rare blood group makes cross-matching difficult.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Flowchart of intraoperative cell salvage from operative-field blood loss to IV reinfusion, with the obstetric-specific leucocyte-depletion step and the discard side-branch.

High-yield exam pointers

- Cell-saver sequence to reproduce: collect → anticoagulate → filter → wash/centrifuge to Hct ~50% → leucocyte-depletion filter (obstetric-specific step) → reinfuse.
- **SALVO trial** (Khan, 2017, *PLoS Med*): 3028 women, caesarean delivery — cell salvage did **not** significantly cut donor transfusion (2.5% vs 3.5%); **zero** amniotic fluid embolism cases.
- **RCOG Green-top 47**: consider cell salvage for caesarean with anticipated major haemorrhage or in a woman declining donor blood.
- **NHLBI rule**: skip preoperative autologous donation if transfusion likelihood is **<10%** (e.g., uncomplicated hysterectomy).
- Ectopic autotransfusion recipe: strain haemoperitoneum through 4–5 layers of gauze into **3.8% citrate** solution, **5:1** blood:citrate ratio — **not routinely advocated**.
- Salvaged blood has **no clotting factors/platelets** — will not correct a coagulopathy.
- RhD-negative recipient of fetal-cell-contaminated salvage → Kleihauer-Betke test + extra anti-D immunoglobulin.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> RCOG Green-top Guideline No. 47 ("Blood Transfusions in Obstetrics") was first published in 2007; its cell-salvage recommendation is the one still reproduced by current obstetric texts, and DC Dutta's account of intraoperative cell salvage for caesarean delivery draws on this guidance.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; Berek & Novak's Gynecology 16e; Arias' High-Risk Pregnancy & Delivery 5e; RCOG Green-top Guideline No. 47 (Blood Transfusions in Obstetrics); SALVO trial (Khan et al., *PLoS Medicine* 2017).

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Bandl's ring

Asked in: Paper I 16-Dec-2023 · Paper IV May 2010 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — *Bandl's ring* (pathological retraction ring) is an abnormally exaggerated form of the normal physiological retraction ring — the transverse ridge that marks the boundary between the actively contracted/retracted, thickened **upper uterine segment** and the passively distended, progressively thinned **lower uterine segment**. It develops in **obstructed labour**, is felt/seen as an oblique

groove rising above the symphysis pubis, and is an important clinical sign of **impending (threatened) rupture of the uterus**.

Pathogenesis

- In normal labour the upper segment contracts and retracts (fibres shorten permanently, wall thickens) while the lower segment and cervix are drawn up and thinned passively; the boundary between the two is the **physiological retraction ring**, situated near the level of the internal os.
- When mechanical **obstruction** (fault in the passage or the passenger) prevents descent of the presenting part despite good uterine contractions, the upper segment goes on contracting and retracting in a vain effort to overcome the obstacle.
- The lower segment is forced to elongate and thin out progressively to accommodate the fetus driven down from above, while the upper segment becomes correspondingly thicker.
- The retraction ring is thereby exaggerated, becomes prominent and **rises progressively upward** (from near the symphysis toward the umbilicus) — this is the **pathological retraction ring of Bandl**.
- **In primigravidae**, the myometrium eventually fatigues and further retraction ceases — a state of **uterine exhaustion/inertia** — labour comes to a standstill (contractions may resume later with renewed vigour).
- **In multiparae**, retraction continues unchecked with progressive circumferential thinning; the ring rises higher and higher and the **lower segment ultimately ruptures** (spontaneous obstructive rupture).

Causes of obstructed labour leading to Bandl's ring

Fault in the passage	Fault in the passenger
Bony: cephalopelvic disproportion, contracted pelvis (primary or secondary, the latter more in multiparae)	Transverse lie
Soft tissue: cervical dystocia (scarring/prolapse), cervical or broad-ligament fibroid below the presenting part	Brow presentation
Impacted ovarian tumour	Congenital malformation — hydrocephalus (commonest), fetal ascites, conjoined ("locked") twins
Non-gravid horn of a bicornuate uterus obstructing the pelvis	Macrosomia, occipitoposterior position; compound presentation

Clinical & differentiating features

Bandl's ring must be distinguished from a **constriction ring** (*Schroeder's ring*) — a localized, reversible, incoordinate contraction that never causes rupture — and from a **false ring** formed by a distended, immobile bladder wedged between the presenting part and the symphysis (urethra compressed, patient unable to void), which can mimic Bandl's ring on abdominal palpation; catheterisation before assessment is essential.

Feature	Pathological retraction ring (Bandl's)	Constriction ring (Schroeder's)
Mechanism	Tonic uterine contraction + retraction secondary to obstruction	Localized incoordinate contraction (undue myometrial irritability)
Site/behaviour	Always at the upper–lower segment junction; position **rises progressively**	Usually at the junction, but may lie around a constricted part of the fetus (e.g., neck); once formed, **position does not change**
Abdominal palpation	Uterus tense, tender; ring felt as an oblique groove; round ligaments taut & tender; fetal parts not easily felt	Uterus normal, not tender; ring not felt per abdomen; fetal parts easily felt
Vaginal examination	Lower segment forcibly pressed by the driven presenting part; ring cannot be felt vaginally; features of obstruction present	Lower segment not pressed; ring occasionally felt above the head; no features of obstruction
Fetal heart sound	Usually absent (fetal distress/death)	Usually present
Reversibility	Irreversible — always pathological	Reversible — abolished by deepening anaesthesia
Risk of rupture	High, especially in multiparae — an impending-rupture sign	Uterus never ruptures
Principle of treatment	Caesarean section, after excluding rupture	Relax the ring (deepen anaesthesia) or cut the ring at caesarean section

Management once Bandl's ring/obstructed labour is recognised

- **Exclude rupture of the uterus first** — check for scar/uterine tenderness, disproportionate shock, cessation of contractions, easily palpable fetal parts per abdomen, and haematuria; catheterise to rule out a false (bladder) ring and to look for blood-stained urine.
- **Resuscitate:**

- Correct dehydration and ketoacidosis with IV Ringer's lactate — at least 1 litre as a running drip, roughly 3 litres total to correct clinical dehydration.
- Send a vaginal swab for culture and sensitivity.
- Group and cross-match blood; keep blood arranged before any operative intervention.
- Antibiotics — **inj. Ceftriaxone 1 g IV** plus IV **metronidazole** for anaerobic cover.
- Adequate analgesia.

- **Absolute contraindications:** oxytocin augmentation and internal podalic version — both risk completing the rupture; there is **no place for "wait and watch."**
- **Definitive delivery:**
  - **Caesarean section** is the treatment of choice and gives the best result if the case is recognised early with the fetus alive.
  - If the case is late/neglected and the fetus is dead with the head low and vaginal delivery not hazardous, a **destructive operation** is preferred to a high-risk caesarean section.
  - **Symphysiotomy** may be considered in resource-limited settings for outlet contraction with vertex presentation and good fetal heart sound.
- **After delivery of the baby and placenta:** mandatory **exploration of the uterine cavity and lower genital tract** to exclude an occult uterine rupture or tear; proceed to laparotomy with repair or hysterectomy if rupture is confirmed.

Complications

- **Maternal:** uterine rupture (chiefly multiparae) with haemorrhage and shock; genital sepsis; postpartum haemorrhage from uterine atony; genitourinary or rectovaginal fistula from pressure necrosis; Sheehan's syndrome after severe haemorrhagic shock; maternal death.
- **Fetal:** hypoxia/acidosis from impaired uteroplacental perfusion, intracranial haemorrhage from supermoulding, birth trauma, stillbirth or early neonatal sepsis.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 25.5A,B — Pathogenesis of retraction ring (Bandl's ring): A. Normal labour; B. Late obstruction, showing circumferential dilatation and stretching of the lower segment with thickening of the upper segment and progressive rise of the retraction ring (DC Dutta's Obstetrics 9e, p.367)*

High-yield exam pointers

- Bandl's ring = **exaggerated physiological retraction ring** at the upper/lower-segment junction in **obstructed labour**; its rise toward the umbilicus is a sign of **impending uterine rupture**.
- **Primigravida → uterine inertia/exhaustion** (labour arrests); **multipara → progressive retraction → rupture** — no protective exhaustion phase.

- Differentiate from **constriction (Schroeder's) ring** — reversible, fixed site, uterus never ruptures, fetal heart sound present.
- Differentiate from the **false ring of a distended bladder** — catheterise before concluding it is Bandl's ring.
- Two absolute "never do" items: **no oxytocin augmentation, no internal version**.
- Resuscitation triad to recall: IV Ringer's lactate (~3 L), **Ceftriaxone 1 g IV** + metronidazole, cross-matched blood — then exclude rupture, then caesarean section (destructive operation only if fetus dead and vaginal delivery is safe).

> **SOURCE & COVERAGE**
>
> DC Dutta's Textbook of Obstetrics 9e; Williams Obstetrics 26e.

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Bethesda classification

Asked in: Paper I 19-Nov-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — The Bethesda System is the standardised, uniform terminology for reporting cervical/vaginal cytology (Pap smear) results, developed at a 1988 National Cancer Institute (NCI) workshop in Bethesda, Maryland, and revised as **Bethesda III (2001)** and again in **2014**. It replaced the older numerical Papanicolaou grading (Groups I–V) and the purely histological dysplasia/CIN (cervical intraepithelial neoplasia) nomenclature with a descriptive, clinically actionable report that states specimen adequacy and a specific interpretation.

Components of a Bethesda report

Component	Content
Specimen type	Conventional Pap smear or liquid-based cytology (LBC)
Specimen adequacy	**Satisfactory** for evaluation vs **unsatisfactory** (specify reason). Satisfactory requires adequate squamous cellularity and, ideally, an identifiable endocervical/transformation-zone component; a smear with more than three-quarters of epithelial cells obscured by blood, inflammation, or air-drying artefact is unsatisfactory
General categorization (optional)	Negative for intraepithelial lesion or malignancy (**NILM**) / epithelial cell abnormality / other
Interpretation/result	The specific diagnostic category (below)

Component	Content
Ancillary testing	Method and result, e.g. high-risk HPV (human papillomavirus) test
Educational notes/suggestions	Optional comments correlating with clinical findings

Interpretation/result — diagnostic categories

Group	Category	Includes
Non-neoplastic findings	Organisms	*Trichomonas vaginalis*; fungal organisms morphologically consistent with *Candida*; shift in flora suggestive of bacterial vaginosis; bacteria morphologically consistent with *Actinomyces*; cellular changes consistent with herpes simplex virus/cytomegalovirus
	Reactive cellular changes	Associated with inflammation, radiation, intrauterine contraceptive device (IUCD), or atrophy
Epithelial cell abnormality — squamous	Atypical squamous cells (ASC)	**ASC-US** (undetermined significance); **ASC-H** (cannot exclude high-grade lesion)
	Low-grade squamous intraepithelial lesion (LSIL)	HPV cytopathic change (koilocytosis) + mild dysplasia/**CIN I**
	High-grade squamous intraepithelial lesion (HSIL)	Moderate/severe dysplasia, carcinoma-in-situ — **CIN II, CIN III**; comment "features suspicious for invasion" if present
	Squamous cell carcinoma (SCC)	Invasive squamous carcinoma
Epithelial cell abnormality — glandular	**Atypical glandular cells (AGC)**	Endocervical, endometrial, or not otherwise specified (NOS)
	AGC, favour neoplastic	Endocervical or NOS
	Endocervical adenocarcinoma-in-situ (AIS)	Pre-invasive glandular lesion
	Adenocarcinoma	Endocervical, endometrial, extrauterine, or NOS

Group	Category	Includes
Other	Endometrial cells	Present in a woman ≥45 years (report even if cytologically benign)

Correlation with dysplasia/CIN nomenclature

Dysplasia (older)	CIN (WHO)	Basal-layer thickness involved	Bethesda
Mild	CIN I	Basal one-third	**LSIL**
Moderate	CIN II	Basal half to two-thirds	**HSIL**
Severe	CIN III	Whole thickness except 1–2 surface layers	**HSIL**
Carcinoma-in-situ	CIS	Whole thickness	**HSIL**

HPV-related koilocytotic change and CIN I are grouped as **LSIL** because they share the same natural history and HPV-type distribution; CIN II and CIN III/CIS are grouped as **HSIL** because their biological behaviour and management are the same.

Cytomorphological basis for grading (dyskaryosis)

Nuclear abnormalities (dyskaryosis) that a cytologist grades on the smear to arrive at the Bethesda category: disproportionate nuclear enlargement, irregular nuclear outline, hyperchromasia, chromatin condensation, and multinucleation.

Cytological grade	Cell type and appearance	Nuclear feature	Bethesda/CIN correlate
Mild dyskaryosis	Superficial/intermediate squamous cells, angular borders, translucent cytoplasm; binucleation common	Nucleus occupies <50% of cytoplasmic area	LSIL / CIN I
Moderate dyskaryosis	Intermediate/parabasal/superficial cells	Nucleus occupies 50–67% of cytoplasm; more hyperchromasia than mild	HSIL / CIN II
Severe dyskaryosis	Basal-type cells — round, oval, polygonal, or elongated ("**fibre cells**"; an elongated cell with a cytoplasmic tail is a "**tadpole cell**")	Nucleus nearly fills the cell or a thin dense rim of cytoplasm remains; coarse chromatin	HSIL / CIN III
Koilocytosis	Perinuclear halo with peripheral cytoplasmic condensation	Irregularly enlarged, hyperchromatic, often multinucleated	HPV cytopathic effect → LSIL

Cytological grade	Cell type and appearance	Nuclear feature	Bethesda/CIN correlate
Carcinoma-in-situ cells	Parabasal type, scanty cytoplasm	High nuclear:cytoplasmic ratio, granular chromatin	HSIL (CIS)
Invasive carcinoma cells	Single cells or clusters; large tadpole cells	Irregular, coarsely clumped chromatin	Squamous cell carcinoma

Clinical triage by category

- **ASC-US** — reflex high-risk HPV testing (preferred, most sensitive for detecting underlying CIN 2/3) or repeat cytology; colposcopy only if HPV-positive or cytology persists abnormal.
- **ASC-H, LSIL, HSIL, SCC** — direct **colposcopy** with directed biopsy; excisional treatment for confirmed HSIL/CIN II–III.
- **AGC (any subtype), AIS** — colposcopy **plus endocervical sampling**, with endometrial sampling added if ≥35 years or with risk factors for endometrial neoplasia (abnormal bleeding, obesity, anovulation).
- **Benign endometrial cells ≥45 years** — correlate clinically; endometrial evaluation if postmenopausal, symptomatic, or otherwise at risk.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
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> ☐ *Fig 23.5 — Smear showing dyskaryotic cells (DC Dutta's Gynaecology 7e, p.285)*

High-yield exam pointers

- **1988 NCI workshop → Bethesda III (2001) → 2014 update**; replaced Papanicolaou Groups I–V.
- Squamous ladder: **ASC-US/ASC-H → LSIL → HSIL → SCC.**
- Glandular ladder: **AGC (endocervical/endometrial/NOS) → AGC favour neoplastic → AIS → adenocarcinoma**.
- **LSIL = CIN I** (HPV/mild dysplasia); **HSIL = CIN II, III, CIS** (moderate–severe dysplasia).
- ASC-US triage = **reflex high-risk HPV test**; all higher categories = **colposcopy**.
- Report must always state **specimen adequacy** first.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

This bank reproduces the **Bethesda III (2001)** categories as printed in the corpus (Berek & Novak 16e; DC Dutta's Gynaecology 7e); the 2014 update kept these squamous and glandular categories unchanged and mainly refined ancillary HPV/genotype-test reporting and transformation-zone-component documentation.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (Ch. 9 — Table 9.3; Ch. 23 — Table 23.1); Berek & Novak's Gynecology 16e (Ch. 16 — Cervical Cytology Screening).

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Blood transfusion in obstetrics

Asked in: Paper II 17-Nov-2022 — RGUHS MS Obstetrics & Gynaecology

Definition — Blood transfusion in obstetrics is the therapeutic administration of whole blood or its components — packed red blood cells (PRBC), fresh-frozen plasma (FFP), cryoprecipitate, and platelets — to a pregnant, labouring, or puerperal woman to correct anaemia or to replace blood and clotting factors lost through obstetric haemorrhage. Pregnancy's physiological haemodilution, hypercoagulable state, and potential for sudden massive blood loss make transfusion practice in obstetrics distinct from general surgical transfusion.

Indications

Category	Indications
Correction of anaemia	Severe anaemia (haemoglobin <7 g/dL) unresponsive to oral/parenteral iron; severe anaemia beyond 36 weeks to improve oxygen-carrying capacity before labour; refractory anaemia despite adequate iron therapy; anaemia with associated infection or cardiac decompensation
Obstetric haemorrhage	Antepartum haemorrhage (placenta praevia, abruption); postpartum haemorrhage (uterine atony, trauma, retained tissue, coagulopathy); ruptured ectopic pregnancy; uterine rupture
Coagulopathy	Disseminated intravascular coagulation (DIC) from abruption, amniotic fluid embolism, severe pre-eclampsia/HELLP, sepsis — replaced with FFP, cryoprecipitate, platelets

Category	Indications
Haemoglobinopathy	Thalassaemia major, sickle cell crisis in pregnancy — repeated or exchange transfusion
Exchange transfusion	Cardiac failure from severe anaemia; severe anaemia needing surgery; severe anaemia near term (packed cell volume <13%) as a safer alternative to simple transfusion

Pre-transfusion testing & blood products

- **ABO and Rh(D) grouping** at the first antenatal visit, repeated at admission for delivery/caesarean section.
- **Antibody (indirect Coombs) screen** at booking to detect irregular alloantibodies (anti-D, anti-c, anti-Kell, anti-E); repeated at 28 weeks in Rh-negative women.
- **Cross-matching** of every donor unit against the recipient's serum immediately before transfusion; a "group and save" sample is kept ready in anticipated high-risk deliveries (placenta praevia/accreta, prior postpartum haemorrhage) so compatible units can be released rapidly if bleeding occurs.
- **Rh(D)-negative women** receive only Rh(D)-negative red cells and platelet packs to avoid sensitisation.

Product	Volume/unit	Contents	Effect
Whole blood	~500 mL, Hct ~40%	RBCs, plasma, 600–700 mg fibrinogen, no platelets	Restores volume and fibrinogen; raises Hct 3–4%/unit
Packed RBCs	250–300 mL, Hct 55–80%	RBCs, minimal fibrinogen, no platelets	Raises Hct 3–4%/unit
Fresh-frozen plasma	~250 mL (30-min thaw)	600–700 mg fibrinogen, all clotting factors	10–15 mL/kg corrects dilutional/consumptive coagulopathy
Cryoprecipitate	~15 mL, frozen	200 mg fibrinogen, factor VIII, von Willebrand factor, factor XIII	15–20 units (3–4 g) raise fibrinogen ~150 mg/dL; used when fibrinogen <150 mg/dL
Platelets	~50 mL, room temperature	Platelet concentrate	1 unit raises count ~5000/µL; single-donor apheresis pack ~50,000/µL; keep count >50,000/µL during active haemorrhage

Massive obstetric haemorrhage — transfusion protocol

- **Activate a massive transfusion protocol (MTP)** once 4–5 units of PRBC have been given (or are anticipated) within about 2 hours of ongoing life-threatening haemorrhage.
- **Escalate in fixed ratios** — plasma:red cell ratios approaching 1:1.4 (one unit FFP per 1.4 units PRBC) improve survival in massive transfusion, versus the highest-mortality ratio of 1:8. The Parkland MTP releases PRBC and FFP in successive rounds, adding a platelet "6-pack" and a unit of cryoprecipitate at alternating rounds.
- **Recheck haemoglobin/haematocrit, platelet count, fibrinogen, and prothrombin/activated partial thromboplastin times** each round; maintain platelets >50,000/μL and fibrinogen >150 mg/dL.
- **Tranexamic acid 1 g IV** as soon as possible after bleeding onset, and within 3 hours of delivery (WOMAN trial) — reduces death from obstetric haemorrhage; ACOG does not recommend it for routine prophylaxis, only for treatment.
- **Refractory bleeding**: recombinant activated factor VII or prothrombin complex concentrate may be added, but recombinant factor VII is ineffective if fibrinogen is <50 mg/dL or platelets <30,000/μL, and carries an arterial thrombosis risk.
- **Whole blood**, where available, is preferred for massive obstetric haemorrhage (fewer donor exposures, replaces fibrinogen along with volume); viscoelastic assays (thromboelastography/rotational thromboelastometry) are increasingly used as point-of-care guides to component replacement.

Complications of blood transfusion

Type	Features	Management
Acute haemolytic reaction	ABO-incompatible unit (usually a labelling/identification error); fever, hypotension, tachycardia, dyspnoea, flank/back pain, haemoglobinuria; may progress to DIC and acute kidney injury	Stop transfusion immediately; IV fluids, treat hypotension/hyperkalaemia, forced alkaline diuresis
Transfusion-related acute lung injury (TRALI)	Dyspnoea, hypoxia, non-cardiogenic pulmonary oedema within 6 hours; ~1 in 12,000 transfusions; donor HLA/HNA antibodies implicated	Supportive care, may need mechanical ventilation
Transfusion-associated circulatory overload (TACO)	Volume-overload pulmonary oedema; the commonest cause of transfusion-related death (~1% incidence)	Slow transfusion rate, diuretics

Type	Features	Management
Infective	Bacterial contamination (chiefly platelets stored at room temperature); viral transmission (HIV/hepatitis C ~1 per 1–2 million units, hepatitis B <1 per 100,000 units on screened blood)	Screening, aseptic collection/storage
Alloimmunisation	Anti-D and other red-cell antibodies risk haemolytic disease of the fetus/newborn in future pregnancies	Rh(D)-matched transfusion; antibody screening
Dilutional coagulopathy	Thrombocytopenia, prolonged prothrombin/activated partial thromboplastin time, hypofibrinogenaemia from crystalloid/PRBC-heavy resuscitation without factor replacement (clinically resembles DIC)	Balanced component replacement (as above)

Precautions and alternatives

- Confirm ABO/Rh grouping, antibody screen, and cross-match before every unit; verify patient identity and unit label at the bedside — labelling error is the leading preventable cause of haemolytic reactions.
- For simple transfusion in antenatal anaemia: give relatively fresh, packed cells only, 80–100 mL at a time; do not repeat within 24 hours to allow circulatory readjustment; cover with an antihistamine and a diuretic and transfuse slowly to reduce reaction and circulatory-overload risk.
- Anticipate at booking — arrange group-and-save/cross-matched units for high-risk pregnancies (placenta praevia/accreta, prior postpartum haemorrhage, coagulation disorder) before caesarean section or induction.
- Intraoperative **cell salvage** is a safe intervention in obstetrics and reduces exposure to donor blood in anticipated major haemorrhage (e.g., placenta accreta spectrum surgery); concern about amniotic fluid embolism has not been substantiated in trials.
- **Preoperative autologous donation** has given disappointing results in obstetrics and is reserved for women with a rare blood type or unusual antibodies.
- Optimise antenatal haemoglobin with iron/folate supplementation to reduce the need for transfusion at delivery.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 23.7 — Techniques of exchange transfusion (DC Dutta's Textbook of Obstetrics 9e, p.346)*

High-yield exam pointers

- Fibrinogen <150 mg/dL and/or platelets <50,000/μL = replacement trigger in obstetric haemorrhage.
- Plasma:PRBC ratio ~1:1.4 (near 1:1) → best survival; 1:8 → worst survival in massive transfusion.
- Tranexamic acid 1 g IV as soon as possible, within 3 hours of delivery (WOMAN trial); not for routine prophylaxis (ACOG).
- Recombinant factor VIIa fails if fibrinogen <50 mg/dL or platelets <30,000/μL; carries arterial thrombosis risk.
- TRALI (~1:12,000 units, donor antibody-mediated) vs TACO (~1%, volume overload, commonest transfusion death) — both present within 6 hours with dyspnoea/hypoxia/pulmonary oedema.
- Simple antenatal transfusion: packed cells only, 80–100 mL/sitting, not repeated within 24 hours.
- Cell salvage is safe in obstetrics; preoperative autologous donation is not routinely useful.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Dutta's simple-transfusion precautions (antihistamine and diuretic cover, small 80–100 mL aliquots for antenatal anaemia) reflect older, non-haemorrhage transfusion practice; current management of major obstetric haemorrhage instead follows a massive transfusion protocol with balanced component ratios, as in Williams Obstetrics and current ACOG/WHO postpartum haemorrhage guidance.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; WOMAN Trial Collaborators (Lancet, 2017); World Health Organization (2017) and American College of Obstetricians and Gynecologists recommendations on tranexamic acid in postpartum haemorrhage.

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Bony pelvis and its obstetrical significance

Asked in: Paper I 15-Nov-2022 — RGUHS MS Obstetrics & Gynaecology

Definition — The bony pelvis is a ring formed by four bones — two **innominate bones**, the **sacrum** and the **coccyx** — united by four joints (two sacroiliac joints, the symphysis pubis and the sacrococcygeal joint). The **pelvic brim** (linea terminalis) divides it into a **false pelvis** above (no obstetric role) and a

true pelvis below, which forms the bony passage of parturition; the size, shape and diameters of the true pelvis at each level determine engagement, the mechanism of labour and the likelihood of a safe vaginal delivery.

Bones, joints, false vs true pelvis

Component	Details
Innominate bone (×2)	Fusion of **ilium** (above acetabulum), **ischium** (below-behind, bears ischial spine and tuberosity) and **pubis** (in front)
Sacrum	5 fused vertebrae; **sacral promontory** is the key posterior landmark for pelvimetry
Coccyx	Mobile at the sacrococcygeal joint; retropulses during crowning
Joints	2 **sacroiliac** joints, **symphysis pubis**, **sacrococcygeal** joint
False pelvis	Above the brim; bounded posteriorly by lumbar vertebrae, laterally by iliac fossae, anteriorly by lower abdominal wall. Supports the gravid uterus; its external shape only crudely predicts true-pelvis configuration — **no true obstetric significance**
True pelvis	Below the brim; bony canal the fetus must negotiate. Landmarks on the brim (anterior→posterior): upper border of symphysis, pubic crest, pubic tubercle, pectineal line, iliopubic eminence, iliopectineal line, sacroiliac joint, ala of sacrum, sacral promontory

Planes and diameters of the true pelvis

Plane	Antero-posterior diameter	Transverse / oblique	Obstetric significance
Inlet (superior strait)	**Obstetric conjugate 10 cm** — shortest AP diameter, sacral promontory to the thickest point on posterior symphysis. **True (anatomical) conjugate 11 cm. Diagonal conjugate 12 cm** (lower border of symphysis to promontory — the only one measurable clinically; OC = DC – 1.5–2 cm)	Transverse **13 cm**; 2 oblique diameters **12 cm** each (sacroiliac joint → opposite iliopubic eminence); sacrocotyloid 9.5 cm	Plane of **engagement** — biparietal diameter of the fetal head crosses here
Cavity (plane of greatest pelvic dimensions)	12 cm (mid-symphysis to S2–S3 junction)	12 cm	Roomiest, almost circular plane — **no obstetric significance**
Midpelvis (plane of least pelvic dimensions)	11 cm (lower border of symphysis to tip of sacrum)	**Bispinous 10.5 cm — narrowest diameter of the entire pelvis**; posterior sagittal 5 cm	**Narrowest plane**; site of **internal rotation**; corresponds to the origin of levator ani; landmark for **pudendal nerve block**; ischial spines mark **station 0**
Outlet (inferior strait)	Anatomical outlet 10.5 cm with coccyx in normal position, extending to **13 cm** with coccyx retropulsed during crowning	**Intertuberous** (TDO) **11 cm**; subpubic angle 90–100°	Governs **crowning** and perineal outcome; pubic arch must accommodate the head as it extends

Caldwell–Moloy classification of pelvic shape

Feature	Gynecoid (50%)	Anthropoid (25%)	Android (20%)	Platypelloid (5%)
Inlet shape	Round	Antero-posteriorly oval	Triangular (heart-shaped)	Transversely oval
Sacral angle/curve	>90°, well curved	>90°, long & narrow	<90°, straight, forward	>90°, short & straight
Side walls	Straight/divergent	Straight/divergent	Convergent	Divergent

Feature	Gynecoid (50%)	Anthropoid (25%)	Android (20%)	Platypelloid (5%)
Ischial spines	Not prominent	Not prominent	Prominent	Not prominent
Subpubic angle	Wide (~85°)	Slightly narrow	Narrow	Very wide (>90°)
Diameter of engagement	Transverse/oblique	Antero-posterior	Transverse/oblique	Transverse
Obstetric outcome	Usual mechanism, no difficulty	No difficulty, but flexion delayed; more face-to-pubis (persistent OP) delivery	Delayed engagement, difficult anterior rotation, arrest above spines, perineal injury	Difficult engagement (exaggerated parietal presentation); once through, easy delivery

Obstetrical significance of the bony pelvis

- **Engagement** — depends on the transverse/oblique diameter of the inlet accommodating the biparietal diameter; delayed or absent engagement at term in a primigravida raises suspicion of cephalopelvic disproportion (CPD), malpresentation, or a high pelvic inclination.
- **Station and internal rotation** — the ischial spines fix **station 0**; the midpelvis, being the narrowest plane, is where internal rotation occurs. Convergent side walls or prominent spines (android pelvis) cause **deep transverse arrest**.
- **Mechanism of labour** — each cardinal movement (engagement, descent, flexion, internal rotation, extension, restitution, external rotation) is dictated by which fetal-head diameter must pass through which pelvic plane; pelvic shape therefore predicts the likely position of the occiput and ease of rotation (Table above).
- **Clinical pelvimetry** — done from 37 weeks or in early labour: sacral curve and promontory reach, sacrosciatic notch (should admit 2 fingerbreadths), ischial spines, side walls, subpubic angle (2 fingers), transverse diameter of outlet (4 knuckles) and diagonal conjugate are assessed bimanually to judge pelvic adequacy before allowing a trial of labour.
- **Imaging pelvimetry** (X-ray, CT, MRI) — reserved for select cases (fractured pelvis, term breech or post-caesarean trial of labour where clinical assessment is equivocal); conventional X-ray pelvimetry delivers ~0.1–0.3 cGy fetal dose and CT ~44–425 mrad, but is a **poor independent predictor** of successful vaginal delivery since it cannot assess fetal size, position or uterine forces — it only supplements, never replaces, clinical examination.
- **Cephalopelvic disproportion / contracted pelvis** — inlet is considered contracted when the obstetric conjugate is <10 cm or the greatest transverse diameter <12 cm (diagonal conjugate <11 cm); **severe** disproportion when OC <7.5 cm, **borderline** at 9.5–10 cm; midpelvis is contracted

when interischial-spinous + posterior sagittal diameters sum ≤13 cm (normal 15 cm). This governs the choice between induction, elective caesarean section, or a supervised **trial of labour**.

- **Instrumental and operative delivery** — an adequate midpelvis and outlet (wide subpubic angle, non-prominent spines) is a prerequisite for safe forceps/vacuum application; an android pelvis with a narrow pubic arch increases the risk of perineal and sphincter injury during instrumental or spontaneous delivery.
- **Decision-making in breech, version and VBAC** — clinical (and, if needed, CT/MRI) pelvimetry is performed before planning a vaginal breech delivery, external cephalic version, or trial of labour after caesarean, since pelvic capacity is one of the few modifiable-in-advance predictors of outcome.
- **Landmark for regional analgesia** — the ischial spine is the anatomical landmark for **pudendal nerve block**.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 9.12 — Composite measurements of the diameters of the inlet, cavity and outlet in centimeters (DC Dutta's Obstetrics 9e, p.109)*
- ☐ *Fig 24.1A–C — Anatomical features of the parent pelvic types: inlet, cavity, outlet (DC Dutta's Obstetrics 9e, p.351)*

High-yield exam pointers

- **10-12-13**: Obstetric conjugate 10 cm (shortest AP, inlet) → Diagonal conjugate 12 cm (clinically measured) → Transverse of inlet 13 cm. OC = DC − 1.5–2 cm.
- **Bispinous 10.5 cm = narrowest diameter of the whole pelvis**; ischial spines fix station 0.
- Four planes: inlet, greatest dimensions (roomiest, no significance), least dimensions (narrowest, site of internal rotation), outlet.
- Caldwell–Moloy percentages: **Gynecoid 50 : Anthropoid 25 : Android 20 : Platypelloid 5**.
- Inlet contraction: obstetric conjugate <10 cm (severe <7.5 cm; borderline 9.5–10 cm); midpelvis contracted if bispinous + posterior sagittal ≤13 cm.
- Normal subpubic angle 90–100°; narrowed in android pelvis → perineal trauma risk.
- X-ray pelvimetry is a poor independent predictor of vaginal delivery success — supplements, never replaces, clinical pelvimetry.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e; Williams Obstetrics 26e.

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Bromocriptine

Asked in: Paper I 24-Sep-2025 · Paper I May 2007 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — Bromocriptine is a semisynthetic **ergot alkaloid** (a bromine-substituted derivative of ergocryptine) that acts as a potent **dopamine D2-receptor agonist**. By reproducing the tonic hypothalamic dopaminergic inhibition of the anterior pituitary lactotroph, it suppresses prolactin secretion and was the original first-line drug for hyperprolactinaemia and prolactin-secreting pituitary adenomas (prolactinoma) in obstetric and gynaecological practice.

Mechanism of action

- Stimulates **D2 dopamine receptors** on anterior pituitary lactotroph cell membranes → activates the inhibitory G-protein (Gi) → falls cyclic AMP → reduces prolactin gene transcription, synthesis and exocytotic release.
- Also inhibits lactotroph **DNA synthesis and cell proliferation**, shrinking a prolactinoma's cell mass rather than merely suppressing its hormone output.
- Fall in circulating prolactin removes its tonic inhibition of the hypothalamic **GnRH pulse generator** → restores pulsatile luteinising hormone (LH)/follicle-stimulating hormone (FSH) secretion → return of ovulatory menstrual cycles.
- The same D2-agonist action underlies its experimental use as adjuvant therapy in **peripartum cardiomyopathy**, where suppressing prolactin (proposed source of a cardiotoxic 16-kDa cleavage fragment) is the rationale.

Pharmacokinetics

Parameter	Feature
Absorption	Oral, incompletely absorbed; extensive first-pass hepatic metabolism
Peak plasma level	About 3 hours after an oral dose
Nadir	By about 7 hours; little drug detectable by 11–14 hours — hence **twice-daily dosing** is required
Elimination	Metabolised in the liver, excreted mainly in **bile/faeces** — use with caution in hepatic impairment
Alternative route	**Vaginal tablet** — better tolerated with higher measured drug exposure; used when oral gastrointestinal side effects limit therapy

Clinical indications in obstetrics & gynaecology

Indication	Use in practice
Hyperprolactinaemia/prolactinoma (micro- and macroadenoma)	First-generation medical therapy of choice; normalises prolactin in ~90%, restores ovulatory menses in ~80%, cures galactorrhoea in ~60% of women
Macroprolactinoma	Shrinks tumour bulk in ~80% of cases; used before, or instead of, transsphenoidal surgery
Anovulatory infertility with hyperprolactinaemia	Restores spontaneous ovulation; may be combined with clomiphene citrate in polycystic ovary syndrome with mild prolactin elevation
Mastalgia/mastodynia and premenstrual breast symptoms	Given where a prolactin-mediated component is suspected
Peripartum cardiomyopathy	Experimental adjuvant (inhibits prolactin secretion); trial evidence is mixed, so it is not yet a standard-of-care indication
Postpartum lactation suppression	Historically used, but pharmacological suppression of lactation is **no longer recommended** — see Note

Dose and administration

Indication/step	Regimen
Starting dose (all indications)	**1.25 mg (half tablet) at bedtime**, taken with food, to minimise first-dose hypotension/nausea
Escalation	Increase by 1.25 mg every week, guided by monthly serum prolactin
Usual maintenance	**2.5 mg twice daily**
Large macroadenoma/very high prolactin	Up to **5 mg twice daily**
Mastalgia	2.5 mg once or twice daily
In pregnancy	Usually stopped once conception is confirmed in microadenoma; continued only if a macroadenoma carries a real growth risk

Adverse effects and contraindications

Category	Details
Common (dose-related)	Nausea, vomiting, headache, postural hypotension, dizziness, fatigue, drowsiness, nasal stuffiness, constipation — minimised by bedtime dosing and slow up-titration

Category	Details
Uncommon/serious	Rare acute psychotic reaction (hallucinations, mood change), reversible on stopping the drug
Postpartum-specific danger	Hypertension, rebound prolactin secretion, seizures, myocardial infarction and puerperal stroke have all been reported when the drug was used for lactation suppression
Contraindications	Uncontrolled hypertension/pre-eclampsia or postpartum hypertension, ischaemic heart disease, severe hepatic impairment, known ergot hypersensitivity, psychiatric illness
Pregnancy safety	A large surveillance series (over 2,500 pregnancies) shows **no increase in congenital malformation or multiple pregnancy** with conception occurring during bromocriptine therapy

Monitoring and drug interactions

- Check serum prolactin **monthly** during dose titration; once normal and stable, monitor every 6–12 months.
- Repeat MRI at 3–6 months in a macroadenoma to confirm shrinkage; formal visual-field testing if chiasmal compression was present at diagnosis.
- Dopamine antagonists — antipsychotics/phenothiazines, metoclopramide, domperidone — oppose bromocriptine's action and should be avoided or substituted where possible.
- Concurrent antihypertensives potentiate postural hypotension; alcohol worsens gastrointestinal intolerance.
- Non-hormonal (barrier) contraception is preferred over combined oestrogen-containing pills until prolactin has normalised and pregnancy is desired, since oestrogen can stimulate lactotroph growth.
- A trial withdrawal of the drug may be considered once prolactin has stayed normal for **2 years or more** with no residual adenoma on MRI, since long-term therapy is not always required.

High-yield exam pointers

- Class: **ergot alkaloid, dopamine D2-receptor agonist** — first approved (1985, USA) for hyperprolactinaemia due to a pituitary adenoma.
- Doses to write exactly: starting **1.25 mg at bedtime**; maintenance **2.5 mg twice daily**; macroadenoma up to **5 mg twice daily**.
- Results to quote: prolactin normalised in ~90%; ovulation restored in ~80%; galactorrhoea cured in ~60%; macroadenoma shrinkage in ~80%.

- Twice-daily dosing is needed because of its short half-life (peak 3 hours, nadir 7 hours) — contrast with **cabergoline** (long half-life, twice-weekly dosing, more potent and better tolerated, but a small long-term valvulopathy risk at high doses).
- **Not** recommended for routine postpartum lactation suppression — risk of hypertension, seizures, myocardial infarction and stroke.
- A drug safe to conceive on, with extensive reassuring pregnancy-surveillance data.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Postpartum lactation-suppression is not a currently recommended indication — the cardiovascular and seizure risks reported with this specific use outweigh any benefit, even though the drug remains a first-line option for prolactinoma/hyperprolactinaemia at standard doses.

> **SOURCE & COVERAGE**
> Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Williams Obstetrics 26e; DC Dutta's Textbook of Gynaecology 7e; DC Dutta's Textbook of Obstetrics 9e; Berek & Novak's Gynecology 16e.

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Cardiovascular changes in pregnancy

Asked in: Paper I May 2019 · Paper I Apr 2006 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — Pregnancy induces major anatomical and haemodynamic adaptations of the maternal cardiovascular system, driven chiefly by hormone-mediated vasodilatation and blood volume expansion, to meet the increased metabolic demands of the mother, the hypertrophied uterus and the fetoplacental unit. The changes begin in the first trimester, are near-maximal by mid-pregnancy, intensify further in labour and the immediate puerperium, and revert to pre-pregnancy values within weeks of delivery.

Anatomical, auscultatory & ECG changes

- The elevated diaphragm (from the enlarging uterus) pushes the **heart upward, outward and rotates it to the left**; the **apex beat shifts to the 4th intercostal space, about 2.5 cm outside the mid-clavicular line**.
- Chest radiograph may show borderline **cardiomegaly** — a normal pregnancy finding that must not be over-read as disease.
- **First heart sound (S1)** becomes louder with wide splitting; a **third heart sound (S3)** from rapid diastolic filling is common, and a fourth (S4) is occasionally heard.

- A soft **mid-systolic ejection murmur** (grade 1–2/6) is audible at the pulmonary area/left sternal border, from reduced blood viscosity and increased flow across the aortic and pulmonary outflow tracts.
- A continuous **"mammary souffle" (venous hum)** may be heard over the 2nd–3rd left intercostal spaces from increased internal-mammary blood flow.
- **ECG** shows an average **15-degree left-axis deviation** (diaphragmatic elevation), a slightly reduced PR interval, and a small Q wave with flattened/inverted T wave in lead III — all normal variants.

Haemodynamic changes

Parameter	Non-pregnant	Pregnancy (term)	Change
Cardiac output (L/min)	4.5	6.2–6.3	**+ 40–43%**
Stroke volume (mL)	65	75	+ 27%
Heart rate (beats/min)	70	85	+ 17%
Mean arterial/diastolic pressure	—	falls 5–10 mm Hg, nadir mid-pregnancy	↓
Systemic vascular resistance	—	—	**– 21%**
Pulmonary vascular resistance	—	—	– 34%
Blood volume	baseline	+ 40–45% (plateaus 32–34 weeks)	↑
Femoral venous pressure (supine)	8–10 cm H_2O	20–25 cm H_2O	+ 100%
Colloid oncotic pressure	20 mm Hg	18 mm Hg	– 14%

- **Cardiac output (CO = stroke volume × heart rate)** starts rising by the 5th week; almost half of the total rise occurs by 8 weeks and it is maximal by mid-pregnancy (Clark, 1989; Capeless, 1989).
- Despite the rise in CO, **blood pressure falls** (BP = CO × SVR) because the fall in SVR outweighs the rise in CO; the fall is caused by the smooth-muscle-relaxing effects of progesterone, nitric oxide, prostacyclin and atrial natriuretic peptide, and by vascular refractoriness to angiotensin II and endothelin-1.
- Central venous pressure and pulmonary capillary wedge pressure remain essentially **unchanged**, because the fall in SVR/PVR and colloid oncotic pressure offsets the added volume and output.
- CO is **highest in the left lateral/knee-chest position and lowest supine or sitting** — the physiological basis of nursing pregnant women in left lateral position for cardiac assessment.

Regional blood-flow redistribution

Organ/bed	Non-pregnant flow	Term flow
Uterus	50 mL/min (~2% of CO)	~750 mL/min (~15% of CO)
Kidney	800 mL/min	+ 400 mL/min (from 16 weeks, plateaus)
Lungs	6000 mL/min	+ 2500 mL/min
Skin	baseline	maximal ~500 mL/min by 36 weeks (explains heat intolerance, sweating, nasal stuffiness)

Postural effects — supine hypotension syndrome

- In late pregnancy the gravid uterus compresses the **inferior vena cava (and aorta)** when the woman lies supine ("aortocaval compression").
- Venous return is normally maintained through paravertebral and azygos collaterals; in about **10%** of women this collateral flow is insufficient.
- These women develop **hypotension, tachycardia, pallor and syncope** — the supine hypotension syndrome.
- Turning the patient to the **left lateral position** promptly restores blood pressure; this is why the left lateral tilt is used for regional anaesthesia, CTG monitoring and resuscitation in pregnancy.
- The same caval compression raises femoral venous pressure (see table), predisposing to dependent oedema, varicose veins, haemorrhoids and deep vein thrombosis; antecubital (upper-limb) venous pressure is unaffected.

Changes in labour and the puerperium

- Each uterine contraction squeezes 300–500 mL of blood from the intervillous space into the systemic circulation — **autotransfusion**.
- Cardiac output rises a further **~50% above pre-labour values** during the first and second stages, augmented by pain- and anxiety-related catecholamine release.
- Immediately after delivery, CO rises to about **70% above pre-labour values**, from autotransfusion, relief of caval compression, and loss of the low-resistance placental circulation.
- Mean arterial pressure also rises transiently in this immediate postpartum period.
- CO returns to pre-labour values by **about 1 hour after delivery**, and to pre-pregnancy levels by about **4 weeks postpartum**.

Clinical significance — physiological versus pathological findings

Physiological (normal pregnancy)	Suggests organic heart disease
Grade 1–2/6 systolic ejection murmur	Systolic murmur ≥ grade 3/6, or **any diastolic murmur**
Loud, widely split S1; audible S3	Cardiomegaly, persistent tachyarrhythmia, persistently split S2
Mild exertional dyspnoea, dependent oedema	Progressive dyspnoea/orthopnoea, nocturnal cough, haemoptysis, syncope, chest pain
15° left-axis deviation on ECG	Cyanosis, clubbing, persistent neck-vein distension

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

No indexed textbook figure matched this physiology topic closely enough to embed; describe instead a **matplotlib line plot** — x-axis: gestational weeks (0 → 40) extending through labour and to 6 weeks postpartum; y-axis: % change from non-pregnant baseline; three lines (cardiac output, blood volume, heart rate) rising steeply to ~20–24 weeks, plateauing near term, spiking further in labour/immediately postpartum (~+50 to +70%), then declining back to the baseline by ~4–6 weeks postpartum.

High-yield exam pointers

- **CO + 40–43%** (Clark, 1989); half the rise by 8 weeks, maximal by mid-pregnancy.
- **Blood volume + 40–45%**, plateauing by 32–34 weeks (Pritchard, 1965).
- **SVR – 21%, PVR – 34%** → BP falls despite ↑CO (BP = CO × SVR).
- CO highest left lateral, lowest supine; **supine hypotension syndrome in ~10%**.
- Labour: CO **+50%**; immediate postnatal **+70%** over pre-labour value (autotransfusion); back to pre-labour value in **1 hour**, pre-pregnancy baseline in **~4 weeks**.
- Apex beat at **4th ICS, 2.5 cm lateral to mid-clavicular line**; ECG shows **15° left-axis deviation**.
- Grade ≥3/6 or diastolic murmur, cardiomegaly, cyanosis/clubbing = **pathological**, not physiological.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e (Table 5.4, Cardiovascular System); Williams Obstetrics 26e (Table 52-1, Figure 52-1, Table 52-2 — Clark, 1989; Capeless, 1989; Pritchard, 1965).

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Cell cycle and its clinical significance

Asked in: Paper I 15-Nov-2022 — RGUHS MS Obstetrics & Gynaecology

Definition — The cell cycle is the ordered sequence of events by which a cell duplicates its DNA and divides into two daughter cells, alternating interphase (growth and DNA synthesis) with mitosis (nuclear and cytoplasmic division). It is driven by cyclins paired with cyclin-dependent kinases (CDKs) and is policed by checkpoints that arrest progression when DNA is damaged or incompletely replicated, safeguarding genomic integrity. Non-dividing cells exit the cycle into a resting **G0 phase**.

Phases and regulation of the cell cycle

Phase	Events	Approx. duration*	Key regulator / checkpoint
G0	Quiescent, non-dividing state; neurons, striated muscle and mature red cells are permanently post-mitotic	Days to a lifetime	Re-entry triggered by growth factors/steroid hormones
G1	Synthesis of enzymes and regulatory proteins needed for DNA replication	7–10 h	**Restriction point (G1/S checkpoint)** — Cdk4/6-cyclin D and Cdk2-cyclin E phosphorylate retinoblastoma (Rb) protein, releasing E2F to commit the cell to division
S	DNA replication — each chromosome duplicates into two sister chromatids	~10 h	Pre-replication complex ensures each origin fires only once
G2	RNA/protein synthesis; proofreading and repair of replication errors	~5 h	**G2/M checkpoint** — Cdk1-cyclin B ("mitosis-promoting factor") held inactive until DNA repair is complete
M	Mitosis — prophase → metaphase → anaphase → telophase — plus cytokinesis	30–60 min	**Spindle-assembly checkpoint** — the anaphase-promoting complex allows chromatid separation only when every chromosome is correctly attached to the spindle

*Total cell-cycle time in dividing human cells ≈ 24 hours (Berek & Novak 16e). Tumour cell-cycle times vary widely (12–217 h) but tumour cells do not divide faster than normal cells — rapid tumour growth instead reflects a larger growth fraction**, i.e., more cells actively cycling and fewer resting in G0 (DC Dutta's Gynaecology 7e).

- **p53**, the "guardian of the genome," enforces the G1 and G2 checkpoints — it arrests cells with damaged DNA to allow repair, or triggers **apoptosis** (programmed cell death) if damage is irreparable.
- Apoptosis normally balances proliferation to maintain tissue mass — physiological examples include endometrial shedding after oestrogen/progesterone withdrawal and androgen-driven granulosa-cell atresia; when proliferation outpaces apoptosis the result is hyperplasia or neoplasia.
- **Ploidy:** mitosis of somatic cells maintains the diploid complement (46 chromosomes); meiosis in gametogenesis produces haploid gametes (23 chromosomes), restored to diploid at fertilisation.

Clinical significance — cancer chemotherapy

Because dividing tumour cells are far more drug-sensitive than resting (G0) cells, knowing which phase a cytotoxic drug targets is the rationale for **combination chemotherapy** — agents of differing cell-cycle specificity and non-overlapping toxicity are combined to raise tumour-cell kill and limit resistance. Antitumour agents kill a constant **fraction**, not a fixed number, of cells with each course (**log-kill hypothesis**), which is why intermittent, repeated courses are used.

Cell-cycle specificity	Phase targeted	Example drugs
Non-specific (CCNS) — kills both cycling and resting cells; suited to bulky, slow-growing tumours	Any phase	Alkylating agents (cyclophosphamide, ifosfamide, melphalan), platinum agents (cisplatin, carboplatin)
Specific (CCS)	G1	Actinomycin D
Specific (CCS)	S phase	Methotrexate (dihydrofolate reductase inhibitor), 5-fluorouracil, doxorubicin
Specific (CCS)	G2	Bleomycin, etoposide
Specific (CCS)	M phase	Vincristine, vinblastine, taxanes (paclitaxel, docetaxel)
Specific (CCS)	G0	Nitrosoureas (BCNU, CCNU)

(DC Dutta's Gynaecology 7e, Table 31.4 — drug activity in the cell cycle)

Clinical significance — radiotherapy

- **Radiosensitivity varies with cell-cycle phase** — cells in **M phase and G2** are the most radiosensitive; cells in **late S phase** are relatively radioresistant.
- **Fractionation** of external-beam radiotherapy (typically 180–220 cGy/fraction, five fractions/week) exploits this difference: repeated small doses let normal tissue repair sub-lethal DNA damage between fractions while cycling tumour cells progressively accumulate lethal damage.
- **Hypoxic tumour cells** need roughly three times the radiation dose for equivalent cell kill (poor oxygen enhancement ratio); chemotherapeutic radiosensitisers (cisplatin, paclitaxel, gemcitabine, doxorubicin) and hypoxic-cell sensitisers (misonidazole, metronidazole) are used to overcome this resistance.
- This is the biological basis for **concurrent chemoradiation** in cervical and endometrial cancer, which combines independent cytotoxic cell-cycle kill with radiosensitisation.

Clinical significance — reproductive biology and genetics

- **Oocyte meiotic arrest:** the primary oocyte is arrested in **diplotene of meiosis I prophase** from fetal life until the pre-ovulatory LH surge triggers resumption; the resulting secondary oocyte then arrests again at **metaphase of meiosis II** and completes division only after fertilisation (extruding the second polar body). This decades-long first-meiotic arrest underlies the age-related rise in oocyte aneuploidy and informs the timing of oocyte/embryo cryopreservation and ovulation triggers in assisted reproduction.
- **Nondisjunction** — failure of homologous chromosomes (meiosis I) or sister chromatids (meiosis II) to separate — produces aneuploid gametes, the mechanism behind trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome).
- **Ploidy abnormalities in gestational trophoblastic disease:** a **complete hydatidiform mole** results from fertilisation of an "empty" ovum (no maternal nuclear DNA) whose paternal haploid genome duplicates (or is fertilised by two sperm), restoring a diploid but wholly androgenetic 46,XX (or 46,XY) karyotype with no embryo. A **partial mole** follows dispermic fertilisation of a normal ovum, giving a triploid karyotype (69,XXX/69,XXY/69,XYY) with an abnormal embryo. This cell-cycle/ploidy disturbance explains the trophoblastic hyperproliferation and malignant potential (persistent gestational trophoblastic neoplasia, choriocarcinoma) that follow, especially, a complete mole.
- **HPV-driven cervical carcinogenesis:** high-risk human papillomavirus (HPV) oncoproteins **E6** and **E7** cause proteolytic degradation of the tumour suppressors **p53** and **Rb** respectively, abolishing the G1/S and DNA-damage checkpoints. Loss of cell-cycle control allows persistently infected cervical cells to proliferate unchecked, driving cervical intraepithelial neoplasia and invasive cervical cancer — the molecular rationale for HPV vaccination and cervical screening.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 6.2 — The cell cycle. (Berek & Novak 16e, p.235)*

Reproduce the four phases (G1 → S → G2 → M) arranged in a circle with the G0 quiescent arm branching off G1; mark the restriction point at G1/S and the checkpoint arrow at G2/M.

High-yield exam pointers

- Four phases with durations: **G1 (7–10 h)** → **S (~10 h)** → **G2 (~5 h)** → **M (30–60 min)**; total cycle ≈24 h; resting cells sit in **G0**.
- Two checkpoints to name: **G1/S (restriction point)** and **G2/M**; master regulator **p53**; **Rb–E2F** controls G1/S commitment.
- Chemotherapy table to reproduce: **CCNS** = alkylating/platinum agents (any phase); **CCS**: G1–actinomycin D, S–methotrexate/5-FU/doxorubicin, G2–bleomycin/etoposide, M–vincristine/vinblastine/taxanes, G0–nitrosoureas.
- Radiosensitivity rule: **M and G2 phase = most radiosensitive; late S phase = most radioresistant**; hypoxic cells need ~3× the dose.
- Oocyte arrest points: **diplotene of meiosis I** (fetal life → LH surge) and **metaphase of meiosis II** (until fertilisation).
- HPV mechanism: **E6 degrades p53, E7 degrades Rb** → checkpoint loss → cervical dysplasia/cancer.
- Molar pregnancy ploidy: **complete mole = diploid, androgenetic, no embryo; partial mole = triploid, embryo present.**

SOURCE & COVERAGE

Berek & Novak's Gynecology 16e (cell-cycle phases and duration, cyclin-CDK/Rb-E2F/p53 regulation, apoptosis, ploidy, hydatidiform mole genetics, nondisjunction and trisomy syndromes); DC Dutta's Textbook of Gynaecology 7e (cell-cycle kinetics and growth fraction, radiosensitivity by cell-cycle phase, chemotherapy cell-cycle-specificity table, HPV E6/E7–p53/Rb pathway); Speroff's Clinical Gynecologic Endocrinology & Infertility 9e (meiosis I and II, oocyte arrest at diplotene and at metaphase II).

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Chlamydial infection

Asked in: Paper I Nov 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — *Chlamydia trachomatis* is an obligate intracellular, Gram-negative bacterium and is now the **commonest bacterial sexually transmitted infection (STI)** worldwide. It has a biphasic life cycle —

an infectious, metabolically inert **elementary body** that attaches to and enters columnar/transitional epithelial cells, and an intracellular, replicating **reticulate body** that forms a cytoplasmic inclusion before re-forming elementary bodies to infect further cells.

Microbiology and serotypes

Feature	Detail
Organism	*Chlamydia trachomatis* — obligate intracellular, Gram-negative bacterium; cannot be grown on ordinary media
Serotypes A–C	Trachoma (ocular) — leading infective cause of blindness worldwide, not sexually transmitted
Serotypes D–K	Genital tract infection — urethritis, cervicitis, PID, neonatal conjunctivitis and pneumonia
Serotypes L1–L3	Lymphogranuloma venereum (LGV) — invasive, lymphatic-tissue-tropic strains
Site of infection	Columnar and transitional epithelium — urethra, endocervix, Bartholin's gland, rectum, conjunctiva
Incubation period	6–14 days (longer than gonorrhoea's 3–7 days)
Transmission	Sexual contact; vertical (mother-to-baby) transmission during vaginal delivery

Clinical manifestations

Site / setting	Features
Lower genital tract (women)	**Asymptomatic in ~75%**; when symptomatic — mucopurulent cervical discharge, cervical oedema/ectopy/friability, dysuria and urethral syndrome, dyspareunia, postcoital or intermenstrual bleeding, Bartholinitis
Ascending / upper genital tract	Endometritis and salpingitis, often subclinical, ascending to **pelvic inflammatory disease (PID)**; **perihepatitis (Fitz-Hugh-Curtis syndrome)** — right hypochondrial pain and "violin-string" adhesions from transperitoneal/lymphatic spread to the liver capsule, seen in 5–10% of acute PID and more often with chlamydia than gonococcus
Long-term sequelae	Tubal-factor infertility, ectopic pregnancy, and chronic pelvic pain from tubal scarring
Effects in pregnancy	Preterm labour, preterm prelabour rupture of membranes, chorioamnionitis, stillbirth, and puerperal endometritis/salpingo-oophoritis

Site / setting	Features
Neonate (vertical transmission, 8–44% of exposed vaginal deliveries)	**Inclusion conjunctivitis** — the commonest neonatal manifestation, onset 5–14 days after birth; **neonatal pneumonia** — afebrile, staccato cough, onset 4–12 weeks
Male partner	Non-gonococcal urethritis — the single commonest cause

Diagnosis

Test	Basis / notes
Nucleic acid amplification test (NAAT)	Test of choice; sensitivity and specificity ~95%; specimen of choice is first-void urine or a vulvovaginal/endocervical swab; detects both symptomatic and asymptomatic infection
Antigen detection (ELISA)	Detects chlamydial lipopolysaccharide antigen on an endocervical swab; less sensitive/specific than NAAT
Tissue culture (McCoy cell monolayer)	100% specific reference standard; expensive, technically demanding, and takes 3–7 days — reserved for medicolegal/research indications
Serology (immunofluorescence / complement fixation)	Antibody titres of limited value for acute lower genital tract disease; raised anti-chlamydial IgG is associated with tubal-factor infertility
Gram stain of vaginal/cervical discharge	Excludes intracellular Gram-negative diplococci of gonococcus; does not itself diagnose chlamydia — a negative gonococcal stain in a woman with cervicitis raises suspicion of chlamydial infection

Management

Uncomplicated urogenital infection — non-pregnant adults

Regimen	Dose
Doxycycline (current first-line)	100 mg orally twice daily × 7 days
Azithromycin (single-dose alternative)	1 g orally, single dose
Levofloxacin (alternative)	500 mg orally once daily × 7 days

In pregnancy

Regimen	Dose
Azithromycin (preferred)	1 g orally, single dose

Regimen	Dose
Amoxicillin (alternative)	500 mg orally three times daily × 7 days
Erythromycin base (older alternative)	500 mg orally four times daily × 7–10 days

Doxycycline and levofloxacin are **contraindicated in pregnancy**. Because of the consequences of untreated infection for both mother and neonate, a test-of-cure by repeat NAAT about 4 weeks after treatment is advised in pregnancy, and screening at the first antenatal visit is recommended for all pregnant women (with third-trimester re-screening for those under 25 years, those with new/multiple partners, or those treated earlier in pregnancy).

Neonatal conjunctivitis / pneumonia

Regimen	Dose
Erythromycin (base or ethylsuccinate)	50 mg/kg/day orally, divided into 4 doses × 14 days

Topical treatment alone is ineffective and does not prevent pneumonia; oral/systemic therapy is mandatory. Universal ocular prophylaxis at birth with erythromycin 0.5% (or tetracycline 1%) ophthalmic ointment reliably prevents gonococcal ophthalmia neonatorum but does **not** reliably prevent chlamydial conjunctivitis or pneumonia, so an exposed or infected infant still needs systemic erythromycin.

Lymphogranuloma venereum (L1–L3 serotypes)

Regimen	Dose
Doxycycline (preferred)	100 mg orally twice daily × 21 days
Azithromycin (alternative)	1 g orally once weekly × 3 weeks

General principles

- Treat **all sexual partners** with the same regimen, regardless of symptoms.
- Advise **abstinence from intercourse for 7 days** after both partners have completed treatment.
- **Retest for reinfection at 3 months** — reinfection rates approach 10% even after successful treatment, including in pregnancy.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 44.5 — Chlamydia trachomatis. (Jeffcoate's Principles of Gynaecology 9e, p.761)*

High-yield exam pointers

- Serotype triad: **A–C trachoma, D–K genital tract, L1–L3 LGV.**
- **75% of genital infection is asymptomatic** — the "silent" STI; partner status is often the biggest clue.

- **NAAT is the diagnostic test of choice** (~95% sensitivity/specificity); tissue culture (McCoy cells) is 100% specific but slow.
- **Fitz-Hugh-Curtis syndrome** (perihepatitis, "violin-string" adhesions) is more chlamydial than gonococcal.
- Non-pregnant: **doxycycline 100 mg BID × 7 days** (first-line) or **azithromycin 1 g single dose** (alternative).
- Pregnancy: **azithromycin 1 g single dose** preferred (doxycycline contraindicated); neonate treated with **oral erythromycin 50 mg/kg/day divided QID × 14 days**.
- LGV clinical sign: the "**groove sign**" — a depression between groups of inflamed inguinal nodes; treated with doxycycline 100 mg BID for 21 days.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Guideline evolution: older textbook tables (citing CDC 2010/2015) list azithromycin and doxycycline as equally acceptable first-line options for non-pregnant chlamydia, but the current CDC Sexually Transmitted Infections Treatment Guidelines (2021) now prefer doxycycline as first-line for non-pregnant adults, with azithromycin retained as the preferred single-dose option in pregnancy.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e; DC Dutta's Textbook of Obstetrics 9e; Berek & Novak's Gynecology 16e; Williams Obstetrics 26e; CDC Sexually Transmitted Infections Treatment Guidelines, 2021.

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Classify Müllerian duct anomalies. Diagnosis and management of imperforate hymen

Asked in: Paper I 19-Nov-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Müllerian duct anomalies (MDAs) are congenital malformations of the female genital tract resulting from failure of formation, fusion, or resorption of the paired paramesonephric (Müllerian) ducts, which normally give rise to the fallopian tubes, uterus, cervix, and upper two-thirds of the vagina. Imperforate hymen is the commonest anatomic obstructive anomaly of the outflow tract — a solid membrane occluding the vaginal introitus that fails to undergo the normal perinatal central dissolution, causing cryptomenorrhea once the endometrium becomes cyclically active at puberty.

Classification of Müllerian anomalies

The **American Fertility Society (AFS, now ASRM) classification (1988)** — based on the earlier Buttram–Gibbons system — is the standard classification and groups anomalies into seven classes by the underlying embryologic defect.

Class	Anomaly	Embryologic defect	Frequency/key point
I	Müllerian agenesis/hypoplasia — vaginal, cervical, uterine (fundal), tubal, combined	Failure of duct development	Complete form = **Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome** (absent uterus/upper vagina, normal ovaries, 46,XX); renal (40%) and skeletal (12%) anomalies coexist
II	Unicornuate uterus ± rudimentary horn (communicating/non-communicating/no cavity)	Failure of development of one duct	~10%; non-communicating horn risks cornual pregnancy/rupture (~16 wk); poorest pregnancy outcome (~40% success)
III	Uterus didelphys	Complete failure of fusion	~8%; best reproductive outcome (~64%); unification surgery not required
IV	Bicornuate uterus — complete (to internal os) or partial	Partial failure of fusion	~26%; fundal indentation ≥1 cm; mid-trimester loss, malpresentation, cervical insufficiency; ~50% successful pregnancy
V	Septate uterus — complete or partial (subseptate)	Failure of septal resorption after fusion	~35% (commonest); worst untreated reproductive outcome but best response to surgery (~86% after metroplasty)
VI	Arcuate uterus	Minor residual fundal concavity	Now classified as a normal variant — no treatment indicated

Class	Anomaly	Embryologic defect	Frequency/key point
VII	Diethylstilbestrol (DES)-related anomalies	In-utero DES exposure	T-shaped cavity, cervical hood/collar, constriction bands; rarely seen now

Distinguishing bicornuate from septate: external fundal contour is divergent/notched (>1 cm indentation, inter-horn angle usually obtuse) in bicornuate, whereas septate uterus has a normal convex or minimally concave fundus with an obtuse-to-acute inter-horn angle — laparoscopy or MRI/3-D ultrasound is used when hysterosalpingography (HSG) cannot differentiate the two, since management (metroplasty route) differs completely.

Investigations for Müllerian anomalies

Investigation	Utility
Ultrasonography (transvaginal/3-D)	First-line; detects septate/bicornuate/unicornuate uterus and associated hematometra
Hysterosalpingography (HSG)	Delineates endometrial cavity contour; cannot assess external fundal shape (cannot distinguish septate from bicornuate alone)
Hysteroscopy	Direct visualization of the cavity/septum; therapeutic (septum resection) in the same sitting
Laparoscopy	Assesses external fundal contour; gold standard combined with hysteroscopy to differentiate bicornuate from septate
MRI	Best anatomical detail of complex anomalies (agenesis, cervical/vaginal atresia); non-invasive
Renal ultrasound/IVU	Renal anomalies coexist in ~40% — mandatory work-up alongside any Müllerian anomaly

Management of Müllerian anomalies

- **Mere presence of a uterine anomaly is not itself an indication for surgery** — treat only if symptomatic (recurrent pregnancy loss, obstruction, dyspareunia, or infertility after excluding other causes).
- **Septate uterus:** hysteroscopic metroplasty (resectoscope/laser resection of septum) — first-line; success rate 80–89%, short hospital stay, permits subsequent vaginal delivery (unlike abdominal metroplasty, which mandates caesarean).
- **Bicornuate uterus (symptomatic, recurrent loss):** abdominal unification (metroplasty) — Strassman/Jones & Jones (excision) or Tompkins (incision) technique.

- **Rudimentary non-communicating horn:** laparoscopic excision to prevent cornual (rudimentary-horn) pregnancy and its rupture (~16 weeks).
- **MRKH syndrome (vaginal agenesis):** non-surgical progressive dilator therapy (Frank technique, 6–12 months) as first-line; surgical neovaginoplasty (McIndoe–Reed with split-skin graft, or bowel/peritoneal vaginoplasty) if dilators fail or are unacceptable; uterine factor infertility managed by gestational surrogacy or emerging uterine transplantation.
- **Arcuate uterus:** no treatment — normal variant.

Diagnosis of imperforate hymen

Clinical features

- Presents typically at **age 14–16 years** (peripubertal, at expected menarche) with normal secondary sexual characteristics (hypothalamic-pituitary-ovarian axis intact).
- **Primary amenorrhea with cyclical lower abdominal/pelvic pain** — cryptomenorrhea from cyclic endometrial shedding trapped behind the membrane.
- Progressive accumulation: **hematocolpos** (distended vagina) → **hematometra** (distended uterine cavity) → **hematosalpinx** in late/neglected cases (fimbrial ends sealed by adhesions).
- **Urinary retention** may be the presenting complaint — due to urethral elongation/compression by the distended vagina.
- Abdominal examination: suprapubic/hypogastric cystic swelling (may mimic a full bladder).
- Vulval inspection: **tense, bulging, bluish membrane** at the introitus, which becomes more prominent on Valsalva (distinguishes it from a transverse vaginal septum, which does not bulge on Valsalva).
- Rectal examination confirms a distended, bulging vagina.
- Untreated/delayed cases risk retrograde menstruation through patent tubes leading to **pelvic endometriosis** and subsequent infertility.

Investigations

- **Ultrasonography** — confirms hematocolpos/hematometra (± hematosalpinx) and is usually sufficient.
- **MRI** — reserved for uncertain anatomy or to differentiate from a transverse vaginal septum/cervical atresia when examination is inconclusive.
- Examination under anaesthesia may be required if the diagnosis is not clear on inspection.
- A diagnostic needle aspiration of the bulge must **never** be performed — it risks converting a sterile hematocolpos into a pyocolpos.

Management of imperforate hymen

- **Definitive surgery should not be delayed** — early relief prevents ascending infection, endometriosis, and future infertility.
- **Standard procedure — cruciate (cross-shaped) incision:** a "+"-shaped incision is made in the bulging hymen down to its base; the resulting quadrants are partially excised (not flush with the vaginal mucosa) to keep the opening patent, allowing spontaneous drainage of the accumulated dark, tarry (altered) blood.
- **Alternative membrane-preserving technique** (where preserving the hymenal ring is desired): a sterile puncture is made centrally and enlarged to about 0.5 cm, a 16-F Foley catheter is inserted and left for about 2 weeks to allow continued drainage; a single prophylactic antibiotic dose is given, and topical estrogen cream is applied to the hymenal ring to aid re-epithelialization.
- **Perioperative cautions:**
  - Do **not** apply pressure over the abdomen/uterus during drainage.
  - Avoid internal (vaginal) examination at the time of the procedure.
  - Nurse with the head end raised; give prophylactic antibiotics.
  - Reassess residual pathology (e.g., persistent hematometra) by internal examination only after the next menstrual period.
- **Follow-up:** encourage tampon use once sexually active to prevent stricture/re-stenosis of the created opening; review to confirm normal, unobstructed menstrual flow.
- If examination reveals the obstructing membrane is actually a **transverse vaginal septum** rather than true hymen, the same drainage principle applies, but the surgical approach (vaginal vs. combined abdomino-vaginal) is tailored to the septum's level and thickness.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 42.1 — American Fertility Society Müllerian anomaly classification. Nonobstructive anomalies (Te Linde 13e, p.2204)*
>
> Also sketch: a bulging, tense, bluish hymenal membrane at the introitus with the vagina distended by altered blood behind it (hematocolpos/hematometra), and mark the sites of the cruciate incision.

High-yield exam pointers

- **AFS/ASRM 1988 — 7 classes:** I Agenesis, II Unicornuate, III Didelphys, IV Bicornuate, V Septate, VI Arcuate, VII DES-related.
- **Approximate frequency among fusion defects:** Septate 35% > Bicornuate 26% > Arcuate 18% > Unicornuate 10% > Didelphys 8%.
- **Renal anomaly association ~40%; skeletal ~12%** — always image the renal tract with any Müllerian anomaly.

- **Reproductive outcome ranking:** Didelphys (64%) > Septate (86% with treatment) > Bicornuate (50%) > Unicornuate (poor, ~40%).
- **Hysteroscopic metroplasty for septum:** success 80–89%; vaginal delivery possible (vs. mandatory caesarean after abdominal metroplasty).
- **Imperforate hymen age of presentation: 14–16 years**, primary amenorrhea + cyclic pain + normal secondary sexual characters.
- **Never needle-aspirate a hematocolpos** — risk of pyocolpos. Cruciate incision is the classic answer.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> DC Dutta's Gynaecology and older editions still cite the original Buttram–Gibbons (1979) six-class scheme without the arcuate/DES subdivisions; the seven-class AFS/ASRM 1988 classification given above is the current, examination-standard version and is what Williams Obstetrics 26e also reproduces.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Te Linde's Operative Gynecology 13e (figure).

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Clinical significance of pouch of Douglas

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — The pouch of Douglas (POD), or rectouterine pouch, is the peritoneal cul-de-sac in the pelvis bounded anteriorly by the peritoneum over the cervix, posterior vaginal fornix and upper third of the posterior vaginal wall; posteriorly by the peritoneum on the anterior rectal wall; and laterally by the uterosacral folds — its floor lies about 6–7 cm above the anal orifice, separated from the vagina below by the rectovaginal septum. Because it is the **most dependent part of the peritoneal cavity** in both the erect and supine posture, free intraperitoneal fluid, blood, pus and shed malignant cells all gravitate here — this single fact underlies every clinical use of the pouch, diagnostic, surgical and obstetric.

Diagnostic significance — detecting what has collected in the pouch

Because collections pool in the POD before spreading elsewhere, it is examined on **per-abdominal, bimanual, and rectovaginal palpation** (through the posterior fornix and confirmed per rectally) and imaged/sampled directly:

Finding in the pouch of Douglas	Method of detection	Suggested diagnosis
Boggy, fluctuant, tender mass through posterior fornix	Bimanual + rectal examination	Pelvic hematocele or pelvic abscess
Free anechoic/echogenic fluid	Transvaginal sonography	Post-ovulatory fluid (physiological) if clear; hemoperitoneum if echogenic, from ruptured/leaking ectopic pregnancy
Unclotted blood on needle aspiration	Culdocentesis (18-gauge spinal needle, 1 cm below the cervicovaginal junction in the posterior fornix)	Disturbed ectopic pregnancy / hemoperitoneum
Pus, white cell count > 30,000/mL	Culdocentesis	Acute pelvic inflammatory disease / pelvic abscess
Firm nodules, uterosacral thickening, "frozen pelvis"	Rectovaginal palpation	Deep infiltrating endometriosis
Hard, fixed nodular deposits	Rectal/rectovaginal palpation	Peritoneal seeding of ovarian/genital malignancy or genital tuberculosis

Culdocentesis and rectovaginal palpation of the pouch therefore remain quick outpatient/bedside tools that can localise pathology before imaging or laparoscopy is arranged.

Disease processes that characteristically localise to the pouch

- **Pelvic hematocele** — encysted blood collecting in the POD after a disturbed tubal ectopic (tubal mole or tubal abortion); presents with irregular bleeding and pain, and an ill-defined, boggy, tender mass through the posterolateral fornix extending into the pouch.
- **Pelvic abscess** — encysted pus in the POD; causes include acute salpingitis/pelvic inflammatory disease, post-abortal sepsis, an infected hematocele, and postoperative pelvic peritonitis; localisation is signalled by a spiking/swinging temperature, rectal tenesmus, diarrhoea, and a bulging fluctuant mass felt per vaginam and per rectum.
- **Endometriosis** — the POD, uterosacral ligaments and rectovaginal septum are among the commonest sites of implantation; deep nodules, uterosacral tenderness, and cul-de-sac obliteration ("frozen pelvis") are classic rectovaginal findings and correlate with dyspareunia.
- **Genital tuberculosis and peritoneal malignancy** — tubercular or malignant deposits seed the dependent pouch and are felt as discrete nodules on rectovaginal examination, a key clinical clue to staging/diagnosis.

- **Enterocele** — herniation of the POD through the posterior vaginal fornix, containing omentum or small bowel; may be a traction enterocele (secondary to uterovaginal prolapse) or a pulsion enterocele (from chronically raised intra-abdominal pressure) — part of vault prolapse.
- **Impacted pelvic mass** — a fibroid or ovarian tumour impacted in the pouch can cause menorrhagia or acute urinary retention by pressure on the bladder neck/urethra.

Surgical and procedural access through the pouch

Procedure	Purpose / technique
Culdocentesis	Transvaginal aspiration of POD fluid to confirm hemoperitoneum (disturbed ectopic) or pelvic abscess (pus, WBC > 30,000/mL)
Culdoscopy	Direct optical visualisation of pelvic structures via an incision in the pouch — largely superseded by laparoscopy
Posterior colpotomy (culdotomy)	Surgical opening of the pouch through the posterior fornix — used to drain a localised pelvic abscess and as the vaginal route for tubal ligation (interval cases, uterus < 12 weeks)
Moskowitz procedure	Abdominal obliteration of the pouch with 3–4 concentric sutures incorporating the uterosacral ligaments and peritoneum over the rectosigmoid — definitive repair of enterocele
Pneumoperitoneum induction	Historically induced via a needle through the pouch before diagnostic laparoscopy

Obstetric significance

- In a **disturbed (ruptured or leaking) ectopic pregnancy**, blood from the tubal mole/abortion collects preferentially in the dependent POD, producing a tender, boggy cul-de-sac mass, cervical excitation tenderness, and sometimes an urge to defecate; transvaginal sonography showing echogenic free fluid in the pouch with an adnexal mass, together with a positive culdocentesis (unclotted blood), supports the diagnosis before laparoscopy/laparotomy.
- **Post-ovulatory physiology**: sonographic or laparoscopic demonstration of fluid in the POD after a collapsed follicle is accepted presumptive/direct evidence of ovulation.
- **Puerperal sepsis**: extrauterine spread of infection localising to the pouch produces a bulging, fluctuant, tender mass (pelvic abscess), evidenced by a swinging temperature and rectal tenesmus, requiring posterior colpotomy for drainage once localised.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 1.5 — Mid-sagittal section of the female pelvis showing relative positions of the pelvic organs (DC Dutta's Gynaecology 7e, p.24)*

- Label on the sketch: uterus, posterior fornix, rectum, the pouch of Douglas as the dependent triangular space between them, the uterosacral folds laterally, and the rectovaginal septum below the floor of the pouch.

High-yield exam pointers

- One-line hook: POD = **most dependent part of the peritoneal cavity** → why blood, pus, and malignant cells all collect there.
- Two collections to pair: **hematocele** (blood, disturbed ectopic) vs **abscess** (pus, salpingitis/PID/postabortal sepsis) — both boggy, tender, fluctuant on posterior fornix.
- Culdocentesis numbers: **18-gauge spinal needle**, **1 cm below the cervicovaginal junction**, **2 cm depth**; WBC > **30,000/mL** in aspirate supports acute PID.
- Access route mnemonic: culdocentesis (needle) → culdoscopy (scope) → posterior colpotomy/culdotomy (open) — all through the same posterior fornix.
- Enterocele repair = **Moskowitz procedure** (obliterates the pouch with concentric uterosacral-peritoneal sutures).
- Nodules in the pouch on rectovaginal exam = triad to recall: **endometriosis, genital tuberculosis, malignant deposits**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

The pouch of Douglas is also called the rectouterine pouch or the cul-de-sac in Western texts (Williams Obstetrics/Berek & Novak) — same structure, used interchangeably with DC Dutta's terminology in this answer.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (pouch of Douglas anatomy, surgical importance list, culdocentesis, pelvic abscess/hematocele); DC Dutta's Textbook of Obstetrics 9e (ectopic pregnancy findings in the pouch, puerperal sepsis spread); Berek & Novak's Gynecology 16e (cul-de-sac findings in endometriosis, adnexal masses, and malignancy).

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Controlled ovarian hyper stimulation

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — Controlled ovarian hyperstimulation (COH) is the pharmacological induction, using exogenous gonadotropins with or without a gonadotropin-releasing hormone (GnRH) agonist/antagonist, of the simultaneous growth of multiple mature ovarian follicles within a single cycle under close ultrasound and hormonal monitoring. It is undertaken for assisted reproductive technology (ART — in vitro fertilisation [IVF]/intracytoplasmic sperm injection [ICSI]) or gonadotropin-stimulated intrauterine insemination (IUI), and differs from simple ovulation induction, whose goal is a single dominant follicle.

Indications

- IVF/ICSI cycles (the principal indication).
- Superovulation with IUI for unexplained infertility, mild male-factor or cervical-factor infertility.
- Anovulatory infertility (WHO Group I/II) after failure of clomiphene citrate.
- Oocyte donation/fertility-preservation cycles.

Stimulation protocols

Down-regulation of the pituitary prevents a premature endogenous LH surge; gonadotropins (urinary FSH [uFSH]/recombinant FSH [rFSH]/human menopausal gonadotrophin [hMG]) then drive multifollicular growth. Starting gonadotropin dose is individualised (150–300 IU daily, guided by age, antral follicle count/anti-Müllerian hormone, body weight and prior response); 150 IU/day is the standard unselected dose.

Protocol	GnRH agonist/antagonist schedule	Gonadotropin timing
Long — follicular down-regulation	Leuprolide acetate 1.0 mg SC daily from cycle day 2 until down-regulation confirmed (serum estradiol <30–40 pg/mL, no follicle >10 mm on transvaginal sonography [TVS]), then reduced to 0.5 mg daily	Started once down-regulation is confirmed
Long — luteal down-regulation (classic long protocol)	Leuprolide 1.0 mg daily begun day 21 (mid-luteal) of the preceding cycle, reduced to 0.5 mg daily after suppression	Same as above
Short/"flare" agonist	Leuprolide acetate 1.0 mg daily on cycle days 2–4, then 0.5 mg daily	Gonadotropins begin cycle day 3, exploiting the agonist's initial flare of endogenous FSH/LH

Protocol	GnRH agonist/antagonist schedule	Gonadotropin timing
GnRH-antagonist	Ganirelix or cetrorelix 0.25 mg SC daily — fixed from stimulation day 5–6, or flexible when the lead follicle reaches 13–14 mm; alternatively a single 3.0 mg cetrorelix dose	Gonadotropins from cycle day 2–3, no prior down-regulation

The antagonist protocol is now the commonest worldwide — shorter, fewer injections, and it permits a GnRH-agonist trigger, which markedly lowers the risk of ovarian hyperstimulation syndrome (OHSS).

Monitoring the stimulated cycle

- Serial transvaginal ultrasonography and serum estradiol (E2) from stimulation day 5–6.
- E2 should rise exponentially (roughly doubling every 2–3 days); an expected level is about 200–300 pg/mL per maturing follicle.
- Dominant follicles grow ~1–2 mm/day; dose is titrated up or down against the E2 trend and follicle number/size.
- Endometrial thickness ("triple stripe") of 8–9 mm or more is the favourable target.

Triggering final oocyte maturation

- **Criterion to trigger:** at least two leading follicles ≥17–18 mm in mean diameter, with the remainder 14–16 mm, and a corresponding E2 rise.
- **Standard trigger:** human chorionic gonadotropin (hCG) 5,000–10,000 IU intramuscularly/subcutaneously (or recombinant hCG 250 μg); oocyte retrieval is timed 34–36 hours later.
- **GnRH-agonist trigger** (e.g., leuprolide 0.5–1.0 mg SC), usable only in antagonist cycles, induces a shorter endogenous LH/FSH surge; it reduces OHSS risk but causes rapid luteolysis, so mandatory progesterone-based luteal support (and often a "freeze-all" strategy) replaces hCG-based support. A low-dose hCG or agonist "dual trigger" is used by some centres.
- **Luteal support:** micronised progesterone (200 mg orally thrice daily, or vaginal, or 50 mg intramuscularly daily) for about 14 days; supplemental hCG boosts (1,500–2,500 IU) raise OHSS risk and are avoided in high responders.

Complications — Ovarian hyperstimulation syndrome (OHSS)

OHSS is an iatrogenic, potentially life-threatening complication of COH — cystic ovarian enlargement with a systemic capillary-leak state driven by vascular endothelial growth factor (VEGF) and other cytokines released after the hCG trigger, causing fluid shift from the intravascular to extravascular space. Onset is 3–7 days after the trigger (early, trigger-driven) or later and more severe if pregnancy supervenes (late, rising endogenous hCG).

Risk factors: age <30 years, low body weight, polycystic ovary syndrome (PCOS), high antral follicle count/anti-Müllerian hormone, rapidly rising or high E2 (>2,500–3,000 pg/mL, or >75% rise over the previous day), numerous intermediate-sized follicles ("necklace sign" on ultrasound), high gonadotropin doses, prior OHSS, and hCG exposure (trigger or luteal support).

Severity	Clinical features
Mild	Abdominal bloating, mild pain; ovarian size <8 cm
Moderate	Nausea, vomiting, diarrhoea; ultrasound ascites; ovarian size 8–12 cm
Severe	Clinical ascites ± hydrothorax; haematocrit >45%, white cell count >15,000/mL; oliguria with normal creatinine; liver dysfunction; anasarca; ovarian size >12 cm
Critical	Tense ascites; haematocrit >55%; white cell count >25,000/mL; oliguria with raised creatinine; renal failure; thromboembolism

Prevention

- Identify anticipated high responders early; individualise starting gonadotropin dose (lower in high-risk women).
- Prefer a GnRH-antagonist protocol with a GnRH-agonist trigger in anticipated high responders.
- "Coasting" — withhold further gonadotropins and delay the hCG trigger 1–3 days until E2 plateaus or falls.
- Use a lower hCG trigger dose (5,000 IU) or an agonist trigger.
- Dopamine agonist (cabergoline) for up to 7 days after the trigger, reducing VEGF-mediated permeability.
- Elective cryopreservation of all embryos ("freeze-all"), avoiding fresh embryo transfer in the stimulated cycle.
- Metformin co-treatment during gonadotropin stimulation in women with PCOS.
- Use progesterone, not hCG, for luteal phase support.

Management (supportive; severity-graded)

- Mild/moderate — outpatient: oral analgesics, oral fluids ≥1 L/day (electrolyte drinks), daily weight, avoid intercourse and strenuous activity (risk of torsion/rupture).
- Admission criteria — intractable pain, tense ascites, dyspnoea, oliguria, hyponatraemia (Na <135 mEq/L), hyperkalaemia (K >5 mEq/L), haemoconcentration, or deranged renal/liver function.
- Inpatient care — strict fluid balance, daily weight/abdominal girth, serial haemogram/electrolytes/renal-liver function, chest X-ray/echocardiogram if effusion is suspected.

- Intravenous normal saline (preferred over lactated Ringer, given the hyponatraemia risk) titrated to urine output; 25% human albumin 50–100 g infused slowly over 4 hours if saline fails to correct hypovolaemia; avoid premature diuretics.
- Ultrasound-guided abdominal or transvaginal paracentesis for tense ascites, oliguria, or dyspnoea refractory to fluids; thoracentesis for a large pleural effusion.
- Thromboprophylaxis — compression stockings/intermittent pneumatic compression and prophylactic anticoagulation in severe disease, continued at least through the first trimester if pregnancy occurs.
- Surgery is reserved for ovarian torsion or haemoperitoneum from cyst rupture.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 48.2 — In vitro fertilisation protocols using gonadotrophin-releasing hormone agonist with gonadotrophin agent, showing long (follicular/luteal down-regulation), short (flare), and antagonist regimens (Jeffcoate's Principles of Gynaecology 9e, p.828)*

High-yield exam pointers

- COH aims for **multiple** mature follicles (ART/IUI); ovulation induction aims for **one**.
- Trigger criterion: **≥2 follicles ≥17–18 mm** + appropriate E2 rise → hCG 5,000–10,000 IU → retrieval at 34–36 hours.
- Antagonist protocol + GnRH-agonist trigger = the modern "OHSS-free" combination.
- OHSS severity numbers to write: **Hct >45% (severe), >55% (critical); ovarian size >12 cm (severe/critical).**
- Luteal support after agonist trigger must be progesterone-based (never hCG) to avoid precipitating late OHSS.
- Risk-factor recall: young, thin, PCOS, high AMH/antral follicle count, high/rapidly rising E2.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's severity table (mild/moderate/severe/critical) is the widely used Indian-exam severity classification for OHSS; current ACOG/American Society for Reproductive Medicine practice increasingly treats OHSS as a clinical continuum rather than four discrete grades, but the numeric cut-offs above remain the exam-relevant reference values.

SOURCE & COVERAGE

Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; DC Dutta's Textbook of Gynaecology 7e; Jeffcoate's Principles of Gynaecology 9e.

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Critically evaluate the role of folic acid/folate in pregnancy

Asked in: Paper I 12-Nov-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — Folate (vitamin B9) is a water-soluble vitamin required for one-carbon transfer in purine/pyrimidine synthesis and in remethylation of homocysteine to methionine; folic acid is its fully oxidised synthetic form used in supplements and fortified food. Requirement rises sharply in pregnancy to support rapid trophoblastic and fetal cell division and, most critically, closure of the neural tube — complete by day 28 after conception, usually before pregnancy is even recognised. This timing is the central argument for periconceptional rather than first-antenatal-visit dosing.

Physiological basis & requirement

Parameter	Detail
Active form	Tetrahydrofolate (THF), formed by dihydrofolate reductase; methyl-THF donates one-carbon units for DNA/RNA synthesis and homocysteine remethylation
Requirement, non-pregnant	~200 µg/day
Requirement, pregnancy	~400 µg/day (increased demand from expanded red-cell mass, trophoblast and fetal growth)
Dietary sources	Green leafy vegetables, liver, legumes, citrus fruits; folate is heat-labile and largely destroyed by prolonged cooking
Deficiency consequence	**Megaloblastic anaemia** from impaired DNA synthesis in erythroid precursors; elevated serum homocysteine

Evidence base for neural-tube-defect prevention — the landmark trials

Trial	Population/design	Intervention	Key result
MRC Vitamin Study (*Lancet* 1991)	Multicentre RCT, women with a previous neural-tube-defect (NTD)-affected pregnancy	4 mg folic acid/day vs placebo, periconceptional	Recurrence risk (baseline 2–5%) reduced by **more than 70 percent**
Czeizel & Dudas (*NEJM* 1992)	Hungarian RCT, women with **no** prior NTD	Periconceptional multivitamin containing folic acid vs trace-element supplement	Reduced the **first-occurrence** risk of NTD, proving benefit extends beyond recurrence prevention

Trial	Population/design	Intervention	Key result
Mechanism	—	—	Low folate impairs methylation and raises homocysteine, disrupting neural tube closure; the *MTHFR* C677T polymorphism compounds the risk

Risk-stratified dosing — current recommendation

Category	Indications	Dose	Timing
Average risk	All women planning pregnancy	**0.4 mg (400 µg)/day**	From ≥4 weeks before conception through 12 weeks gestation
High risk	Previous NTD-affected pregnancy or family history, antiepileptic drug therapy (valproate, carbamazepine), pregestational diabetes, obesity, malabsorption syndromes, multifetal gestation, haemoglobinopathy	**4 mg/day**	1 month before conception to end of the first trimester

Other proposed benefits — critical appraisal of the evidence

Claimed benefit	Evidence quality / verdict
Megaloblastic anaemia prevention/treatment	Established indication — but coexistent iron or vitamin B12 deficiency must be excluded/corrected too
Orofacial clefts, some congenital heart defects	Observational reduction reported; evidence weaker and less consistent than for NTD
Pre-eclampsia prevention	Directly tested — *Wen* et al. RCT, ~2500 high-risk women given 4 mg folic acid vs placebo: **no reduction** in incidence (~14% in both arms), refuting the homocysteine-based hypothesis
Preterm birth / fetal growth restriction	Trial evidence inconsistent; not an established indication
Recurrent pregnancy loss	No robust randomised evidence of benefit beyond correcting overt deficiency

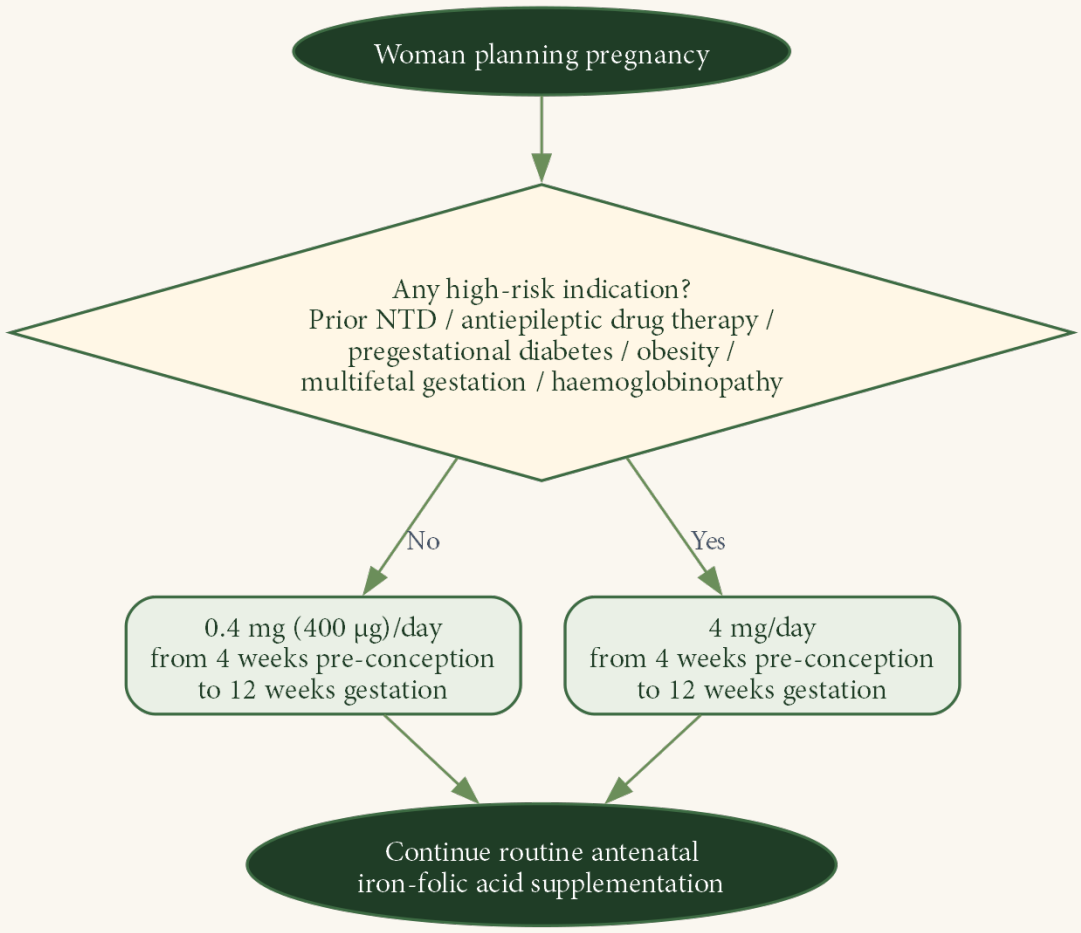
Limitations, risks & controversies

- High-dose folic acid can correct the anaemia of coexistent vitamin B12 deficiency while allowing subacute combined degeneration of the cord to progress unrecognised — B12 status should be checked before high-dose folate therapy for anaemia.
- Antiepileptic drugs impair folate metabolism, but the dose needed for seizure-related deficiency is not automatically the NTD-prevention dose — both indications converge on the same 4 mg high-risk regimen, which is a coincidence of dosing rather than a shared mechanism.
- Mandatory food fortification raises population folate intake without depending on individual compliance, but the resulting cumulative intake (fortified staples plus supplements) has raised debate about exceeding the tolerable upper limit in some subgroups.
- Because folate is heat-labile, dietary counselling alone cannot reliably deliver the periconceptional dose — supplementation is required.

Public health delivery

- **United States**: mandatory folic acid fortification of cereal grain products since 1998 — measurably lowered population NTD rates.
- **India**: iron-folic acid (IFA) supplementation is the Government of India's antenatal standard, and the Food Safety and Standards Authority of India has mandated fortification of wheat/maize atta and edible oil in parallel.
- **Coverage gap**: since a large proportion of pregnancies are unplanned, opportunistic preconceptional dosing misses many at-risk women — the strongest argument for fortification over supplementation-alone strategies.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Risk-stratified periconceptional folic-acid algorithm.

High-yield exam pointers

- MRC Vitamin Study 1991: 4 mg folic acid cut NTD **recurrence** by >70%.
- *Czeizel* & Dudas 1992 (*NEJM*): proved benefit for **first-occurrence** prevention too.
- Dose rule: 0.4 mg average risk vs **4 mg** high risk — a 10-fold step, not an additive one.
- Critical window: 4 weeks before conception to end of first trimester (neural tube closes by day 28).
- *Wen* 2018 RCT: 4 mg folic acid did **not** prevent pre-eclampsia (~14% incidence in both arms) — a key "negative trial" to quote.
- Always exclude/correct vitamin B12 deficiency before high-dose folate in anaemia (masking risk).

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Textbook of Obstetrics 9e states two different average-risk doses within the same chapter — 4 mg in its preconceptional-counselling text versus 0.4 mg in its own end-of-chapter summary; the current standard (Williams Obstetrics 26e, reflecting ACOG/USPSTF 2019) reserves 4 mg for the high-risk indications listed above and uses 0.4 mg for average-risk women, and that current standard is what is followed here.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; MRC Vitamin Study Group (*Lancet* 338:131, 1991); Czeizel AE & Dudas I (*N Engl J Med* 327:1832, 1992); Wen SW et al. (cited in Williams Obstetrics 26e); ACOG/USPSTF 2019 recommendations (as cited in Williams Obstetrics 26e).

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Describe anatomy of perineum and write the management of third degree perineal tear

Asked in: Paper I May 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — The **perineum** is the diamond-shaped region of soft tissue below the pelvic floor, between the thighs, containing the external genitalia and anal canal. A **third-degree perineal tear** is an obstetric laceration extending from the perineal skin through the perineal body to involve the **anal sphincter complex** (external and/or internal anal sphincter) while sparing the anorectal mucosa.

Anatomy of the perineum

Boundary	Structure
Superior	Inferior surface of the pelvic floor (levator ani)
Inferior	Skin between the two thighs
Anterior (apex)	Pubic symphysis / subpubic arch
Posterior	Tip of the coccyx
Lateral	Ischiopubic rami, ischial tuberosities, sacrotuberous ligaments

A transverse line joining the two ischial tuberosities (the posterior border of the urogenital diaphragm) divides this diamond into two triangles.

- **Urogenital triangle** (anterior) — pierced by the urethra and vagina; obstetrically important. It contains two fascial compartments:
  - *Superficial perineal pouch* (between Colles' fascia below and the perineal membrane above): **bulbospongiosus**, **ischiocavernosus**, **superficial transverse perineal muscles**, vestibular bulbs, and **Bartholin's glands**.
  - *Deep perineal pouch* (within the urogenital diaphragm): **deep transverse perineal muscle** and **sphincter urethrae membranaceae** (external urethral sphincter).
- **Anal triangle** (posterior) — contains the anal canal with the **external anal sphincter (EAS)**, the anococcygeal body, and the paired **ischiorectal fossae** (fat-filled spaces bounded by obturator internus laterally and levator ani medially, transmitting the pudendal nerve and internal pudendal vessels through the **pudendal canal / Alcock's canal**).

Perineal body (central point of perineum) — a pyramidal fibromuscular mass, roughly 4 cm × 4 cm at its base, situated between the lower vagina and the anal canal. It is the point of convergence of **eight to nine muscles**, "like spokes to the hub of a wheel":

- Bulbospongiosus (both sides)
- Superficial transverse perineal muscles (both sides)
- Deep transverse perineal muscles (both sides)
- External anal sphincter
- Pubovaginalis fibres of levator ani
- External urethral sphincter fibres

Clinical relevance: the perineal body maintains the normal vaginal axis and indirectly supports the uterus, bladder and rectum; it is torn in every second-, third- and fourth-degree laceration and must be reconstructed in any perineal repair. The superficial (Colles') fascia is firmly attached to the ischiopubic rami and posteriorly to the perineal body/urogenital diaphragm but is continuous anteriorly with Scarpa's fascia of the abdominal wall — hence a urethral extravasation or vulval haematoma tracks upward onto the abdominal wall but not onto the thigh. Sensory and motor supply is via the **pudendal nerve (S2–S4)** through Alcock's canal (inferior rectal, perineal, and dorsal nerve of clitoris branches).

Classification of third-degree perineal tear

Degree	Structures torn
First	Vaginal epithelium / perineal skin only
Second	Perineal muscles (bulbospongiosus, superficial transverse perineal) — sphincter intact

Degree	Structures torn
Third	Anal sphincter complex torn — **3a**: <50% of external anal sphincter (EAS) thickness torn; **3b**: >50% of EAS torn, internal anal sphincter (IAS) intact; **3c**: both EAS and IAS torn
Fourth	As third degree + anorectal mucosa torn

If the depth of injury is in doubt, it is always graded to the higher (more severe) category (RCOG classification of obstetric anal sphincter injury, OASI).

Management of third-degree perineal tear

A. Timing

- **Recent tear** (identified at delivery): repair immediately after delivery of the placenta — minimises infection and blood loss.
- **Missed/delayed tear** (>24 hours since delivery): defer primary repair, start antibiotics, and perform a **delayed (interval) repair after 3 months** once oedema and inflammation have settled.

B. Pre-repair principles

- Repair in an operating theatre with good lighting and assistance, by a clinician trained in anal sphincter repair (or under direct supervision).
- **Anaesthesia:** regional (spinal/epidural) or general anaesthesia is preferred for adequate relaxation and exposure of the retracted sphincter ends; local infiltration of 1% lignocaine (10–15 mL) or pudendal block is used only if regional/general anaesthesia is unavailable.
- Lithotomy position, antiseptic cleaning, urethral catheterisation.

C. Surgical steps (from within outward)

- Retracted ends of anorectal mucosa are grasped and sutured from ~1 cm above the apex down to the anal verge with a continuous or interrupted submucosal stitch of 3-0 vicryl/PDS, knots tied within the lumen or buried, avoiding full-thickness bites (risk of recto-vaginal fistula).
- **Internal anal sphincter (IAS)** — identified as the glistening white fibrous layer between the anorectal submucosa and the EAS; repaired separately with interrupted or continuous 2-0/3-0 PDS or vicryl.
- **External anal sphincter (EAS)** — retracted ends exposed with Allis's tissue forceps and reconstructed by one of two equally effective techniques:
  - *End-to-end (approximation)* — the torn ends and surrounding capsule are apposed with interrupted figure-of-eight and mattress sutures (2-0/3-0 PDS or vicryl) at the 3, 6, 9 and 12 o'clock positions; suitable for 3a/3b tears.
  - *Overlapping* — the two ends are overlapped and secured with two rows of mattress sutures; used only when the EAS is completely divided (3c/fourth degree).

Both techniques give comparable long-term continence outcomes.

- Perineal muscles (bulbospongiosus, transverse perinei) are re-approximated with interrupted 0-vicryl/PDS to reconstruct the **perineal body** and restore the vaginal axis.
- Vaginal epithelium is closed with a continuous 2-0 vicryl suture, and the perineal skin with a subcuticular stitch.
- A per-rectal examination is done at the end to confirm no suture has breached the rectal mucosa; needle and swab counts are reconciled.

Layer	Suture material
Anorectal mucosa	3-0 vicryl or 3-0 PDS
Internal anal sphincter	2-0/3-0 PDS or vicryl
External anal sphincter	2-0/3-0 PDS (monofilament) or polyglactin 910
Perineal body/muscles	0 vicryl or PDS
Vaginal/perineal skin	2-0 vicryl, continuous/subcuticular

D. Perioperative antibiotic prophylaxis: a single intravenous dose of a second-generation cephalosporin (e.g., cefuroxime 1.5 g) at the time of repair, or clindamycin if penicillin-allergic, to reduce infective morbidity.

E. Aftercare

- Regular analgesia (paracetamol/NSAIDs); avoid rectal diclofenac in the immediate post-repair period.
- Stool softener/laxative (e.g., lactulose, titrated up to 15 mL twice daily) continued for 1–2 weeks with a normal, fibre-containing diet to keep stools soft and prevent straining; enemas and suppositories are avoided.
- Continue broad-spectrum antibiotic cover; metronidazole 400 mg thrice daily for 5–7 days to cover anaerobic faecal contamination.
- Pelvic floor physiotherapy/exercises.
- Intercourse is deferred until after the first postpartum visit.
- **Follow-up at 6–12 weeks** — clinical review of continence; if flatal/faecal incontinence persists, arrange **endoanal ultrasound and anorectal manometry**, with referral to a colorectal surgeon if a residual defect is found.

F. Counselling for future delivery — women who are asymptomatic with normal endoanal ultrasound/manometry may be offered a further vaginal delivery; those with persistent symptoms or an abnormal scan/manometry are offered elective caesarean delivery.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 1.20 — Anatomy of the pelvic floor, perineal view. (Te Linde 13e, p.91)*

Label: urogenital triangle vs anal triangle, perineal body with its nine converging muscles, ischiorectal fossa, and the anal sphincter complex (EAS/IAS) in relation to the anorectal mucosa.

High-yield exam pointers

- OASI classification: 3a <50% EAS, 3b >50% EAS (IAS intact), 3c EAS + IAS both torn; 4th degree adds anorectal mucosa.
- If depth of tear is uncertain — always grade to the **higher** degree.
- Delayed presentation rule: >24 h → antibiotics + **repair after 3 months** (interval repair).
- EAS repair: **overlap only for 3c/complete division**; end-to-end for 3a/3b — outcomes equivalent.
- Suture of choice for sphincter: **PDS or polyglactin (vicryl)**, not chromic catgut (higher breakdown rate).
- Single-dose IV cephalosporin at repair; stool softener (not enemas) for 1–2 weeks after.
- Perineal body = 9 converging muscles ("hub of a wheel"); its restoration maintains the vaginal axis.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Some Indian texts still advise a "low-residue diet" for the first few postoperative days after complete perineal tear repair; current practice instead favours a normal/high-fibre diet with a stool softener, since constipation and straining — not stool bulk — risk wound dehiscence.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; Te Linde's Operative Gynecology 13e (figure); RCOG Green-top Guideline No. 29 (classification and management of obstetric anal sphincter injury); ACOG Practice Bulletin No. 198 (Prevention and Management of Obstetric Lacerations at Vaginal Delivery).

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Describe lymphatic drainage of uterine corpus and cervix with it's clinical significance

Asked in: Paper I 16-Dec-2023 — RGUHS MS Obstetrics & Gynaecology

Definition — The uterus has an **intrinsic lymphatic plexus** (basal endometrial layer and a subserosal layer, connected by channels running through the myometrium) that feeds **extrinsic pathways** running

alongside the ovarian, round-ligament, and uterine vessels. The corpus and the cervix empty into *different* regional node groups, and this segmental, region-specific pattern determines both the natural spread and the surgical staging of endometrial and cervical malignancy.

Lymphatic drainage of the uterine corpus

Region of corpus	Lymphatic pathway	Draining node group
Fundus & adjoining upper body	Along **ovarian lymphatics**, through the infundibulopelvic (suspensory) ligament	**Superior lumbar (para-aortic)** nodes — bypasses the pelvis entirely
Cornu	Along the **round ligament**	**Superficial inguinal** nodes (horizontal group)
Rest of the body	Direct	**External iliac** nodes
Lower body, adjacent to cervix	Continuous with cervical plexus	Cervical lymphatics (see below)

- Two anastomosing intrinsic plexuses exist — one in the **basal layer of the endometrium**, one **subserosal**; the basal-layer lymphatics traverse the myometrium alongside the blood vessels to join the subserosal plexus before leaving the uterus.
- There is free cross-anastomosis of the ovarian lymphatics of the two sides across the **uterosacral ligament** and via the subperitoneal fundal plexus, so a unilateral tubo-ovarian growth can spread to contralateral and para-aortic nodes.

Lymphatic drainage of the cervix

The cervical lymphatics course **alongside the uterine veins** and drain into two tiers of nodes.

- **Primary groups**
  - **Parametrial nodes** — small, inconsistently present, near the point where the ureter crosses the uterine artery
  - **Obturator nodes**
  - **Internal iliac (hypogastric) nodes**
  - **External iliac nodes** — anterior (middle) and medial groups specifically (the lateral group is not primarily involved)
  - **Sacral nodes** — lateral to the rectum and in front of the sacral promontory
- **Secondary group** — all primary groups drain onward into the **common iliac nodes**, then the **superior lumbar (para-aortic) nodes**, which finally empty via the **cisterna chyli** (over the body of T12) into the **thoracic duct**, opening into the **left subclavian vein** at its junction with the left internal jugular vein.

In carcinoma cervix, it is specifically the medial and middle groups of the external iliac nodes, together with the obturator and internal iliac nodes, that constitute the first-echelon (sentinel) basin.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 2.2 — Schematic representation of the lymphatic drainage of the body of uterus (DC Dutta's Gynaecology 7e, p.42)*
- ☐ *Fig 2.3 — Schematic representation of the lymphatic drainage of the cervix (DC Dutta's Gynaecology 7e, p.43)*

Clinical significance

Clinical scenario	Basis in lymphatic anatomy	Significance
Carcinoma cervix — radical hysterectomy	First-echelon nodes are parametrial, obturator, internal iliac and the medial/middle external iliac groups	*Wertheim's* radical hysterectomy removes the parametrium **en bloc with these node groups**; nodal metastasis, regardless of tumour size, upstages disease to **FIGO 2018 stage IIIC — IIIC1** (pelvic nodes only) or **IIIC2** (para-aortic nodes ± pelvic), with an **r** (radiology) or **p** (pathology) suffix recording how the nodes were confirmed
Sentinel lymph-node (SLN) mapping in early cervical cancer (tumour <2 cm, per NCCN)	Cervix injected with dye/radiocolloid technetium-99/indocyanine green at the **3 and 9 o'clock** positions	Sentinel nodes are typically found **medial to the external iliac, ventral to the hypogastric (internal iliac), or in the superior obturator space**; a negative SLN allows the remaining nodal basin dissection to be omitted (sensitivity 65–87%, negative predictive value 90–97%)
Carcinoma endometrium, especially fundal tumours	Fundus drains along ovarian lymphatics directly to **para-aortic** nodes, bypassing the pelvic groups	Explains why isolated para-aortic nodal disease can occur even in apparently low-risk disease; complete surgical staging needs **pelvic + para-aortic lymphadenectomy** (or sentinel node mapping with indocyanine green, now validated by the FIRES trial), and nodal status again defines **stage IIIC1 (pelvic) / IIIC2 (para-aortic)**
Growth at the **cornu** of the uterus	Drains along the round ligament to **superficial inguinal** nodes	Rare but recognised route by which a cornual/fundal uterine tumour can present with inguinal nodal metastasis, mimicking vulval drainage

Clinical scenario	Basis in lymphatic anatomy	Significance
Ascending genital infection / puerperal sepsis	Cervical and lower-uterine-segment lymphatics communicate with the **parametrium and broad ligament**	Explains lymphatic spread of infection after delivery, abortion or instrumentation to cause **parametritis, pelvic cellulitis and broad-ligament abscess**
Pelvic ± para-aortic lymphadenectomy (cervical/endometrial cancer surgery)	Interruption of the normal external/internal/common iliac and para-aortic channels	Predisposes to **lower-limb lymphoedema and pelvic lymphocyst**; this morbidity is the main driver for adopting sentinel-node mapping in place of complete lymphadenectomy
Ovarian/tubal malignancy	Ovarian lymphatics anastomose across both sides via the uterosacral ligament/subperitoneal fundal plexus	Explains **contralateral and para-aortic nodal spread** even from an apparently unilateral tubo-ovarian growth

High-yield exam pointers

- **Fundus → ovarian lymphatics → para-aortic nodes** (bypasses pelvis) — the single most commonly tested line.
- **Cornu → round ligament → superficial inguinal nodes.**
- **Rest of body → external iliac; adjacent to cervix → cervical lymphatics.**
- Cervix primary groups (mnemonic — "POISE"): Parametrial, Obturator, Internal iliac, external iliac (Specifically medial + middle), sEcral.
- Carcinoma cervix classically involves the **medial and middle external iliac groups** first.
- **FIGO 2018/2019 cervical staging**: any pelvic/para-aortic nodal metastasis = **stage IIIC** (IIIC1 pelvic, IIIC2 para-aortic), with r/p imaging-pathology notation — write this line verbatim.
- **SLN cervical injection sites: 3 and 9 o'clock**, for tumours **<2 cm**.
- Final common lymphatic pathway: **cisterna chyli (T12) → thoracic duct → left subclavian vein.**

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
>
> The endometrial-cancer staging table available in the corpus is the FIGO 2009 revision (stage IIIC1 = positive pelvic nodes, IIIC2 = positive para-aortic nodes); FIGO's 2023 update further stratified endometrial cancer by histology and molecular profile but did not change this underlying pelvic-versus-para-aortic nodal split, so the anatomy and clinical-significance points above remain current.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (Chapter 2 — Blood Vessels, Lymphatic Drainage and Innervation of Pelvic Organs); Berek & Novak's Gynecology 16e (pelvic lymphatic anatomy; cervical cancer — FIGO staging and sentinel lymph-node evaluation; endometrial cancer — surgical staging and sentinel node mapping); FIGO Committee Report, "Revised FIGO staging for carcinoma of the cervix uteri," Int J Gynecol Obstet 2019.

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Describe primary and secondary immune response and immunological changes in pregnancy

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — A **primary immune response** is the immune system's reaction on first contact with an antigen; it has a long lag phase and a low antibody titre. A **secondary (anamnestic/booster) response** occurs on re-exposure to the same antigen and is faster, larger, and more durable because memory B and T lymphocytes generated during the primary response persist. Normal pregnancy is an immunological paradox — a semi-allogeneic fetal allograft carrying paternal antigens is tolerated for 9 months not by global immunosuppression but by an actively regulated, regional shift in maternal immunity at the maternal-fetal interface.

Primary vs secondary immune response

Feature	Primary response	Secondary response
Trigger	First exposure to an antigen	Re-exposure to the same antigen
Lag/induction period	Long (5–10 days)	Short (1–3 days)
Antibody class	**IgM** appears first, followed by a low-titre IgG	**IgG** predominates rapidly and in high titre (secretory IgA also boosted at mucosae)
Peak antibody titre	Low	High (10–100-fold greater)
Rate of antibody rise	Slow	Rapid
Antibody affinity	Lower	Higher (affinity maturation via somatic hypermutation in germinal centres)
Duration	Short-lived, declines quickly	Long-lasting — memory cells persist for years
Cells responsible	Naive B and T lymphocytes	Memory B and T lymphocytes (rapid clonal expansion)

Feature	Primary response	Secondary response
Clinical/exam correlate	First infection; first vaccine dose	Booster vaccine dose; re-infection; basis of repeat anti-D dosing on re-exposure to Rh(D) antigen

Mechanisms of maternal-fetal immune tolerance

- **Trophoblast MHC restriction ("no-classical-HLA" principle)** — the villous trophoblast, which bathes directly in maternal blood in the intervillous space, expresses **no classical HLA class I or class II molecules** and is therefore immunologically inert to maternal T cells. The invading extravillous trophoblast expresses only the **non-classical HLA-G** (with HLA-E/HLA-C) but never HLA-A, HLA-B, or class II molecules — this protects it from cytotoxic T-cell recognition while HLA-G actively signals decidual immune cells to tolerate invasion.
- **Decidual/uterine natural killer (uNK) cells** — constitute about 70% of decidual leukocytes in the first trimester but, unlike circulating NK cells, **lack cytotoxic function**. They are progesterone-dependent, interact with trophoblast HLA-G/HLA-C, and secrete IL-8, interferon-inducible protein-10, VEGF, and placental growth factor to drive trophoblast invasion and spiral-artery remodelling rather than attack it.
- **Systemic T-helper (Th) cytokine shift** — maternal immunity shifts from a **Th1** (pro-inflammatory: interleukin-2, interferon, tumour necrosis factor — cell-mediated) profile toward a **Th2** (anti-inflammatory: interleukins-4, 6, and 10 — humoral) profile. This Th2 predominance is protective for the fetal allograft and explains why Th1-driven autoimmune disease (e.g., rheumatoid arthritis) often improves in pregnancy, while Th2-associated disease (e.g., systemic lupus erythematosus) may flare postpartum.
- **Immunosuppressive humoral factors** — estradiol, progesterone, human chorionic gonadotropin, and prolactin act systemically; alpha-fetoprotein, pregnancy-associated glycoproteins (α2-macroglobulin), and placental interferon add further suppression; amniotic fluid is rich in immunosuppressive phospholipids.
- **Maternal-fetal microchimerism** — bidirectional trafficking of cells and cell-free fetal DNA across the placenta throughout gestation leaves low-level chimeric cell populations in both mother and fetus, thought to contribute to mutual tolerance.
- **Antibody formation without rejection** — anti-paternal HLA and anti-T-cell antibodies do form during pregnancy, but these have no major adverse effect on outcome in most women; immunological tolerance here is regulated through complement and cytokine control rather than mimicking transplant rejection biology.

Changes in maternal systemic immune parameters

Parameter	Change in pregnancy
Total leukocyte count	Rises through gestation (upper normal ~15,000/μL); during labour and early puerperium can physiologically reach ≥25,000/μL
Lymphocyte subsets	B-lymphocyte numbers unchanged; absolute T-lymphocyte numbers rise; CD4:CD8 ratio unchanged
Cervical/mucosal immunity	Peak IgA and IgG levels in cervical mucus form an immunoglobulin-rich mucus plug that barriers ascending infection
Placental IgG transfer	Bulk of maternal IgG crosses to the fetus in the third trimester, conferring passive immunity ahead of birth
Acute-phase markers	C-reactive protein rises in normal pregnancy and becomes a less reliable marker of infection; erythrocyte sedimentation rate rises because of increased fibrinogen and plasma globulins
Complement	C3 and C4 levels significantly rise during the second and third trimesters
Procalcitonin	Low/undetectable in mid-pregnancy; rises near term and through the first postpartum days; a genuine rise still favours bacterial sepsis but poorly predicts chorioamnionitis after membrane rupture
Net clinical effect	Pregnancy is **not** a globally immunodeficient state — women mount effective humoral and cell-mediated responses to infection and vaccination; the changes above reflect a regionally targeted, actively regulated tolerance of the fetal allograft plus a systemic Th2 shift

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 21.8 — Immune tolerance and activation at the maternal-fetal interface (Williams Obstetrics 26e, p.419)*

Also sketch/plot the classic **primary vs secondary antibody response curve**: X-axis = time (days) after antigen exposure; Y-axis = serum antibody titre (log scale). Plot two exposure events — a first antigen dose at day 0 producing a curve with a long lag, an early small IgM peak, and a low delayed IgG peak that quickly declines; and a second (booster) dose at roughly day 30 producing a curve with a short lag and a much taller, longer-lasting IgG-dominant peak. Label the lag phase, the IgM-to-IgG class switch, and the higher/faster secondary peak.

High-yield exam pointers

- Pregnancy is **immunologically active, not immunosuppressed** — write this line explicitly.
- Th1 → Th2 shift is the single most testable line for "immunological changes in pregnancy."
- "No-HLA" rule: villous trophoblast = no HLA at all; extravillous trophoblast = HLA-G only (never classical HLA-A/B or class II).
- uNK cells = ~70% of first-trimester decidual leukocytes, non-cytotoxic, progesterone-dependent.
- Primary response = IgM first, slow, low titre; secondary response = IgG-dominant, fast, high titre, driven by memory cells — link to repeat anti-D dosing after re-exposure.
- Physiological leukocytosis in labour can reach ≥25,000/μL — do not over-call sepsis on white count alone.
- CRP, ESR, and complement (C3/C4) are all physiologically raised in normal pregnancy and are unreliable in isolation for diagnosing infection.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Some recent immunology literature further subdivides the T-helper response into Th1/Th2/Th17/regulatory-T-cell subsets, but the Th1-to-Th2 shift remains the exam-standard explanatory framework used by DC Dutta's Obstetrics and Williams Obstetrics.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e (Chapter 39, "Immunology in Obstetrics"); Berek & Novak's Gynecology 16e.

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Describe the anatomical features and clinical significance of lower uterine segment

Asked in: Paper I 16-Dec-2023 — RGUHS MS Obstetrics & Gynaecology

Definition — The lower uterine segment (LUS) is the thin, distensible, relatively passive part of the parturient uterus that develops from the isthmus of the non-pregnant uterus and is fully formed only during labour. It lies between the actively contracting-and-retracting upper (active) segment above and the cervix below, and together with the fully dilated cervix it forms the smooth continuation of the birth canal. Because of its thin wall, poor retractility, and loose anterior peritoneal attachment, it is the anatomical basis for placenta previa, lower-segment caesarean section (LSCS), and obstetric rupture.

Formation and boundaries

Aspect	Detail
Origin	Develops from the **isthmus** — a narrow (0.5–1 cm) zone between the body and the cervix of the non-pregnant uterus
Boundaries before labour	Above — **anatomical internal os**; below — **histological internal os**
Onset and progression	Isthmus hypertrophies and elongates (up to 3× its length) from the first trimester; from about **12 weeks** it progressively unfolds from above downward and is incorporated into the uterine cavity
Maximal formation	Occurs during the **first stage of labour**, especially after rupture of the membranes; becomes a fully formed, cylindrical tube by the **second stage**
Boundaries in labour	Above — the **physiological retraction ring** (junction between the thick, retracted upper/active segment and the thin lower segment); below — the fibromuscular junction of cervix and uterus
Length when fully formed	**7.5–10 cm**
Postpartum fate	Becomes thin, flabby and collapsed immediately after delivery; reverts over a few weeks to the size and shape of the isthmus

Structural features distinguishing it from the upper segment

Feature	Lower uterine segment	Upper (active) segment
Muscle arrangement	Thin wall; largely lacks the thick, criss-crossing oblique "figure-of-8" fibres	Three layers — outer longitudinal, inner circular, and a thick interlacing intermediate layer that occludes the vessels running through it on contraction (the "**living ligature**")
Behaviour in labour	Passive — undergoes stretching, thinning and dilatation ("receptive relaxation")	Active — contracts and retracts, becomes progressively thicker
Retractile power	Poor	Strong
Haemostatic capacity	Poor — cannot occlude vessels by retraction	Excellent — living-ligature action secures haemostasis after placental separation
Peritoneal attachment	Loose anteriorly (vesico-uterine pouch), permitting the bladder to be reflected off during surgery; firmly adherent posteriorly	Firmly adherent to the myometrium throughout
Wall thickness	≤1.5 cm at term, becomes paper-thin as labour progresses	Thickens progressively through labour

Clinical significance

Clinical setting	Significance of the lower segment
Formation of the birth canal	Receptive relaxation of the lower segment, together with full cervical dilatation, creates the continuous, smooth-walled canal through which the fetus is expelled
Placenta previa	Implantation of the placenta over or adjacent to the internal os = **placenta previa**; poor decidual reaction here also predisposes to **morbidly adherent placenta** (accreta spectrum)
Antepartum/postpartum haemorrhage	Poor retractile property means a placenta implanted here cannot achieve haemostasis by living-ligature action, so bleeding from this site (previa, or a lower-segment placental bed after delivery) is difficult to control

Clinical setting	Significance of the lower segment
Lower-segment caesarean section (LSCS)	The thin, less vascular lower segment is deliberately used for the uterine incision: thin margins appose well, blood loss is less, reperitonisation is complete, and post-operative morbidity/mortality is lower than with a classical incision; the resulting scar is stronger, with a future rupture risk of only **0.5–1.5%** versus **4–9%** for a classical scar
Obstructed labour	Poor retractility means unrelieved obstruction causes progressive thinning of the lower segment; when extreme, this produces the **pathological retraction ring of Bandl**, a warning sign of impending lower-segment/uterine rupture
VBAC / scar assessment	Ultrasound assessment of lower-segment scar thickness informs counselling for **vaginal birth after caesarean (VBAC)** — a thickness of **≥4 mm is reassuring (RCOG)**, whereas a full myometrial thickness **<2.3 mm** carries a high (about **9%**) risk of scar rupture

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 13.7A–C — Sequence of development of the active (upper) and passive (lower) segments of the uterus: A. uterus at term; B. early labour; C. late second stage, showing the physiological retraction ring at the junction (DC Dutta's Obstetrics 9e, p.142)*

High-yield exam pointers

- Origin: **isthmus** — bounded above by the anatomical internal os, below by the histological internal os (non-pregnant/early pregnancy).
- In labour, bounded above by the **physiological retraction ring**; fully formed length **7.5–10 cm**.
- Muscle mnemonic: upper segment = 3 layers with the criss-cross "**living ligature**"; lower segment lacks this → poor retraction → poor haemostasis.
- Three linked clinical facts to write together: **placenta previa** (implantation site) → **PPH/APH** (poor retraction) → **LSCS** (deliberately incises this same segment).
- Rupture-risk numbers to quote: LSCS scar rupture **0.5–1.5%** vs classical **4–9%**; scar thickness **≥4 mm** reassuring (RCOG), **<2.3 mm** → ~9% rupture risk.
- Extreme thinning in obstructed labour → pathological **Bandl's ring**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

The scar-thickness cut-offs quoted are the current RCOG-referenced sonographic thresholds used for VBAC counselling in DC Dutta's Obstetrics 9e; no single value is universally validated, so these are used as risk-stratifying guides, not absolute cut-offs.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e (Table 13.1 — Lower Segment of Uterus and its Clinical Significance; Table 37.4 — Merits and Demerits of Lower Segment Operation over Classical; scar-thickness/VBAC section); Williams Obstetrics 26e (physiological retraction ring, Bandl's ring, hysterotomy/lower-segment incision technique).

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Describe the anatomy of internal iliac artery and its clinical implications

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — The internal iliac artery (formerly the *hypogastric artery*) is the principal artery of the pelvis, arising as the smaller terminal branch of the common iliac artery. It supplies the pelvic viscera, perineum, gluteal region and part of the thigh, and its surgical control is central to managing intractable pelvic and obstetric haemorrhage.

Origin, course and termination

Feature	Description
Origin	Bifurcation of the **common iliac artery**, anterior to the sacroiliac joint, at the level of the **lumbosacral (L5–S1) intervertebral disc**/pelvic brim
Side accompanied by	Internal iliac **vein**, lying **posterior and medial** to the artery (injury here causes torrential, hard-to-control venous bleeding)
Length	About **4 cm** in the adult
Course	Descends into the true pelvis along the posterolateral pelvic wall, medial to the external iliac vessels and psoas major, anterior to the sacroiliac joint
Termination	Divides at the upper margin of the **greater sciatic foramen** into an **anterior division** and a **posterior division** (division pattern is variable)

Feature	Description
Fetal remnant	Its anterior continuation, the umbilical artery, becomes the **superior vesical artery** postnatally; the obliterated distal part forms the **medial umbilical ligament**

Relations

Relation	Structure
Anterior	Ureter, which crosses **the bifurcation of the common iliac artery into external and internal iliac arteries** — the classical surgical landmark used to identify and protect the ureter during pelvic surgery
Posterior	Internal iliac vein, lumbosacral trunk, sacroiliac joint
Medial	Peritoneum of the pelvic cavity, ovary (in the ovarian fossa)
Lateral	Obturator nerve, external iliac vein, psoas major
Ureter re-crossed	At the level of the **internal cervical os**, ~1.5–2 cm lateral to the cervix, where the **uterine artery crosses anterior to the ureter** ("water under the bridge") — the second classical point of surgical risk to the ureter

Branches

Division	Branches	Chief supply
Anterior division (visceral, mainly)	Superior vesical (umbilical artery continuation), inferior vesical, **uterine**, vaginal, middle rectal, **obturator**, internal pudendal, inferior gluteal	Bladder, uterus, vagina, rectum, perineum, medial thigh/gluteal region
Posterior division (parietal)	Iliolumbar, lateral sacral, **superior gluteal**	Posterior pelvic wall, buttock, back of thigh

- The **uterine artery** typically arises from the anterior division (sometimes as a common trunk with the superior vesical artery), runs medially in the base of the broad ligament, crosses over the ureter, ascends along the lateral uterine border giving arcuate → radial → spiral arteries, and anastomoses with the ovarian artery at the cornu — this **dual (uterine + ovarian) supply** is the anatomical basis for uterine viability even after uterine or unilateral internal iliac artery ligation.
- The posterior division's branches (superior gluteal, lateral sacral, iliolumbar) supply the buttock and lumbosacral region — ligation performed **proximal** to (i.e., involving) the posterior division

risks gluteal/buttock ischaemia and sciatic neuropathy, so surgical ligation is always placed **distal to the posterior division's origin**.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
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> ☐ *Fig 5.9 — The blood supply to the pelvis. A: The sagittal view of the pelvis without the viscera. (Berek & Novak 16e, p.174)*
>
> Label: common iliac bifurcation, internal iliac artery, its anterior and posterior divisions with their branches (uterine, obturator, superior vesical, internal pudendal, inferior gluteal anteriorly; iliolumbar, lateral sacral, superior gluteal posteriorly), the ureter crossing the bifurcation, and the internal iliac vein lying posteromedial to the artery.

Clinical implications

Clinical application	Anatomical basis / key points
Internal iliac (hypogastric) artery ligation for intractable pelvic/postpartum haemorrhage (uncontrolled PPH, broad ligament haematoma, pelvic trauma, after failed conservative measures)	Ligation is performed **unilaterally or bilaterally**, ~2.5–3 cm **distal to the origin** of the internal iliac artery and **distal to its posterior division**, to spare the gluteal circulation. Mechanism: converts the pulsatile arterial pressure distal to the ligature into a **venous-like, low-pressure flow**, reducing pulse pressure by up to **85%** (Burchell, 1968), which favours clot stabilisation rather than reducing total pelvic blood flow (extensive collateral anastomoses maintain perfusion, so pelvic tissue necrosis does not occur)
Step-wise obstetric devascularization for atonic/traumatic PPH	Sequence: (1) uterine artery ligation (O'Leary suture), (2) bilateral uterine artery ligation, (3) low uterine/cervical branch ligation, (4) utero-ovarian anastomosis ligation, (5) internal iliac artery ligation, (6) hysterectomy as last resort — reflects the anatomical order of collateral supply
Surgical hazard during ligation	The internal iliac **vein** lies immediately **posterior and lateral** to the artery — inadvertent injury during dissection/clamp passage causes severe, difficult-to-control venous haemorrhage; the **ureter crossing the bifurcation** must be identified and retracted before clamp placement
Fertility after bilateral ligation	Because of rich collateral circulation (uterine–ovarian anastomosis, contralateral vessels), bilateral internal iliac ligation **does not compromise subsequent fertility or menstrual function**

Clinical application	Anatomical basis / key points
Selective angiographic embolization (interventional radiology)	Alternative/adjunct to surgical ligation for PPH — catheterizes branches (usually uterine or anterior division) and occludes with gel-foam/coils; success rate **>90%**, uterus- and fertility-preserving, avoids hysterectomy
Prophylactic balloon occlusion in placenta accreta spectrum	Balloon catheters placed in the internal iliac (or uterine/aortic) arteries preoperatively to reduce blood loss during caesarean hysterectomy; however, a randomized trial (Yu et al., 2020) found **no reduction in postpartum haemorrhage** with prophylactic internal iliac artery balloon occlusion, and complications (buttock/lower-limb ischaemia) are reported — current society guidance does not universally recommend it
Radical (Wertheim's) hysterectomy and pelvic lymphadenectomy	Visceral branches of the anterior division (uterine, vaginal, vesical) are ligated during parametrial and paracolpial dissection; the ureteric tunnel (**tunnel of Wertheim**) where the ureter passes beneath the uterine artery near the anterior vaginal fornix is a key site of ureteric injury during radical surgery; **internal iliac (hypogastric) lymph nodes** are part of the pelvic node dissection template for cervical and endometrial cancer staging
Ureteric injury prevention landmark	Surgeons trace the ureter cephalad along the common iliac artery to its **bifurcation into external and internal iliac arteries** to positively identify it before pelvic sidewall dissection, hysterectomy, or endometriosis surgery
Ovarian fossa / lateral pelvic wall surgery	The internal iliac artery, ureter and obturator neurovascular bundle form the floor of the **ovarian fossa** — relevant to safe adnexal and pelvic sidewall surgery, and to the risk of ureteric/vascular injury during oophorectomy or endometriosis excision in a distorted pelvis

High-yield exam pointers

- Origin: bifurcation of common iliac artery at the **lumbosacral (L5–S1) disc level**; terminates at the greater sciatic foramen into **anterior (visceral) + posterior (parietal)** divisions.
- Recall the anterior division's 7 branches as "**3 visceral pairs + obturator + 2 gluteal-perineal**": superior vesical, inferior vesical, middle rectal, uterine, vaginal, obturator, internal pudendal, inferior gluteal. Posterior division has only 3: **iliolumbar, lateral sacral, superior gluteal**.

- Two classic surgical points where the **ureter is at risk**: (1) at the **common iliac bifurcation** (crossed anteriorly), (2) at the **internal os**, 1.5–2 cm lateral to the cervix, where the **uterine artery crosses over the ureter** ("water under the bridge").
- Ligation site: **distal to the posterior division**, ~2.5 cm from its origin — reduces distal pulse pressure by **85%** (Burchell, 1968).
- Internal iliac **vein lies posterior/lateral** to the artery — the chief hazard during ligation.
- Angiographic embolization success rate **>90%**; bilateral ligation preserves fertility.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> The randomized-trial evidence on prophylactic internal iliac artery balloon occlusion in placenta accreta spectrum is recent and still debated — cite it as evolving practice rather than a fixed guideline recommendation.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e.

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Describe the anatomy of pelvic ureter. What are the sites and likely conditions in which ureter can be injured during gynecologic surgeries

Asked in: Paper I Jun 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — The ureter is a paired, entirely retroperitoneal muscular tube, about 25–30 cm long, carrying urine from the renal pelvis to the bladder; it is conventionally divided into an abdominal and a pelvic part of roughly equal length. The **pelvic ureter** extends from where it crosses the pelvic brim (over the common iliac vessel bifurcation) to its oblique termination in the bladder trigone, measuring about 12–15 cm, and its intimate relationship to the ovarian vessels, uterine artery, cardinal ligament and vaginal fornix makes it the structure most at risk during gynaecologic surgery.

Course and relations of the pelvic ureter

Level	Relations
Pelvic brim	Crosses in front of the bifurcation of the common iliac artery, just medial to the ovarian vessels, over the sacroiliac joint (behind the root of the small-bowel mesentery on the right, behind the apex of the mesosigmoid on the left)

Level	Relations
Lateral pelvic wall	Descends adherent to the peritoneum of the medial leaf of the broad ligament, anterior to the internal iliac artery; forms the **posterior boundary of the ovarian fossa**
Ischial spine level	Reaches the pelvic floor, then turns forwards and medially at the base of the broad ligament
Base of broad ligament / cardinal ligament	Crossed **anteriorly, from above, by the uterine artery** — the classical "**water flows under the bridge**" relationship — about 1–2 cm lateral to the supravaginal cervix; here it enters the **ureteric tunnel (tunnel of Wertheim)** within the cardinal ligament
Anterior vaginal fornix	Runs a short distance medial to and just above the lateral fornix
Intramural (intravesical) part	Pierces the bladder wall obliquely for about 1.5–2 cm at the lateral angle of the trigone; the oblique course acts as a valve preventing vesico-ureteric reflux

Points of relative narrowing (surgically and clinically important — sites of stone impaction and of surgical vulnerability): (1) at the pelvic brim, (2) where crossed by the uterine artery, (3) in the intravesical part.

Structure (outside inwards): fibrous sheath derived from the visceral (endopelvic) fascia → muscularis of outer and inner longitudinal smooth muscle with an intermediate circular layer → mucosa of transitional epithelium.

Blood supply: segmental, with contributions from the renal, gonadal (ovarian), common iliac and internal iliac arteries (uterine, vesical, vaginal, middle rectal branches); these anastomose in a fine **longitudinal plexus running within the periureteric adventitial sheath**. This is why the sheath must never be stripped or "skeletonised" during dissection — doing so devascularises a segment and causes delayed ischaemic necrosis, stricture or fistula even without a direct cut.

Lymphatics: lower pelvic ureter drains to external and internal iliac nodes; the upper/abdominal ureter to lumbar (para-aortic) nodes.

Nerve supply: sympathetic from the hypogastric and pelvic plexuses, parasympathetic from the sacral (pelvic splanchnic) plexus; peristalsis itself is myogenic.

Sites of ureteric injury during gynaecologic surgery

Anatomical site	Operative step most at risk	Usual mechanism
Infundibulopelvic ligament at the pelvic brim, where the ureter runs parallel and medial to the ovarian vessels and forms the posterior boundary of the ovarian fossa	Clamping/ligation of the ovarian vessels during salpingo-oophorectomy, especially for an adnexal mass	Ligation, transection, thermal spread
Lateral pelvic wall below the ischial spine, where the ureter lies just lateral to the peritoneum overlying the uterosacral ligament	Division of the uterosacral ligaments during hysterectomy; uterosacral-ligament vault suspension; presacral neurectomy	Ligature incorporation, kinking
Base of the broad/cardinal ligament, ~1–2 cm lateral to the cervix, where the uterine artery crosses over the ureter	Clamping/ligation of the uterine vessel pedicle during abdominal or radical hysterectomy — particularly **re-clamping a slipped pedicle**	Crush injury, ligature, transection
Ureteric tunnel (tunnel of Wertheim) in the cardinal ligament, over the anterior vaginal fornix, where the ureter turns medially towards the bladder	Vaginal hysterectomy (clamping the cardinal/uterosacral pedicle and vault angles), radical (Wertheim's) hysterectomy, colporrhaphy sutures	Crush/kinking, suture inclusion
Intramural (intravesical) part traversing the bladder wall	Anterior colporrhaphy, Burch colposuspension, retropubic mid-urethral sling, apical/vault suspension sutures	Suture entrapment, kinking
Pelvic peritonisation — ureter adherent to the posterior leaf of peritoneum	Closing the peritoneum at the end of hysterectomy	Inadvertent inclusion in a running suture

Conditions and operations that carry a high risk of ureteric injury

Predisposing condition / procedure	Why the ureter is at risk
Cervical or broad-ligament fibroid	Distorts and displaces the normal ureteric course, often medially or into the tumour capsule
Pelvic endometriosis (especially of the uterosacral ligaments/ovarian fossa)	Dense fibrosis and adhesions obliterate normal surgical planes, tethering the ureter
Ovarian/adnexal malignancy, tubo-ovarian mass, broad-ligament tumour	Obliterated pararectal/paravesical spaces; direct tumour infiltration or gross distortion

Predisposing condition / procedure	Why the ureter is at risk
Pelvic inflammatory disease, chronic pelvic hematoma, dense adhesions (prior surgery/ovarian remnant excision)	Adhesions obscure normal anatomy, promoting blind dissection
Re-clamping a slipped uterine-artery pedicle	A second, often hurried, blind clamp placed without direct visualisation of the ureter
Radical (Wertheim's) hysterectomy / pelvic lymphadenectomy	Extensive parametrial and paracervical dissection close to the ureteric tunnel
Vaginal hysterectomy	Rare, but reported with marked uterine descent, cervical elongation, or a narrow vaginal access
Laparoscopic-assisted vaginal hysterectomy / total laparoscopic or robotic hysterectomy	Thermal spread from monopolar/bipolar energy or laser used near the infundibulopelvic ligament or uterine pedicle; stapler misfire
Colposuspension (Burch), retropubic mid-urethral sling, uterosacral vault-suspension procedures	Paravaginal/vault sutures placed close to the intramural ureter or the ureter at the ischial-spine level
Congenital duplex ureter	An ectopic or aberrant limb is more vulnerable at any of the above sites

Overall incidence of ureteric injury is about 0.5–1% of pelvic operations; roughly 75% of all iatrogenic ureteric injuries follow gynaecologic surgery, and abdominal/laparoscopic hysterectomy is now the single commonest cause.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
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> ☐ *Fig 20 — The broad ligament from the side showing the relation of the ureter to the uterine artery, and how the latter supplies branches to the corpus, cervix and vagina (Jeffcoate's Principles of Gynaecology 9e, p.23)*

High-yield exam pointers

- Pelvic ureter = **12–15 cm**; total ureter **25–30 cm**, entirely retroperitoneal.
- **"Water flows under the bridge"** — the uterine artery crosses **above** the ureter, about **1–2 cm lateral to the cervix**.
- **Three points of narrowing**: pelvic brim, uterine-artery crossing, intravesical part.
- **Blood supply travels longitudinally within the adventitial sheath** — never strip/skeletonise the ureter, or ischaemic necrosis and fistula follow even without a direct cut.
- Five classic injury sites to reproduce verbatim: **infundibulopelvic ligament → pelvic sidewall near the uterosacral ligament → uterine-artery crossing in the cardinal ligament → ureteric tunnel of Wertheim over the anterior fornix → intramural/intravesical part**.
- **75% of all ureteric injuries follow gynaecologic surgery**; hysterectomy (increasingly laparoscopic, thermal mechanism) is the leading operation.

- High-risk pathology to name: fibroid (cervical/broad-ligament), endometriosis, malignancy/tubo-ovarian mass, and a re-clamped slipped uterine pedicle.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Reported measurements for the pelvic ureter's length (12–15 cm) and its distance from the cervix (1–1.5 cm in DC Dutta and Jeffcoate vs up to 2 cm in Berek & Novak) vary slightly between textbook editions; the figures above reflect the range quoted across current standard texts and are all acceptable in an exam answer.

> **SOURCE & COVERAGE**
> Jeffcoate's Principles of Gynaecology 9e; DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Te Linde's Operative Gynecology 13e.

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Describe the course and anatomy of pelvic ureter. Discuss the clinical significance of pelvic ureter obstetrics and Gynaecology

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — The ureter is a muscular, retroperitoneal tube conveying urine from the renal pelvis to the bladder; total length is about 25 cm, divided into abdominal and pelvic parts. The **pelvic ureter** extends from where it crosses the pelvic brim (at the common iliac bifurcation) to its oblique termination at the bladder trigone, measuring about 13 cm with a lumen diameter of 5 mm. Its intimate relation to the uterine artery, broad ligament, and cervix makes it the single most important structure to identify safely in pelvic surgery.

Course and key relations of the pelvic ureter

- **Entry at the pelvic brim** — crosses in front of the bifurcation of the common iliac artery, over the sacroiliac joint; on the right side it lies behind the root of the small-bowel mesentery, on the left behind the apex of the mesosigmoid. The **ovarian (gonadal) vessels cross over the ureter** here and lie in close lateral proximity as it enters the pelvis.
- **Along the pelvic side wall** — descends adherent to the peritoneum of the lateral pelvic wall, anterior to the internal iliac artery, forming the **posterior boundary of the ovarian fossa**; here it runs within the broad ligament just lateral to the uterosacral ligament, separating the uterosacral ligament from the mesosalpinx, mesovarium, and ovarian fossa.
- **At the level of the ischial spine** — turns forward and medially onto the pelvic floor and base of the broad ligament, where it is **crossed anteriorly/superiorly by the uterine artery** — the classic

"**water under the bridge**" relationship (ureter = water, uterine artery = bridge). This divides the parametrium into a supra-ureteric part around the uterine vessels and an infra-ureteric paracervix around the vaginal vessels continuing into the uterosacral ligament. At this point the ureter lies only **1.5–2 cm (up to 2–3 cm) lateral to the supravaginal cervix**.

- **Through the "ureteric tunnel"** in the cardinal ligament, close to the cervix, then **crosses the anterior fornix of the vagina** for a short distance.
- **Termination** — courses obliquely through the bladder wall for about 1.5–2 cm before opening at the lateral angle of the trigone.

Three sites of natural constriction (clinically relevant for calculus impaction and ureteroscopy): (i) at the pelvic brim, (ii) where crossed by the uterine artery, (iii) the intramural/intravesical segment.

Structure, blood and nerve supply

Feature	Detail
Mucosa	Transitional epithelium
Muscularis	Three layers — inner and outer longitudinal, middle circular
Adventitia	Fibrous sheath adherent to overlying peritoneum; carries a longitudinal anastomotic vascular network
Blood supply	**Segmental**, from vessels it lies medial to as it passes them — renal, gonadal (ovarian), common iliac, and branches of the anterior division of the internal iliac (uterine, superior vesical, vaginal, middle rectal); supply reaches the ureter from the **lateral** side via the periureteric sheath — hence the ureter must never be skeletonised circumferentially during surgery
Venous drainage	Corresponds to the arteries (uterine, vaginal, vesical, superior gluteal)
Lymphatics	Lower ureter → external/internal iliac nodes; upper ureter → lumbar (para-aortic) nodes
Nerve supply	Sympathetic — hypogastric and pelvic plexus; parasympathetic — sacral (S2–S4) plexus
Intraoperative identification	Pale, glistening white cord; visible peristalsis; can be "flicked" and seen to spring back

Clinical significance in Obstetrics

Situation	Significance
Physiological hydroureter/hydronephrosis of pregnancy	Dilatation above the pelvic brim from mid-pregnancy, more marked on the **right side** — dextrorotated uterus compresses the right ureter, dilated right ovarian vein complex overlies it, and the sigmoid colon cushions the left; progesterone-related smooth-muscle relaxation adds to it. Must be distinguished from true obstruction on imaging
Predisposition to pyelonephritis of pregnancy	Ureteral stasis from the above dilatation promotes ascending infection; commoner on the right
Caesarean section/hysterectomy	Vulnerable during extension of a lower-segment tear into the broad ligament, securing a bleeding angle, or ligating uterine vessels for caesarean hysterectomy, especially with broad-ligament haematoma
Obstetric fistula	Prolonged obstructed labour or instrumental delivery can rarely cause a **ureterovaginal fistula** (far less common than vesicovaginal fistula) — continuous leakage despite normal voiding

Clinical significance in Gynaecology

A. Sites of ureteric injury during gynaecological surgery (abdominal/vaginal/laparoscopic hysterectomy is the commonest cause of iatrogenic ureteric injury)

- At the **infundibulopelvic ligament**, while clamping the ovarian vessels (salpingo-oophorectomy) — ureter crosses just medial/close to these vessels at the pelvic brim.
- At the **side of the cervix/cardinal ligament**, while clamping the uterine vessels and descending cervical artery — the single commonest site, corresponding to the "water under the bridge" relation.
- At the **vaginal angle**, as the ureter traverses the anterior fornix during colpotomy or vault closure.
- During **pelvic peritonisation**, since the ureter runs in the posterior leaf of the peritoneum.
- During **uterosacral ligament vault suspension**, given the ureter's proximity (2–3 cm lateral to the cervix) to the ligament used for the suspending stitch.

B. Risk factors for injury: endometriosis, pelvic inflammatory disease, broad-ligament fibroid/tumour, malignancy, dense adhesions, and re-clamping (more injurious than primary clamping).

C. Conditions in which the ureter itself is clinically affected

Condition	Mechanism / significance
Broad-ligament fibroid	Displaces ureter (usually down and lateral, occasionally medial); risk of hydroureter/hydronephrosis; pre-operative intravenous urography advised; enucleation before hysterectomy minimises injury
Pelvic/deep infiltrating endometriosis	Extrinsic compression (commoner than intrinsic mural disease) causes silent hydroureteronephrosis, sometimes progressing to renal impairment before symptoms appear; intravenous urography/CT urogram indicated; may need segmental resection with reimplantation
Cervical carcinoma	Parametrial spread surrounds and compresses the ureter → hydroureteronephrosis, pyelonephritis, uraemia; ureteric obstruction/non-functioning kidney defines **FIGO 2018 Stage IIIB**, independent of tumour size
Radical hysterectomy	Direct transection is uncommon, but stripping the ureter off the peritoneum during parametrial/nodal dissection can devitalise it, causing delayed sloughing and fistula
Intracavitary radiotherapy	**Point A** (2 cm cephalad and 2 cm lateral to the external os) is defined at the uterine artery–ureter crossing; ureteric tolerance is up to ~7000 cGy, guiding dose planning

D. Diagnosis and management of ureteric injury

- Intraoperative: direct visualisation, cystoscopy after IV indigo carmine/methylene blue (efflux from both orifices confirms patency).
- Postoperative: flank pain, fever, oliguria/anuria (if bilateral), urinoma, or a delayed **ureterovaginal fistula** (continuous leakage despite normal voiding) — differentiated from vesicovaginal fistula by the tampon dye test (methylene blue stains it in VVF; oral pyridium/IV indigo carmine in ureterovaginal fistula). CT urogram confirms site/degree.
- Management: double-J **stenting** for partial injury; **ureteroureterostomy** for mid-ureteric transection; **ureteroneocystostomy** (psoas hitch/Boari flap) for lower-third injury; **transureteroureterostomy** for extensive loss.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 2.20 — The broad ligament from the side showing the relation of the ureter to the uterine artery (Jeffcoate's Principles of Gynaecology 9e, p.23)*

High-yield exam pointers

- Mnemonic "**water under the bridge**" — the single most-tested relation (uterine artery over, ureter under, at the ischial-spine level).
- Write the numbers: **25 cm** total ureter, **13 cm** pelvic ureter, **5 mm** diameter, **1.5–2 cm** lateral to cervix.
- Commonest injury site in hysterectomy = clamping the uterine vessels at the cervix; laparoscopic hysterectomy = highest-risk procedure overall.
- FIGO 2018 **Stage IIIB** cervical cancer is defined partly by ureteric obstruction/non-functioning kidney.
- Tampon dye test: methylene blue → VVF; oral pyridium/IV indigo carmine → ureterovaginal fistula.
- Never skeletonise the ureter circumferentially — its blood supply enters from the lateral (medial-approach) side only.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Cross-checked FIGO 2018 cervical-cancer staging (Berek & Novak 16e) against DC Dutta's Gynaecology 7e, which broadly agrees on ureteric obstruction defining Stage III/IIIB disease.

SOURCE & COVERAGE

Williams Obstetrics 26e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e; DC Dutta's Textbook of Obstetrics 9e; Te Linde's Operative Gynecology 13e; Jeffcoate's Principles of Gynaecology 9e; FIGO 2018 cervical cancer staging.

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Describe the course of ureter in pelvis. How to prevent ureteric injuries during surgery?

Asked in: Paper I 24-Sep-2025 — RGUHS MS Obstetrics & Gynaecology

Definition — The ureter is a muscular, peristaltic tube (~25–30 cm total) carrying urine from the renal pelvis to the bladder. Its **pelvic part** begins as it crosses the pelvic brim and ends at the ureteric orifice in the bladder trigone, measuring about **13 cm in length and 5 mm in diameter**. Sound knowledge of

its pelvic course is essential to gynaecological and obstetric surgery, since about 75% of all iatrogenic ureteric injuries occur during gynaecological procedures, most often hysterectomy.

Course of the pelvic ureter

Segment	Course and relations
1. Pelvic brim (entry)	Crosses the bifurcation of the common iliac artery, entering the pelvis within about 1 cm of this bifurcation; lies just **medial to the ovarian vessels**, which cross it here — this is the first surgically important relation (danger during clamping the infundibulopelvic/IP ligament).
2. Descent along the pelvic side wall	Runs downward adherent to the peritoneum of the **medial leaf of the broad ligament/pelvic side wall**, anterior to the internal iliac artery; forms the **posterior boundary of the ovarian fossa** (bounded superiorly by external iliac vein, laterally by obturator vessels/nerve). Because it stays attached to the peritoneum rather than the vessels, it is carried medially when the peritoneal space is opened.
3. Through the parametrium/cardinal ligament	At about the level of the ischial spine/internal os, the ureter passes **beneath the uterine artery** — the classic "**water flows under the bridge**" relationship — then runs through the "**ureteric tunnel**" in the cardinal ligament, lying **1–2 cm lateral to the supravaginal cervix**. This divides the parametrium into a supra-ureteric part (around the uterine vessels) and an infra-ureteric part (paracervix, continuous with the uterosacral ligament).
4. Terminal/vesical part	Turns medially onto the **anterior vaginal wall/anterior fornix**, running close to the upper third of the vagina, then enters the bladder wall obliquely for about 1.5–2 cm before opening at the trigone.

- **Three physiological constrictions:** at the pelvic brim, where crossed by the uterine artery, and the intramural (intravesical) part — all clinically relevant sites for calculus impaction and surgical narrowing.
- **Blood supply is segmental** and reaches the ureter from *lateral* sources as it passes the common iliac, internal iliac, uterine and vesical vessels, forming a longitudinal anastomotic network on its adventitial sheath — hence over-stripping this sheath during dissection devascularises the ureter.
- **Recognition at surgery:** pale glistening tubular structure showing visible peristalsis, with fine longitudinal vessels on its surface.

Common sites & mechanisms of ureteric injury (why prevention targets these points)

Surgical step	Site/mechanism of injury
Clamping/ligating the **infundibulopelvic ligament**	Upper pelvic ureter, as it lies close to the ovarian vessels at the pelvic brim
Clamping the **cardinal ligament** with the descending cervical/uterine artery	Commonest site — ureter in the ureteric tunnel, 1–2 cm lateral to the cervix; risk rises with **reclamping** for bleeding
Securing the **vaginal angle** during colpotomy	Distal ureter on the anterior vaginal wall/fornix
Posterior peritonisation of the pelvic floor	Ureter lies in the posterior leaf of peritoneum and may be caught in the suture
Laparoscopic energy devices (monopolar/bipolar/ultrasonic)	Thermal injury anywhere along the course, often with delayed presentation
Radical hysterectomy	Direct clamp injury uncommon; over-stripping the ureter off the peritoneum devascularises it → sloughing necrosis

Risk is markedly increased by **endometriosis, pelvic inflammatory disease, broad-ligament fibroid, adnexal masses and malignancy**, which distort normal anatomy. Ninety-one percent of injuries occur at the level of the pelvic ureter (only 2% upper, 7% middle third); **laparoscopic hysterectomy carries the highest rate** of ureteric injury and **vaginal hysterectomy the lowest**.

Prevention of ureteric injury during surgery

- **Preoperative risk assessment** — anticipate distorted anatomy in large fibroids, endometriosis, malignancy or previous pelvic surgery; obtain imaging (IV urogram/CT urogram) to define ureteric course when displacement is suspected.
- **Deliberate retroperitoneal identification, not blind dissection** — incise the posterior leaf of the broad ligament lateral to the infundibulopelvic ligament and locate the ureter first at the pelvic brim (within ~1 cm of the common iliac bifurcation), then trace it visually down to the ureteric tunnel, confirming identity by its peristalsis rather than assuming its position.
- **Gentle, targeted mobilisation** — when mobilisation is needed, grasp the peri-ureteric sheath (not the ureter itself), use push-spread dissection at right angles to the ureter over a short segment only, to avoid stripping a long length and devascularising it.
- **Clamp and ligate close to the uterus/cervix**, keeping pedicles medial to the ureter's course; avoid wide lateral bites of the cardinal ligament and avoid blind reclamping in a bleeding field — control haemorrhage by pressure and exposure, then clamp under direct vision.

- **Adequate bladder mobilisation** off the anterior vagina/cervix before colpotomy, so the distal ureter (which lies directly on the anterior vaginal wall) is carried safely away from the vaginal angle sutures.
- **Caution with energy sources** near the ureteric tunnel and pelvic side wall — minimise thermal spread, avoid unipolar coagulation close to the ureter, and keep it in view before applying any energy device.
- **Careful posterior peritonisation** — visualise the ureter before placing the peritoneal closure suture.
- **Selective prophylactic ureteric stent placement** in anticipated difficult cases (large broad-ligament fibroid, severe endometriosis, malignancy) — aids intraoperative palpation/identification, though it does not eliminate the risk of thermal injury.
- **Intraoperative cystoscopy with an intravenous dye** (indigo carmine or methylene blue) to confirm bilateral ureteric efflux/patency at the end of the procedure — contemporary practice increasingly favours this as routine after laparoscopic hysterectomy, since it detects the majority of unsuspected injuries before the patient leaves the operating room.
- **Prompt intraoperative repair** if injury is recognised — immediate repair (stenting, uretero-neocystostomy, or end-to-end anastomosis as appropriate) gives far better outcomes than delayed diagnosis, which classically presents days later with flank pain, fever, leukocytosis, or later a uretero-vaginal fistula.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 37.2 — Abdominal and pelvic portions of the ureter showing relation to aorta, psoas muscle, common iliac vessels and pelvic side wall (Te Linde 13e, p.1942)*

High-yield exam pointers

- Pelvic ureter: **~13 cm long, 5 mm diameter**; 3 constrictions — pelvic brim, uterine artery crossing, intramural part.
- Mnemonic relation: **"water (ureter) flows under the bridge (uterine artery)"** — ureter lies **1–2 cm lateral to the cervix** in the ureteric tunnel of the cardinal ligament.
- **91% of injuries at the pelvic ureter**; laparoscopic hysterectomy = highest risk, vaginal hysterectomy = lowest.
- Four classic clamp sites to recall: **infundibulopelvic ligament, cardinal ligament (with cervical/uterine artery), vaginal angle, posterior peritonisation.**
- Prevention triad for the exam: **identify (retroperitoneal dissection) → clamp/ligate close to the uterus → confirm patency (cystoscopy + IV dye).**
- Risk multipliers to name: endometriosis, broad-ligament fibroid, PID, malignancy/radical hysterectomy, reclamping.

SOURCE & COVERAGE

Te Linde's Operative Gynecology 13e; Williams Obstetrics 26e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e.

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Describe the development of female internal genital organs. Discuss the mullerian anomalies and the clinical significance

Asked in: Paper I Nov 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — The female internal genital organs (fallopian tubes, uterus, cervix and upper vagina) develop from the paired **paramesonephric (Müllerian) ducts**. Müllerian anomalies are congenital malformations arising from defective duct agenesis, unilateral development, failed midline fusion, or failed septal resorption/canalisation. Because the ovaries arise separately from the genital ridge, ovarian function is normal even in severe Müllerian anomalies.

Development of the female internal genital organs

Approx. age	Event
5th week	Paramesonephric (Müllerian) ducts invaginate from coelomic epithelium lateral to the mesonephric (Wolffian) ducts
6th–7th week	Absent testicular **anti-Müllerian hormone (AMH)** (no Sertoli cells) allows the ducts to persist; in the male fetus, Sertoli-cell AMH causes Müllerian regression
7th–10th week	Ducts grow caudally, cross medial to the Wolffian ducts, and meet in the midline; the unfused cranial (upper) segments remain separate as the two **fallopian tubes**, their coelomic ends becoming the abdominal ostia
~10th week	Fusion of the mid and lower vertical segments forms the **uterovaginal canal**, giving the **uterine corpus and cervix**; fusion starts centrally and extends both cranially and caudally, producing the pyriform uterine shape; the cervix differentiates from the corpus by the 10th week
10th week–5th month	The septum between the two fused ducts is progressively resorbed (complete by the 5th month), converting the double canal into a single uterine cavity

Approx. age	Event
From ~8th week	The fused caudal Müllerian tip contacts the urogenital sinus and induces paired **sinovaginal bulbs**, which fuse to form a solid vaginal plate
Up to 20th week	The vaginal plate canalises to form the vaginal lumen — the **upper three-fifths** of the vagina from the Müllerian uterovaginal canal, the **lower two-fifths** from the urogenital sinus; the residual hymeneal membrane (Müllerian tubercle mesoderm + sinus endoderm) persists as the hymen

Classification of Müllerian anomalies

The **American Fertility Society (AFS, 1988)** classification — the system used by Williams Obstetrics and DC Dutta's Gynaecology — groups anomalies by the embryological step that failed: agenesis, unilateral maturation, non-fusion, or non-canalisation.

Class	Anomaly	Sub-types	Approx. relative frequency
I	Segmental Müllerian agenesis/hypoplasia	Vaginal, cervical, uterine (fundal), tubal, combined — e.g. *Mayer-Rokitansky-Küster-Hauser (MRKH)* syndrome	Uncommon
II	Unicornuate uterus	With/without rudimentary horn (communicating, non-communicating, no cavity, no horn)	~10%
III	Uterus didelphys	Two separate hemiuteri, two cervices, single or septate vagina	~8%
IV	Bicornuate uterus	Complete (to internal os, "bicollis") or partial ("unicollis")	~26%
V	Septate uterus	Complete or partial (subseptate) septum	~35% — commonest fusion anomaly needing treatment
VI	Arcuate uterus	Mild concave fundal indentation only	~18% — commonest anomaly in the general population, usually benign

Class	Anomaly	Sub-types	Approx. relative frequency
VII	Diethylstilbestrol (DES)-related	T-shaped cavity, cervical collar/cockscomb cervix, vaginal adenosis	Historical (in-utero DES exposure)

Clinical significance

Domain	Significance
Associated anomalies	Concurrent **renal tract anomaly in ~40%** (commonly unilateral renal agenesis) and **skeletal anomaly in ~12%** — image the urinary tract in every case. *MRKH* may extend to the **MURCS association** (Müllerian aplasia, Renal aplasia, Cervicothoracic Somite dysplasia). *Uterus didelphys* with an obstructed hemivagina and ipsilateral renal agenesis is the **OHVIRA/Herlyn-Werner-Wunderlich syndrome**
Gynaecological	Primary amenorrhoea (Class I agenesis); cryptomenorrhoea and haematometra/haematocolpos with a non-communicating rudimentary horn or obstructed septum; dysmenorrhoea, dyspareunia, menorrhagia; infertility
Obstetric	Recurrent first- and second-trimester miscarriage (highest, up to ~60%, with septate uterus — the septum is poorly vascularised); preterm labour; malpresentation (breech with bicornuate/unicornuate, transverse with arcuate/subseptate); fetal growth restriction; cervical insufficiency; obstructed labour from a non-gravid horn/septum; malposition of the placenta over a septum causing retained placenta and postpartum haemorrhage; increased caesarean delivery rates
Ectopic risk	Pregnancy in a non-communicating rudimentary horn is a **cornual ectopic** that classically ruptures around 16–20 weeks with life-threatening haemorrhage — prophylactic excision of the rudiment (and its tube) is recommended once diagnosed

Domain	Significance
Diagnosis	Two/three-dimensional transvaginal sonography (2-D/3-D TVS), hysterosalpingography (HSG), MRI (best for distinguishing septate from bicornuate uteri by external fundal contour), hysteroscopy and laparoscopy combined to define both internal cavity and external contour
Management	A uterine anomaly per se is **not** an indication for surgery. **Hysteroscopic septal resection** is offered for septate uterus with recurrent pregnancy loss (live-birth success ~80–89%). **Abdominal metroplasty** (Strassman/Jones for excision, Tompkins for incision) is reserved for select bicornuate/didelphys cases with otherwise unexplained loss. Non-communicating rudimentary horns are excised. Cervical cerclage may benefit those with coexisting cervical insufficiency

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 3.4A to D — Schematic representation of the development of the genitourinary system (internal genital organs) (DC Dutta's Gynaecology 7e, p.48)*
- ☐ *Fig 13.7A–G — Classification of uterine (Müllerian) anomalies (Jeffcoate's Principles of Gynaecology 9e, p.235)*

High-yield exam pointers

- Classification = **AFS 1988, Classes I–VII** (agenesis → unicornuate → didelphys → bicornuate → septate → arcuate → DES-related).
- **Arcuate** = commonest overall, mildest, usually asymptomatic; **septate** = commonest anomaly needing surgical treatment and the worst pregnancy-loss risk among fusion defects.
- **Renal anomaly ~40%, skeletal ~12%** — always image the kidneys with any Müllerian anomaly.
- **MRKH** = vaginal/uterine agenesis with 46XX karyotype and normal ovaries/secondary sexual characters; extended form = **MURCS**.
- **OHVIRA (Herlyn-Werner-Wunderlich)** = uterus didelphys + obstructed hemivagina + ipsilateral renal agenesis.
- Rudimentary-horn (cornual) pregnancy ruptures ~16–20 weeks — excise the rudiment prophylactically.
- Hysteroscopic metroplasty success ~80–89% versus lower success and mandatory caesarean delivery after abdominal metroplasty.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Gynaecology 7e and Williams Obstetrics 26e both still teach the original AFS 1988 seven-class system, which remains the exam standard; newer schemes (e.g., ESHRE/ESGE 2013) exist in the literature but are not the RGUHS-expected classification.

SOURCE & COVERAGE

Williams Obstetrics 26e (Chapter 3 — Congenital Genitourinary Abnormalities); DC Dutta's Textbook of Gynaecology 7e (Chapter 4 — Congenital Malformation of Female Genital Organs); Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e (Fig 13.7).

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Describe the development of Mullerian duct

Asked in: Paper I 29-Jul-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — The **Müllerian (paramesonephric) ducts** are a bilateral pair of tubes that arise as an invagination of the coelomic epithelium on the lateral aspect of each mesonephros at 5–6 weeks of intrauterine life. In a normal female fetus — in the absence of **anti-Müllerian hormone (AMH)** and androgen — each duct elongates caudally, crosses the *Wolffian (mesonephric) duct*, and fuses with its fellow in the midline to form the **fallopian tubes, uterus, cervix, and the muscular coat of the upper vagina**; the Wolffian ducts themselves regress. Müllerian duct differentiation is essentially complete by the 12th week, with the residual midline septum resorbing by the 5th month.

Origin and chronology of development

Gestational age (CR length)	Event
5–6 weeks (10 mm)	Ingrowth of coelomic epithelium lateral to the mesonephros forms a groove, then a solid tube that sinks below the surface — the Müllerian duct
Immediately after	Duct grows caudally **alongside the Wolffian duct, which acts as its obligatory migrational guide/template** — if the Wolffian duct fails to form, the Müllerian duct on that side also fails; it crosses the Wolffian duct ventrally, then turns medially towards its fellow. Three segments are laid down: **cranial vertical, middle horizontal, caudal vertical**
7–8 weeks (22 mm)	The two ducts meet in the midline; **fusion of the intermediate horizontal and adjoining vertical parts begins**, forming the body of the uterus

Gestational age (CR length)	Event
9 weeks	Solid, fused caudal tips project into the dorsal wall of the urogenital sinus as the **Müllerian tubercle**
10 weeks	Cervix differentiates from the corpus
12 weeks	Fusion of the vertical parts is complete, creating a single **Y-shaped uterovaginal canal**; Müllerian differentiation is essentially finished
3rd–5th month	Fusion continues to "zip" cranially; as the ducts are drawn medially away from the posterior body wall they drag a fold of peritoneum with them, forming the **broad ligament**
5th month (~20 weeks)	The septum remaining between the two fused ducts is resorbed, leaving a **single uterine cavity**

Hormonal and molecular control

Factor	Role in Müllerian duct development
Wolffian duct	Obligatory physical/migrational template — its presence is a prerequisite for Müllerian duct formation, though it makes no direct structural contribution
***Lim1* (Lhx1) gene**	Selects the coelomic epithelial cells destined to become the Müllerian duct
Wnt4, Wnt7a, Wnt9b	Drive epithelial invagination and initial duct formation
***Pax2* (with *Pax8*)**	Required for craniocaudal duct elongation and its differentiation into uterus and vagina
Retinoic acid receptors	Direct regional patterning of the duct into tube, uterine, cervical and vaginal segments
Anti-Müllerian hormone (AMH)	Secreted by fetal Sertoli cells (induced by *SOX9*) from about the 7th week; causes **ipsilateral Müllerian duct regression by the 8th week** in the male fetus. Gene on chromosome **19p13.3**; receptor **AMHR2** on chromosome **12q13**
Testosterone	Stabilises and promotes the *ipsilateral Wolffian* duct in the male; has no direct effect on the Müllerian duct itself
Absence of AMH (normal female, or absent/dysgenetic gonad)	Permits full, unopposed growth and fusion of the Müllerian duct system

The three segments and their adult derivatives

Segment of the Müllerian duct	Structure it forms
Cranial (unfused) vertical part	Fallopian tube; its open cranial end becomes the **abdominal ostium** (fimbriated end)
Middle horizontal part + adjoining vertical part (fuse in midline)	**Body and fundus of the uterus**
Caudal fused vertical parts	**Cervix**; also give the **muscular coat of the upper (proximal) vagina** — the vaginal mucosa and hymen are urogenital-sinus derivatives, covered separately
Mesenchyme surrounding the fused ducts	**Myometrium and endometrial stroma** (the lining epithelium and glands of endometrium/endocervix arise instead from the coelomic epithelium lining the duct lumen)
Point of fusion of the two ducts with the gubernaculum	Divides the gubernaculum into the **ovarian ligament** (proximal) and **round ligament** (distal)
Peritoneal fold dragged medially during fusion	**Broad ligament**, containing vestigial mesonephric remnants (epoophoron, paroophoron, Gartner's duct) in its mesosalpinx

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 5-2 — The embryonic development of the female genital tract: formation of the uterus and vagina by fusion of the paramesonephric (Müllerian) ducts, "zippering" cranially to drag the broad ligament, with the sinovaginal bulbs forming the inferior vagina (Berek & Novak 16e, p.151)*

High-yield exam pointers

- Numbers to write verbatim: duct appears **5–6 weeks** → fusion begins **7–8 weeks** → cervix differentiates from corpus **10 weeks** → fusion complete, Y-shaped uterovaginal canal **12 weeks** → septum resorbs **5th month (~20 weeks)**.
- "No Wolffian duct, no Müllerian duct" — the mesonephric duct is only a migrational guide, not a structural contributor, but its absence causes ipsilateral Müllerian agenesis (explains the renal–Müllerian anomaly association).
- Three segments, three fates: **cranial → tube; middle+adjoining vertical (fused) → body/fundus; caudal (fused) → cervix** (+ upper vaginal muscle coat).
- AMH is Sertoli-cell derived, gene **19p13.3**, receptor AMHR2 on **12q13**, causes regression by **8 weeks** — its *absence* is why the female duct persists.
- Gene sequence for molecular recall: ***Lim1** *(selection)* → **Wnt4/Wnt7a/Wnt9b** *(invagination)* → **Pax2/Pax8** *(elongation + differentiation)* → *retinoic acid receptors** (regional patterning).

- Fusion of the ducts drags peritoneum to form the **broad ligament**; the point of fusion splits the gubernaculum into **ovarian + round ligaments**.
- Failure of fusion/resorption at any stage is the embryological basis of the congenital uterine anomalies (didelphys, bicornuate, septate, unicornuate) — asked separately.

> **SOURCE & COVERAGE**
> Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e.

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Describe the Endocrinological and physiological changes during normal menstruation

Asked in: Paper I 19-Nov-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Menstruation is the visible manifestation of cyclic, physiologic uterine bleeding caused by shedding of the endometrium, following an invisible interplay of hormones along the hypothalamo-pituitary-ovarian (HPO) axis. A normal cycle lasts 21–35 days (mean 28), menstrual flow lasts 4–5 days, and average blood loss is 20–80 mL (mean ~35 mL), with nearly 70% lost in the first 2 days. Three parallel, hormone-driven cycles — ovarian, endometrial, and cervico-vaginal — run in synchrony under fluctuating estrogen and progesterone.

Hormonal (Endocrinological) Changes — HPO Axis

Gonadotropin-releasing hormone (GnRH) is released in a pulsatile manner from the hypothalamus; both its amplitude and frequency vary through the cycle and drive the reciprocal FSH/LH pattern from the same gonadotroph cells.

Cycle days	Endometrial phase	Ovarian phase	GnRH pulse frequency	FSH	LH	Estrogen/progesterone
1–5	Menstrual	Early follicular	Rapid (~1 pulse/hour)	Rises from the low nadir (loss of prior cycle's negative feedback)	Low	Both low

Cycle days	Endometrial phase	Ovarian phase	GnRH pulse frequency	FSH	LH	Estrogen/progesterone
6–14	Proliferative	Late follicular	~1 pulse/hour	Falls to a base level by day 5, then a brief mid-cycle surge	Rising to a mid-cycle surge	Estrogen rising to a peak
15–28	Secretory	Luteal	Slower (1 pulse/2–3 hours)	Low (suppressed)	Low, tonic (sustains corpus luteum)	Progesterone rising to a mid-luteal peak

Ovarian Cyclical Events

- **Follicular recruitment & selection** — a cohort of antral follicles is FSH-rescued each cycle; by day 5–7 the follicle with the richest estrogenic, FSH-receptor-dense microenvironment becomes the **dominant follicle**, reaching ~20 mm just before ovulation while the rest become atretic.
- **LH surge and ovulation** — sustained estradiol >200 pg/mL for 24–48 hours in the late follicular phase exerts a **positive feedback** on the hypothalamo-pituitary axis, triggering the LH surge (effective surge duration ~24 hours). A concurrent FSH surge (aided by rising 17-α-hydroxyprogesterone) activates the plasminogen–plasmin system that lyses the follicular wall. **Ovulation occurs 10–12 hours after the LH peak, or 32–36 hours after the onset of the LH surge.**

Event before ovulation	Timing
Estradiol rise begins	83 hours before
Onset of LH surge	34–36 hours before
Estradiol peak	24–36 hours before
LH peak	10–12 hours before
Progesterone rise begins	8 hours before

- **Corpus luteum** — the ruptured follicle luteinises through four stages: proliferation → vascularisation → maturation (peak secretory activity by day 7–8 after ovulation; progesterone peaks ~8 days after the LH peak, reaching 10–20 ng/mL mid-luteal versus <1 ng/mL pre-ovulation) → regression (starts day 22–23) if pregnancy does not occur. It secretes predominantly progesterone, plus estrogen, inhibin and relaxin, and has a fixed lifespan of about **12–14 days**; its

withdrawal (loss of tonic LH support) removes the negative feedback on FSH, initiating the next follicular recruitment.

Endometrial (Physiological) Changes

Phase	Cycle day	Thickness	Key histology	Driving hormone
Regeneration	Begins before menses ends, complete by day 2–3	~2 mm	Cuboidal surface epithelium and glands regrow from the basal zone	Rising estrogen
Proliferative	Day 5/6–14	10–12 mm at ovulation	Tubular glands, columnar pseudostratified epithelium, straight spiral vessels, mitotically active stroma	Estrogen
Secretory	Day 15–28	Up to 12 mm	**Subnuclear vacuolation** (the earliest histological sign of ovulation, seen at 36–48 hours), glycogen secretion into gland lumina, corkscrew glands, coiled spiral arterioles, pre-decidual stromal change after day 21	Progesterone acting on an estrogen-primed endometrium
Menstrual	Day 1–5	Functional layer shed	Ischaemic/enzymatic breakdown of the functional zone; basal zone (~1 mm) unaffected and regenerates the next cycle	Estrogen + progesterone withdrawal

Mechanism of Normal Menstrual Bleeding

- **Trigger** — corpus luteum regression (day 22–23) causes a fall in estradiol, progesterone and inhibin.
- **Vascular events** — withdrawal of steroid support causes intense spasm of the spiral arterioles in the basal endometrium, producing stasis and focal tissue anoxia.
- **Enzymatic autodigestion** — the contemporary model (supplementing the classic ischaemia theory): destabilisation of lysosomal membranes releases proteases and matrix

metalloproteinases; leukocyte infiltration (up to 40% of the stroma pre-menstrually) adds further cytokines and enzymes, digesting the extracellular matrix and vessel walls, causing interstitial haemorrhage.

- **Prostaglandins** — synthesised locally from arachidonic acid: **PGF2α** causes myometrial contraction and vasoconstriction (the dominant mediator of normal menstrual physiology and cramping); PGE2 causes contraction with vasodilatation; PGI2 (prostacyclin) causes relaxation, vasodilatation and inhibits platelet aggregation — the balance between them determines flow and pain.
- **Haemostasis** — combined effect of prolonged vasoconstriction, myometrial contraction, and platelet/fibrin plugging of vessel stumps; **plasmin** liquefies intracavitary clot, which is why menstrual blood is usually unclotted.
- **Repair** — rapid re-epithelialisation from residual gland stumps and basal-layer stem cells, largely oestrogen-independent initially, complete by around day 5.

Associated Cyclical (Physiological) Changes

Feature	Follicular phase	Luteal phase
Cervical mucus	Thin, watery, stretchable beyond 10 cm (spinnbarkeit), ferns on drying	Thick, viscid, loses stretchability and ferning
Internal os	Funnel-shaped, patent	Tightly closed
Vaginal cytology	Superficial cornified cells with pyknotic nuclei; clear background	Navicular (intermediate) cells; dirty background (leukocytes, bacilli)

Ovulatory mid-cycle events may produce transient mittelschmerz (unilateral iliac fossa pain) with scant vaginal spotting and mucoid discharge; the premenstrual phase commonly brings irritability, mastalgia, pelvic discomfort, bloating and acne as physiological correlates of the hormone withdrawal described above.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
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> ☐ *Fig 7.5 — Fluctuation of different hormone levels during menstrual cycle (ovulatory) (DC Dutta's Gynaecology 6e, p.90)*

High-yield exam pointers

- Cycle 21–35 days (mean 28); flow 4–5 days; loss 20–80 mL (mean 35 mL), 70% in first 2 days.
- Ovulation = **10–12 h after LH peak / 32–36 h after LH surge onset**; sustained estradiol >200 pg/mL x 24–48 h triggers the surge (positive feedback).
- GnRH pulse frequency: **~1/hour in follicular phase, 1 pulse/2–3 hours in luteal phase**.

- Corpus luteum lifespan **12–14 days**; progesterone peaks ~8 days post-LH peak (10–20 ng/mL); regression begins day 22–23.
- **Subnuclear vacuolation** = earliest (36–48 h) histological marker of ovulation.
- **PGF2α** dominates normal menstrual vasoconstriction/cramping; PGI2 opposes it.
- Menstrual blood does not clot in the cavity because of **plasmin**-mediated fibrinolysis.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older texts (including DC Dutta) describe menstruation chiefly as vasospastic ischaemic necrosis; contemporary evidence (Speroff 9e) shows minimal true endometrial hypoxia and attributes initiation mainly to enzymatic autodigestion of the functional layer, with vasoconstriction remaining central to how bleeding is limited and stopped — both frameworks are given together above as either may be examined.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e (cross-checked for hormone-pattern and mechanism concordance).

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Describe the obesity related complications and management of obese mothers from pre-gravid to post-partum

Asked in: Paper I 12-Nov-2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Obesity is a body mass index (BMI, weight in kg / height^2 in m) ≥30 kg/m^2; overweight is BMI 25.0–29.9 kg/m^2. Obesity is sub-classed as class I (30.0–34.9), class II (35.0–39.9) and class III/"morbid" (≥40.0 kg/m^2), with "supermorbid" obesity at ≥50 kg/m^2 (World Health Organization/National Institutes of Health criteria, endorsed by the American College of Obstetricians and Gynecologists, ACOG, Practice Bulletin 230, 2021). South Asian/Indian women develop metabolic

complications at lower BMI, so the WHO Asia-Pacific consensus lowers the cut-offs to ≥23 kg/m^2 (overweight) and ≥25 kg/m^2 (obese) for this population.

Obesity-related complications (pre-gravid to postpartum)

Phase	Maternal complications	Fetal/neonatal complications
Pre-gravid/early pregnancy	Anovulation, subfertility (often with polycystic ovary syndrome); combined oral contraceptive failure and venous thromboembolism (VTE) risk are higher; 2–3-fold higher miscarriage and recurrent-miscarriage risk; inaccurate early dating on ultrasonography	Neural tube defects (2–3-fold), congenital heart defects, omphalocele — linked to folate status and undiagnosed hyperglycaemia
Antenatal	Gestational diabetes mellitus (odds ratio, OR, ≈4 for BMI ≥30 vs normal BMI); gestational hypertension/pre-eclampsia (OR ≈3–5, rising further above BMI 40); obstructive sleep apnoea; non-alcoholic fatty liver disease; antenatal VTE (OR ≈2.6); degraded ultrasound anomaly/growth detection; postdated pregnancy	Macrosomia/large-for-gestational-age fetus; stillbirth (risk rises linearly with BMI, several-fold higher in extreme obesity); preterm prelabour rupture of membranes and preterm birth
Intrapartum	Slower labour progression, higher failed-induction and Caesarean delivery rates; difficult external fetal monitoring; difficult neuraxial block placement and failed/difficult intubation for general anaesthesia; postpartum haemorrhage (PPH)	Shoulder dystocia and birth injury (brachial plexus palsy); meconium aspiration; umbilical-artery acidaemia
Postpartum/long-term	PPH from uterine atony/overdistension; wound infection and dehiscence (up to 3-fold risk, higher again with diabetes); endometritis; VTE; delayed lactogenesis and lower breastfeeding rates; postnatal depression (risk rises with obesity class); persistent weight retention and metabolic syndrome	Childhood and adult obesity, metabolic syndrome, and cardiometabolic disease in offspring (fetal programming)

Management — preconception to postpartum

Preconception

- Structured weight-loss programme (diet + supervised exercise) before conception; refer for bariatric surgery if BMI ≥40 (or ≥35 with comorbidity); advise a 12–18-month interval after bariatric surgery before conceiving to allow weight stabilisation and correction of micronutrient deficiencies.
- High-dose folic acid 4–5 mg/day from at least 3 months preconception until 12 weeks (obesity is an independent risk factor for neural tube defects, so it is managed as a high-risk-for-NTD group).
- Screen and optimise comorbidities — HbA1c, blood pressure, thyroid function, screen for obstructive sleep apnoea if symptomatic.
- Counsel on reduced efficacy and higher VTE risk of combined oral contraceptives; prefer long-acting reversible contraception until ready to conceive.
- Multidisciplinary preconception clinic (obstetrician, physician, dietitian, and anaesthetist for class III obesity).

Antenatal

- Calculate and document booking BMI; risk-stratify by class and plan the level of antenatal/intrapartum care accordingly.
- Early dating scan; counsel that anomaly-scan sensitivity is reduced with increasing BMI and a repeat/extended view may be needed.
- Target gestational weight gain per the Institute of Medicine (2009)/ACOG-endorsed table: total gain 11–20 lb (≈5–9 kg) at ≈0.5 lb/week in the 2nd and 3rd trimesters for BMI ≥30 kg/m^2 — weight loss in pregnancy is not advised.
- Screen for gestational diabetes early at booking in addition to the standard 24–28-week 75-g oral glucose tolerance test.
- Low-dose aspirin (75–150 mg/day, typically 81 mg per ACOG) from 12 weeks until delivery if obesity coexists with ≥1 other moderate risk factor for pre-eclampsia (nulliparity, maternal age ≥35, family history, prior adverse pregnancy outcome) — ACOG moderate-risk aspirin-prophylaxis criterion.
- Serial growth scans (fundal height is unreliable) for macrosomia/large-for-gestational-age and fetal-growth surveillance.
- Assess VTE risk each trimester; thromboprophylaxis with low-molecular-weight heparin (e.g., enoxaparin, weight-adjusted dosing) if class III obesity coexists with a thrombophilia, prior VTE, or per Royal College of Obstetricians and Gynaecologists (RCOG) Green-top 37a risk-scoring.
- Obstetric anaesthetic assessment antenatally for BMI ≥40 kg/m^2.

- Dietitian referral and lifestyle intervention; avoid routine metformin for weight/outcome improvement — a Cochrane review found no benefit.

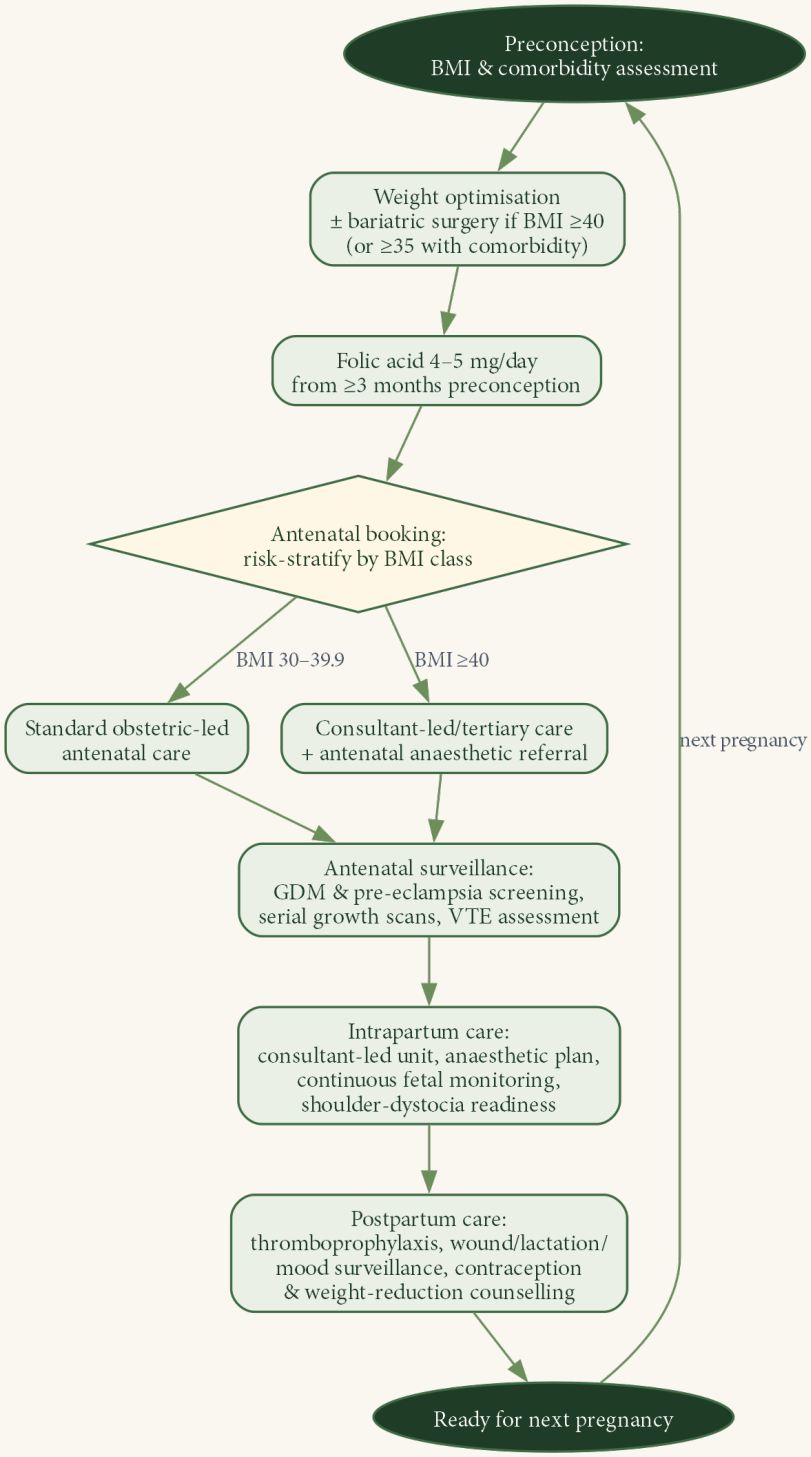
Intrapartum

- Deliver in a consultant-led/tertiary unit for BMI ≥35–40 kg/m^2, with anaesthetic and neonatal input arranged in advance.
- Site neuraxial analgesia early given higher failure/re-attempt rates; combined spinal–epidural is favoured for Caesarean delivery.
- Continuous electronic fetal monitoring; use a fetal scalp electrode if external monitoring is technically difficult.
- Do not induce labour for obesity alone (RCOG) — reserve induction for an obstetric/medical indication; anticipate a higher failed-induction and Caesarean rate.
- Anticipate shoulder dystocia and rehearse the drill.
- For Caesarean delivery: individualise the skin incision (vertical periumbilical incision is preferred by some for very high BMI to access the lower segment); cefazolin prophylaxis 2 g (3 g if weight ≥120 kg per Centers for Disease Control and Prevention; ACOG accepts either dose ≥80 kg) with redosing if surgery is prolonged.
- Mechanical thromboprophylaxis (pneumatic compression) for all, plus pharmacological low-molecular-weight heparin per RCOG/Society for Maternal-Fetal Medicine criteria.
- Active management of the third stage with prophylactic uterotonics given the higher PPH risk.

Postpartum

- Continue thromboprophylaxis with early mobilisation and graduated compression stockings.
- Monitor for wound complications; close subcutaneous tissue if depth ≥2 cm to reduce wound-complication rates.
- Proactive lactation support for delayed lactogenesis and lower breastfeeding rates.
- Screen for postnatal depression, which rises with obesity class.
- Repeat 75-g oral glucose tolerance test 6 weeks postpartum if gestational diabetes mellitus was diagnosed.
- Contraception counselling favouring long-acting reversible methods.
- Structured weight-reduction counselling/referral before any subsequent pregnancy, since obesity begets obesity and worsens outcomes cumulatively across pregnancies.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Care pathway for the obese mother, preconception through postpartum, looping back for subsequent pregnancies.

High-yield exam pointers

- BMI classes: overweight 25–29.9, class I 30–34.9, class II 35–39.9, class III (morbid) ≥40, supermorbid ≥50 kg/m^2; Asian cut-offs ≥23/≥25.
- Institute of Medicine (2009) weight-gain target for obesity: 11–20 lb total, ≈0.5 lb/week in trimesters 2–3 — never advise weight loss in pregnancy.
- Folic acid 4–5 mg/day preconceptionally (obesity = independent neural-tube-defect risk factor).
- Aspirin 75–150 mg/day from 12 weeks if obesity plus another moderate pre-eclampsia risk factor.
- Cefazolin prophylaxis 2 g (3 g if ≥120 kg) for Caesarean delivery in obesity.
- Bariatric surgery: wait 12–18 months before conceiving; monitor vitamin B12, D, folate, and calcium.
- Mnemonic for complications: "GDM–HTN–VTE–CS–PPH–Wound–Depression" tracks the antenatal-to-postpartum cascade.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Guideline aspirin doses differ slightly by source (75 mg per World Health Organization/NICE, 81 mg per ACOG); use whichever your unit's protocol specifies, as the principle (start 12 weeks, continue to delivery) is identical across all of them.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e (Chapter 51, Obesity); Arias' High-Risk Pregnancy & Delivery 5e (Chapter 25, Obesity and Pregnancy); DC Dutta's Textbook of Obstetrics 9e (Obesity in Pregnancy); ACOG Practice Bulletin No. 230 (2021); Society for Maternal-Fetal Medicine (2020); RCOG Green-top Guideline No. 37a; Institute of Medicine (2009) weight-gain guidelines; WHO Asia-Pacific BMI consensus.

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Development of genital tract

Asked in: Paper I Jun 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — The genital tract passes through an early "indifferent stage" (up to the 7th week) that is morphologically identical in both sexes, followed by sex-specific differentiation of the gonad, the paired genital ducts and the external genitalia. Male differentiation is an active, gene-driven process (SRY →

testis-determining factor); female development is the constitutive pathway that proceeds in the absence of testosterone and anti-Müllerian hormone (AMH).

Timeline and hormonal control of differentiation

- **Week 4–5:** Genital (gonadal) ridge forms medial to the mesonephros; primordial germ cells migrate from the yolk sac along the dorsal mesentery of the hindgut (from the level of the 10th thoracic somite) into the ridge.
- **Week 5–6:** Paramesonephric (**Müllerian**) ducts arise as an invagination of coelomic epithelium lateral to the mesonephric (**Wolffian**) ducts.
- **Week 6–7:** Indifferent gonad — both cortex and medulla present, sex not yet determined.
- **Week 7:** *SRY* gene (short arm of the Y chromosome) up-regulates **SOX9**, driving Sertoli cell differentiation and testis formation; Sertoli cells secrete AMH, which causes ipsilateral Müllerian duct regression, and Leydig cells secrete testosterone (→ dihydrotestosterone via 5α-reductase), which sustains the Wolffian duct and virilises the external genitalia.
- **In the absence of SRY:** *WNT4* and *RSPO1* actively repress *SOX9* — ovarian development is not merely passive default but a gene-driven pathway; without AMH the Müllerian ducts persist, and without testosterone the Wolffian ducts regress.
- **Week 12:** External genitalia become clinically distinguishable; genital tubercle, folds and swellings have diverged along male/female lines.
- **Week 20:** Vaginal plate canalises; oogonial numbers peak (~6–7 million) before entering meiotic arrest as primary oocytes.

Derivatives of the bipotential urogenital structures

Embryonic structure	Female derivative	Male derivative
Gonadal cortex	Ovarian (cortical) follicles	Regresses
Gonadal medulla	Regresses (vestige: rete ovarii)	Seminiferous tubules, rete testis
Paramesonephric (Müllerian) duct — unfused cranial part	Fallopian tube, abdominal ostium	Appendix testis (vestige)
Paramesonephric duct — fused caudal part	Uterus, cervix, muscular coat of upper vagina	Regresses (prostatic utricle, vestigial)
Mesonephric (Wolffian) duct/tubules	Epoophoron, paroophoron, Gartner's duct (vestigial)	Epididymis, vas deferens, seminal vesicle, ejaculatory duct
Genital tubercle	Clitoris	Glans penis
Urogenital folds	Labia minora	Ventral (penile) urethra
Labioscrotal swellings	Labia majora	Scrotum

Embryonic structure	Female derivative	Male derivative
Urogenital sinus	Bladder, urethra, vestibule, lower vagina, Bartholin's & Skene's glands	Bladder, urethra, prostate, bulbourethral (Cowper) glands
Müllerian tubercle/sinus tubercle	Hymen	Seminal colliculus
Gubernaculum	Ovarian ligament + round ligament	Gubernaculum testis

Development of the ovary

- Genital ridge forms (week 4–5) from proliferating coelomic epithelium and condensed mesenchyme medial to the mesonephros.
- Primordial germ cells (endodermal, yolk-sac origin) invade the ridge and induce the primitive (cortical) sex cords; without this induction the gonad cannot develop.
- In the absence of *SRY*/testis-determining factor, cortical sex cords fragment into clusters that envelop the germ cells, becoming **primordial follicles**; the medulla regresses to a vestige (rete ovarii).
- Germ cells differentiate into oogonia → primary oocytes arrested in prophase of the first meiotic division; numbers peak at ~6–7 million by 20 weeks, falling to ~2 million at birth through atresia.
- **Descent:** the ovary migrates from its thoracic origin to the pelvic brim by the 7th–9th month, guided by the gubernaculum, which becomes divided at its point of attachment to the fusing Müllerian ducts into a proximal **ovarian ligament** and a distal **round ligament**.

Development of the uterus, tubes and vagina

- Each paramesonephric duct develops three segments — cranial vertical, middle horizontal, caudal vertical — and crosses ventral to the Wolffian duct.
- The two caudal vertical segments fuse in the midline (beginning week 7–8, complete by week 12) to form the **uterovaginal canal**, which differentiates into the **uterus and cervix**; the intervening septum resorbs by the 5th month. The unfused cranial parts remain separate as the **fallopian tubes**, with the coelomic opening becoming the abdominal ostium.
- Fusion of the ducts drags two peritoneal folds together to form the **broad ligaments**, dividing the pelvis into vesico-uterine and recto-uterine pouches.
- The fused Müllerian tip meets the posterior urogenital sinus wall at the **sinus (Müllerian) tubercle**, stimulating endodermal proliferation into paired **sinovaginal bulbs**, which elongate cranially as a solid **vaginal plate**.
- The vaginal plate canalises by central desquamation from about the 12th to the 20th week — mucosal lining is endodermal (urogenital sinus origin), the fibromuscular wall is mesodermal

(Müllerian origin). The sinovaginal bulbs form roughly the lower one-fifth of the vagina; the fused uterovaginal canal contributes the upper four-fifths.

- The **hymen** persists as the membrane at the junction of the canalised vaginal plate and the urogenital sinus.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 5.2 — The embryonic development of the female genital tract: formation of the uterus and vagina (Berek & Novak 16e, p.151)*

Label: paired paramesonephric (Müllerian) ducts crossing ventral to the mesonephric ducts, midline fusion forming the uterovaginal canal and broad ligaments, sinovaginal bulbs at the urogenital sinus, and the unfused cranial ducts opening as the fallopian tubes.

High-yield exam pointers

- **SRY → SOX9 → AMH (Sertoli) + testosterone/DHT (Leydig)** is the male cascade; **WNT4/RSPO1 repressing SOX9** drives the female pathway (not purely "passive default").
- Female genital tract = **Müllerian (paramesonephric) duct**; male tract = **Wolffian (mesonephric) duct** — opposite duct regresses under AMH (female) or absent testosterone (male).
- Vagina has a **dual origin**: upper four-fifths from the fused Müllerian uterovaginal canal (muscularis) + sinovaginal bulb-derived mucosa; lower one-fifth from the urogenital sinus. Canalisation completes by **week 20**.
- Vestiges to name on sight: **epoophoron, paroophoron, Gartner's duct cyst** (Wolffian remnants); **hydatid of Morgagni** (Müllerian remnant at the fimbria).
- Gubernaculum → **ovarian ligament (proximal) + round ligament (distal)** in the female; gubernaculum testis in the male.
- Oogonia: **~6–7 million at 20 weeks → ~2 million at birth** (atresia); all arrested as primary oocytes in meiotic prophase I by birth.
- External genitalia are indistinguishable until the **12th week**; unicornuate, bicornuate, septate, didelphys and Müllerian agenesis all arise from faults in this fusion/canalisation sequence.

SOURCE & COVERAGE

Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e (molecular control of gonadal differentiation — SOX9/WNT4/RSPO1).

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Discuss the blood supply of pelvic organs. Describe its clinical importance

Asked in: Paper I Nov 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — The pelvic organs (uterus, cervix, vagina, ovaries, fallopian tubes, bladder, rectum, and vulva) are supplied chiefly by the anterior division of the **internal iliac (hypogastric) artery**, supplemented by the **ovarian artery** (a direct branch of the abdominal aorta) and, for the vulva/perineum, by the internal and external pudendal arteries. A dense network of arterial anastomoses links these sources, and this collateral network is the basis of most of the clinical and surgical importance discussed below.

Arterial supply — organ by organ

Organ	Artery/arteries	Origin & key course
Uterus	**Uterine artery** (each side)	Branch of anterior division of internal iliac artery (occasionally a common trunk with the superior vesical artery); crosses **anterior to the ureter** ~1.5–2 cm lateral to the internal os ("water under the bridge"); ascends along the lateral uterine border in the broad ligament, giving off arcuate → radial → spiral/basal arteries; terminal tubal and ovarian branches anastomose with the ovarian artery at the cornu
Cervix & upper vagina	Cervicovaginal branch of uterine artery + vaginal artery	Vaginal artery arises from the uterine artery or directly from the anterior division of the internal iliac artery
Vagina (whole length)	Cervicovaginal + vaginal artery (upper), middle rectal artery (posterior wall), internal pudendal artery (lower/distal walls)	These anastomose on each side to form two longitudinal **azygos arteries** (anterior and posterior) running the length of the vagina
Ovary	**Ovarian artery**	Direct branch of the abdominal aorta just below the renal artery; runs in the infundibulopelvic (suspensory) ligament; terminal branch anastomoses with the ovarian branch of the uterine artery at the cornu

Organ	Artery/arteries	Origin & key course
Fallopian tube	Tubal branch of uterine artery (medial two-thirds) + ovarian artery branches through the mesosalpinx (lateral one-third)	Dual supply from both anastomosing arteries
Bladder	Superior vesical artery (from the patent proximal umbilical artery) + inferior vesical artery	Both from anterior division of internal iliac artery
Rectum	Superior rectal (from inferior mesenteric artery), middle rectal and inferior rectal (internal iliac/internal pudendal)	Superior rectal is the sole portal-system supply — see venous note below
Vulva & perineum	External pudendal artery (from femoral artery) + internal pudendal artery (terminal branch of anterior division of internal iliac, via Alcock's canal)	Internal pudendal gives the inferior rectal artery, then supplies the perineum, vestibular bulb and clitoris (dorsal artery of clitoris)
Pelvic ureter	Segmental twigs from nearly all visceral branches of the anterior division of internal iliac artery (uterine, vaginal, vesical, middle rectal)	Explains why ureteric devascularisation can occur even without direct transection

Internal iliac artery — divisions supplying the pelvis

Division	Branches	Territory
Anterior division	Superior & inferior vesical, middle rectal, uterine, vaginal, obturator, internal pudendal, inferior gluteal, and the umbilical artery (patent part → superior vesical)	Pelvic viscera and perineum
Posterior division	Iliolumbar, lateral sacral, superior gluteal	Buttock and posterior pelvic wall — spared during ligation to avoid gluteal ischaemia

Venous drainage and key anastomoses

- Uterine, vaginal and vesical veins accompany their arteries and drain via the **internal iliac vein** → common iliac vein → inferior vena cava (IVC).
- **Ovarian veins** are asymmetric: the right drains directly into the IVC; the **left drains into the left renal vein** — surgically important during retroperitoneal dissection and in ovarian/renal vein thrombosis.

- Rectal venous drainage is **porto-systemic**: superior rectal vein → inferior mesenteric vein → portal system, while middle/inferior rectal veins drain into the internal iliac (systemic) system; free anastomosis here explains haematogenous liver metastasis from pelvic genital malignancy and is the anatomical site of haemorrhoids.
- Vulval/perineal drainage is via richly anastomotic **internal pudendal veins**, predisposing to vulval varicosities in pregnancy.

Clinical importance

- **Ureteric injury in pelvic surgery** — the uterine artery crosses anterior to the ureter close to the internal os ("water under the bridge"); this is the commonest site of iatrogenic ureteric injury during abdominal/vaginal hysterectomy, along with the infundibulopelvic ligament (ovarian vessel pedicle), the point where the cardinal ligament is clamped lateral to the cervix, and the vaginal angle. Careful ureteric dissection off the "ureteric tunnel" is central to radical (Wertheim's) hysterectomy for cervical cancer.
- **Collateral circulation permitting arterial ligation for haemorrhage control** — the dual uterine–ovarian anastomosis and the azygos vaginal anastomoses create a vascular reserve, so the uterine artery, and even both internal iliac arteries, can be ligated for postpartum haemorrhage (PPH) without causing uterine or pelvic-organ ischaemic necrosis.
- **Internal iliac (hypogastric) artery ligation** — performed ~5 cm distal to the common iliac bifurcation, deliberately distal to the posterior division, to spare the gluteal branches. Its principal mechanism is an **~85% reduction in pulse pressure** distal to the ligation (Burchell, 1968), converting the arterial circuit toward a venous-pressure system that favours clot formation. It is technically demanding and controls PPH in only about half of cases (more effective for placenta previa bleeding than for atony); bilateral ligation does not impair subsequent fertility.
- **Stepwise surgical devascularisation for PPH** — escalating ligation of the uterine artery (O'Leary suture), then the utero-ovarian vessels, then the internal iliac artery, is used before resorting to hysterectomy; uterine compression (B-Lynch "brace") sutures act by compressing these same arcuate/radial vessels.
- **Uterine artery embolisation (UAE)** — transfemoral angiographic occlusion exploits this same collateral-tolerant anatomy and is used for intractable obstetric haemorrhage, prophylactic balloon occlusion in placenta accreta spectrum surgery, and symptomatic fibroids.
- **Uterine artery Doppler velocimetry** — a persistent diastolic notch or raised resistance (failure of physiological spiral-artery remodelling by trophoblast) on second-trimester uterine artery Doppler is used to screen for pre-eclampsia and fetal growth restriction.
- **Broad ligament haematoma** — because the uterine vessels run within the base of the broad ligament, a tear here (uterine rupture, cervical laceration extending laterally, difficult

instrumental delivery) causes a broad ligament haematoma rather than free intraperitoneal bleeding.

- **Pregnancy-related vascular changes** — marked hypertrophy of the pelvic vasculature (the ovarian vascular pedicle widens from 0.9 cm to 2.6 cm at term) predisposes to round ligament varicosities (which can mimic an inguinal hernia) and vulval varicosities.
- **Preserved perfusion after proximal ligation** — anastomoses between the internal pudendal artery and the external pudendal artery (from the femoral artery) maintain vulval and bladder perfusion even after ligation of the anterior division/vesical branches of the internal iliac artery.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 2.35 — Blood supply of the internal genital organs. (Jeffcoate's Principles of Gynaecology 9e, p.23)*

High-yield exam pointers

- Ovarian artery = direct branch of aorta, just below the renal artery; left ovarian vein drains into the **left renal vein**, right ovarian vein drains directly into the IVC.
- Uterine artery crosses **anterior to the ureter** ~1.5–2 cm from the cervix/internal os — "water under the bridge"; the single most-tested fact in this topic.
- Internal iliac artery ligated **5 cm distal to the common iliac bifurcation**, distal to the posterior division; mechanism = **85% fall in distal pulse pressure** (Burchell, 1968); success only ~50% for PPH.
- Two **azygos arteries** (anterior + posterior) run the length of the vagina, formed by anastomoses of the cervicovaginal, vaginal, middle rectal and internal pudendal arteries.
- Dual uterine–ovarian anastomosis = the anatomical basis for safe uterine/internal iliac artery ligation in PPH.
- Stepwise PPH devascularisation order: uterine artery → utero-ovarian vessels → internal iliac artery (before hysterectomy).
- Uterine artery embolisation used in PPH, placenta accreta spectrum, and fibroids.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Williams Obstetrics 26e describes the uterine artery crossing the ureter "approximately 2 cm lateral to the cervix," while DC Dutta's texts cite "about 1.5 cm" from the internal os — both texts agree on the essential operative teaching point (close proximity, artery anterior to ureter); the exact centimetre figure varies only by the reference landmark used.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e.

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Discuss the cardiovascular and haematological changes in pregnancy and their clinical significance

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — Pregnancy is a state of physiological hypervolaemia and hyperdynamic circulation, in which blood volume, cardiac output and coagulability all rise progressively to meet the metabolic demands of the fetoplacental unit and to pre-compensate for blood loss at delivery. These adaptations begin as early as the 5th–6th week, peak around 28–34 weeks, and are exaggerated further in labour and the immediate puerperium.

Cardiovascular changes

Anatomical/clinical findings (elevated diaphragm pushes the heart up, outward and rotates it left):

- **Apex beat** shifted to the 4th intercostal space, ~2.5 cm lateral to the mid-clavicular line.
- **Soft systolic ejection murmur** (grade 1–2/6) at the pulmonary/apical area — from reduced blood viscosity and torsion of great vessels.
- **Mammary souffle** — a continuous murmur over the 2nd–3rd left intercostal space from increased internal mammary flow.
- **Third heart sound (S3)** from rapid diastolic filling; rarely a fourth sound.
- **ECG** — left axis deviation; otherwise normal.
- **Echocardiography** — increased left ventricular end-diastolic diameter and left/right atrial diameters.

Haemodynamic changes (*DC Dutta's Obstetrics 9e*, Table 5.4; corroborated by *Williams Obstetrics 26e*, Table 4-5):

Parameter	Non-pregnant	Near term	Change
Cardiac output (L/min)	4.5	6.2–6.3	**+40–43%**
Stroke volume (mL)	65	75	+27%
Heart rate (/min)	70	83–85	+17%
Diastolic BP / MAP	—	—	↓ 5–10 mm Hg (mid-pregnancy nadir)

Parameter	Non-pregnant	Near term	Change
Femoral venous pressure	8–10 cm H_2O	~25 cm H_2O	+100%
Colloid osmotic pressure (mm Hg)	20	18	−14%
Systemic vascular resistance	—	—	−21%
Pulmonary vascular resistance	—	—	−34%
Central venous pressure / PCWP	—	—	No significant change

Cardiac output rises from the 5th week, peaks (+40–50%) at **28–34 weeks**, plateaus till term, then rises further in **labour (+50%)** and is highest **immediately postpartum (+70%)** due to relief of caval compression and *autotransfusion* from the emptying, contracting uterus. It returns to pre-labour values by 1 hour and to pre-pregnant levels by 4 weeks postpartum. Uterine blood flow rises from 50 mL/min to ~750 mL/min at term (10% of maternal cardiac output).

Clinical significance of cardiovascular changes

Physiological finding	Clinical implication
Ejection systolic murmur, S3, mammary souffle, sinus tachycardia, ECG left-axis deviation	Mimic organic heart disease; a **diastolic or grade ≥3/6 systolic murmur is always pathological** and needs cardiac work-up
Peak CO at 28–34 weeks, and further surges in the **second stage of labour** and **first 24–72 h postpartum**	The three periods of maximum haemodynamic stress — highest risk of decompensation/pulmonary oedema in women with valvular or structural heart disease, and the classic window for **peripartum cardiomyopathy**
↓ SVR and ↓ PVR despite ↑ cardiac output	Explains why MAP/CVP/PCWP stay essentially unchanged — a normal heart copes easily, a diseased heart cannot
Supine hypotension syndrome — gravid uterus compresses the inferior vena cava/aorta in the supine position; in ~10% collateral (paravertebral/azygos) flow fails to open	Hypotension, tachycardia, syncope in late pregnancy; corrected promptly by turning to the **left lateral position**
Mid-pregnancy fall in diastolic BP/MAP	A rising trend back toward or above booking BP in the third trimester is an early clue to **pre-eclampsia**
Raised femoral venous pressure, venous distensibility	Predisposes to dependent oedema, varicose veins, haemorrhoids and deep vein thrombosis

Haematological changes

Parameter	Non-pregnant	Near term	Change
Blood volume (mL)	4000	5500	**+30–40%** (up to 45% at 30–34 wk)
Plasma volume (mL)	2500	3750	**+40–50%**
Red cell volume (mL)	1400	1750	+20–30%
Total haemoglobin (g)	475	560	+18–20%
Haematocrit (whole body)	38%	32%	Diminished
Total leucocyte count	~7,000/mm^3	8,000–9,000/mm^3 (up to 20,000–25,000 in labour)	Neutrophilic leucocytosis
Platelet count	1.6–2.0 lakh/mm^3	Static or ~15% fall	Mild dilutional/consumptive fall
Fibrinogen (mg/dL)	200–400	300–600	**+50%**
ESR (mm/h)	10	40	4-fold rise
Clotting factors VII, VIII, IX, X, I (fibrinogen)	—	—	Increased
Factors XI, XIII; protein S	—	—	Decreased
Clotting time	—	—	Unchanged

The rise in plasma volume outstrips the rise in red-cell mass, producing **haemodilution** — the fall in Hb (~2 g/dL from baseline) and haematocrit is the so-called **physiological (dilutional) anaemia of pregnancy**. Levels of coagulation factors and leucocytes normalise by 2 weeks and 1–12 weeks postpartum respectively.

Clinical significance of haematological changes

- **Physiological vs true anaemia** — a fall to Hb ~10–11 g/dL is expected dilution; **anaemia in pregnancy is diagnosed only when Hb <11 g/dL or haematocrit <32%** (WHO cut-off, as adopted in DC Dutta's Obstetrics). Values below this need iron/folate work-up, not reassurance.
- **Iron demand rises sharply** — total requirement ≈1000 mg (300 mg fetoplacental, 400 mg expanded red-cell mass, ~200 mg obligatory loss), concentrated in the second half, reaching 6–7 mg/day; this is the rationale for routine antenatal iron-folic acid supplementation.

- **Benefits of haemodilution** — lower blood viscosity improves uteroplacental gas exchange, protects against the haemodynamic effects of posture change, and buffers the mother against the blood loss of delivery.
- **Hypercoagulable state** — ↑fibrinogen and clotting factors, ↓protein S and depressed fibrinolysis give pregnancy a 4–6-fold increased risk of **venous thromboembolism**, especially peripartum and postpartum; this same hypercoagulability helps limit postpartum haemorrhage after placental separation.
- **Gestational thrombocytopenia** (mild fall, usually >1 lakh/mm^3) is benign and does not increase bleeding risk — it must be distinguished from pre-eclampsia-associated or immune thrombocytopenia.
- **Neutrophilic leucocytosis** can mimic or mask infection/appendicitis in pregnancy; a normal count does not exclude sepsis and a mildly raised one does not confirm it.
- **ESR is unreliable in pregnancy** (four-fold physiological rise) and should not be used to diagnose inflammatory disease.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 16.2 — Haemodynamic changes during pregnancy relate to increased cardiac output and a fall in systemic vascular resistance (Arias High-Risk Pregnancy 5e, p.976)*

Alternatively sketch a curve of cardiac output and systemic vascular resistance against gestational age (non-pregnant → each trimester → labour → postpartum) to show the timing of peak haemodynamic stress.

High-yield exam pointers

- CO **+40% peak at 28–34 weeks**, further **+50% in labour**, **+70% immediately postpartum** — the three danger windows for cardiac decompensation.
- Blood volume **+30–45%**, plasma **+50%** > RBC mass **+20–30%** → dilutional (physiological) anaemia; true anaemia = **Hb <11 g/dL or Hct <32%**.
- SVR **−21%**, PVR **−34%** — MAP/CVP stay unchanged despite rising CO.
- Fibrinogen **+50% (200–400 → 300–600 mg/dL)**; factors VII, VIII, IX, X ↑, protein S ↓ → hypercoagulable state, 4–6× VTE risk.
- **Supine hypotension syndrome** — corrected by left lateral tilt (IVC decompression).
- **ESR rises 4-fold** — no diagnostic value in pregnancy.
- Iron requirement **≈1000 mg total**, **6–7 mg/day** in the second half of pregnancy.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Williams Obstetrics gives a comparable cardiac output rise of +43% (6.2 vs 4.3 L/min) with identical −21% SVR and −34% PVR, confirming DC Dutta's figures.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e (Chapter 5, Physiological Changes during Pregnancy — Tables 5.1, 5.3, 5.4); Williams Obstetrics 26e (Chapter 4, Maternal Physiology — Table 4-5); figure from Arias High-Risk Pregnancy 5e.

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Discuss the etiopathogenesis of Disseminated Intravascular Coagulation in obstetrics

Asked in: Paper I 15-Nov-2022 — RGUHS MS Obstetrics & Gynaecology

Definition — Disseminated intravascular coagulation (DIC), better termed **consumptive coagulopathy**, is a clinicopathological syndrome in which an obstetric trigger causes widespread intravascular activation of the coagulation cascade with diffuse fibrin deposition throughout the microcirculation. Platelets and clotting factors are consumed faster than the liver can resynthesise them, so the same patient shows microvascular thrombosis (organ ischaemia) and a bleeding diathesis side by side. **DIC is always secondary to an underlying obstetric or medical condition — it is never a primary disorder.**

Pregnancy as a predisposing hypercoagulable state

Parameter	Change in normal pregnancy
Procoagulants — fibrinogen (I), VII, VIII, IX, X	Progressively increased
Plasminogen	Increased, but plasminogen activator inhibitor-1 and -2 (PAI-1, PAI-2) rise even more → net **fibrinolysis suppressed**
Platelet count	Mildly reduced (subclinical, low-grade consumption)
Net physiological state	A finely balanced, **compensated hypercoagulable state** that maintains the uteroplacental interface — any pathological trigger easily tips it into overt DIC

Etiology — obstetric triggers classified by mechanism of activation

Endothelial injury	Tissue factor (thromboplastin) release	Phospholipid/procoagulant release
Severe pre-eclampsia, eclampsia, HELLP syndrome	**Abruptio placentae***	Fetomaternal haemorrhage
Septicaemia / septic abortion (endo-/exotoxin)	Amniotic fluid embolism	Incompatible blood transfusion
Chorioamnionitis, acute pyelonephritis	Dead fetus syndrome (retained IUFD)	Haemolysis
Hypovolaemic/haemorrhagic shock	Hydatidiform mole	Septicaemia
Acute fatty liver of pregnancy (also ↓ hepatic factor synthesis)	Caesarean section	
	Intra-amniotic hypertonic saline instillation (mid-trimester abortion)	

*Abruptio placentae is the single most common cause of severe consumptive coagulopathy in obstetrics.

Pathogenesis

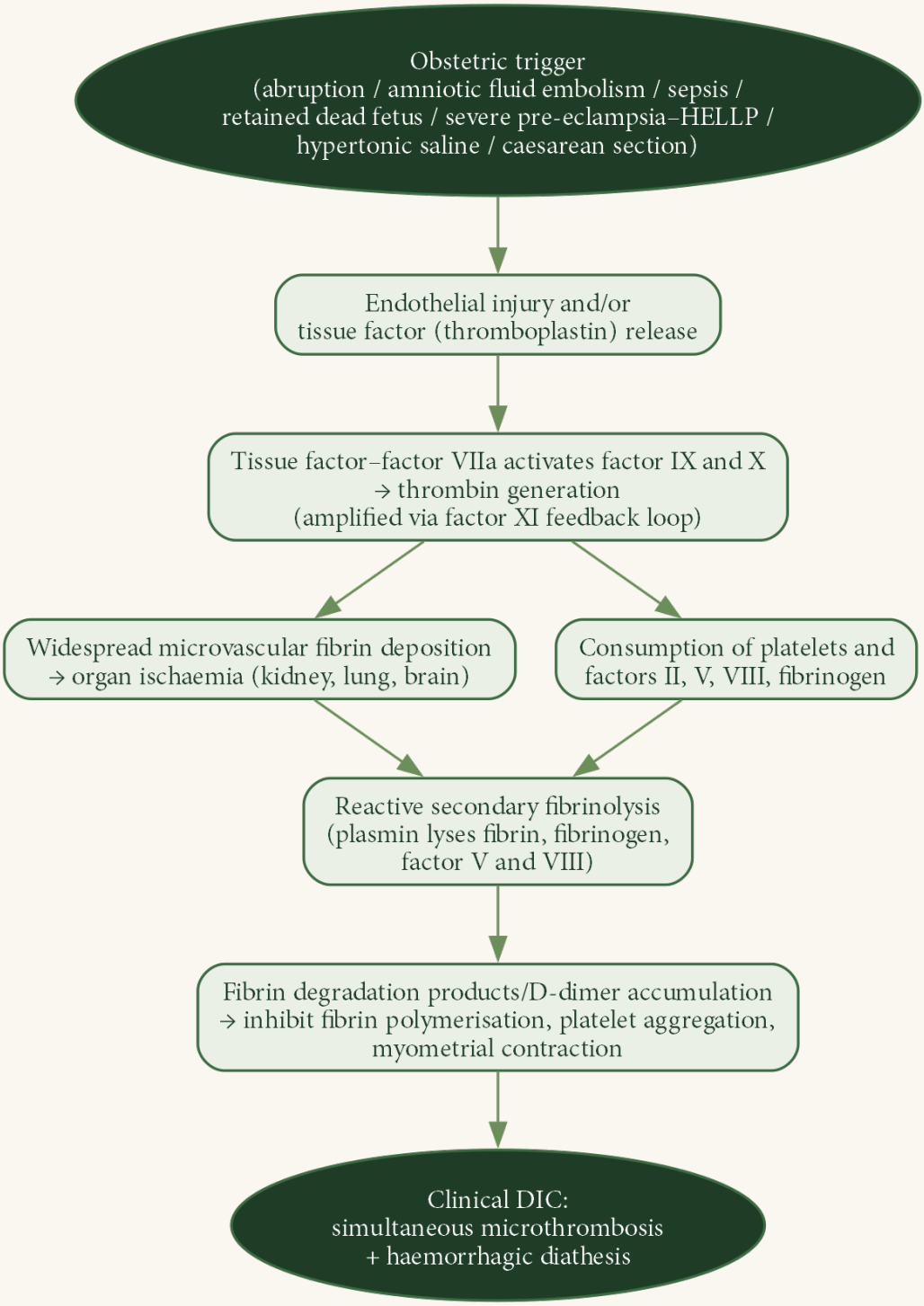
- **Central initiating pathway (current concept).** Tissue factor — a subendothelial membrane glycoprotein exposed by injury or liberated as "thromboplastin" from decidua, placenta, or amniotic fluid — is the principal initiator of coagulation, replacing the older stepwise intrinsic/extrinsic "waterfall" model. Tissue factor complexes with factor VIIa to activate factors IX and X; factor Xa generates thrombin, which converts fibrinogen to fibrin. The initial thrombin produced also activates factor XI, creating a feedback amplification loop (the process formerly labelled the "intrinsic pathway"). The end result is widespread fibrin formation through the microvasculature.
- **Trigger-specific mechanisms:**
  - **Abruptio placentae** — the retroplacental clot sequesters fibrinogen and other procoagulants; clot retraction then expresses serum (with residual thromboplastin) back into the circulation; thromboplastin liberated from the damaged decidua and myometrium enters the maternal bloodstream and precipitates DIC; concurrent haemorrhagic shock impairs hepatic resynthesis of clotting factors.
  - **Amniotic fluid embolism** — thromboplastin-rich amniotic fluid and fetal debris enter the maternal circulation through a breach in the membranes, placenta, or uterine veins, lodge in and injure the pulmonary vasculature, and trigger the coagulation cascade with massive pulmonary fibrin deposition. If the woman survives the cardiorespiratory collapse, fibrinolytic activators released from the damaged pulmonary endothelium produce severe

secondary fibrinolysis (lysis of fibrin, fibrinogen, and factors V and VIII) superimposed on the primary consumptive process.

- **Sepsis / septic abortion / endotoxaemia** — endotoxin (gram-negative organisms) or exotoxins (Group A *Streptococcus pyogenes*, *Staphylococcus aureus*, *Clostridium perfringens/sordellii/novyi*) activate endothelium and monocytes, provoking cytokine release and diffuse coagulation activation — comparable to a generalised Shwartzman-type reaction, for which a single stimulus suffices in the already hypercoagulable pregnant state. In the shock phase, hypoxic capillary endothelial injury and blood stasis further favour DIC.
- **Severe pre-eclampsia, eclampsia, HELLP syndrome** — endothelial activation/injury is the pathogenic hallmark, driving platelet adhesion, activation, and consumption; clinically significant overt DIC occurs in roughly 10% of HELLP cases.
- **Retained dead fetus (chronic/compensated DIC)** — slow, continuous absorption of thromboplastin from the degenerating placenta, decidua, and amniotic fluid produces a gradual fall in fibrinogen and factor VIII with mild thrombocytopenia; overt defibrination is uncommon before 4 weeks of fetal death but develops in up to a quarter of cases after a month of retention.
- **Mid-trimester induced abortion** (intra-amniotic hypertonic saline instillation, or dilation and evacuation) — the necrobiotic effect of hypertonic saline on the placenta, fetus, and decidua releases thromboplastin into the circulation.
- **Caesarean section** — thromboplastin and amniotic fluid can enter the circulation through open venous sinuses at the uterine incision, and the injured uterine wound itself releases excess plasminogen activator.

- **The consumption–fibrinolysis vicious circle:** widespread thrombin generation → fibrin trapped in the microcirculation (renal, pulmonary, cerebral ischaemia) plus platelets and factors II, V, VIII, and fibrinogen consumed faster than hepatic synthesis can replace them → fibrinogen falls toward the critical haemostatic threshold → **reactive ("secondary") fibrinolysis** is triggered as a protective mechanism to restore microcirculatory patency, converting plasminogen to plasmin, which lyses fibrin/fibrinogen and also factors V and VIII → fibrin degradation products (FDPs) and D-dimers accumulate and themselves impair platelet aggregation, fibrin polymerisation, and myometrial contraction → this compounds the haemorrhagic diathesis (bruising, venepuncture-site oozing, postpartum haemorrhage despite a well-contracted uterus).

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Pathogenesis of DIC in obstetrics — from the obstetric trigger through tissue-factor-driven thrombin generation, the parallel microthrombosis/consumption limbs, reactive fibrinolysis, and the resulting simultaneous microthrombosis-plus-haemorrhage picture.

High-yield exam pointers

- One-line definition to reproduce: "consumptive coagulopathy — always secondary, never primary."
- Modern initiator of coagulation: **tissue factor**, not the older intrinsic/extrinsic "waterfall" model.
- Single most common obstetric cause of severe DIC: **abruptio placentae**.
- Three-column classification to draw from memory: endothelial injury / thromboplastin release / phospholipid release.
- Retained dead fetus → **chronic/compensated DIC**; overt defibrination usually only after **4 weeks** of fetal death.
- HELLP syndrome → overt DIC in roughly **10%** of cases.
- "Secondary/reactive fibrinolysis" superimposed on primary consumption explains the rise in FDP/D-dimer and the worsened bleeding.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> DC Dutta's Obstetrics still frames coagulation activation using the classical intrinsic/extrinsic cascade terminology; current teaching (Williams Obstetrics 26e) attributes initiation to tissue factor with a factor XI feedback amplification loop — both describe the same final common pathway of thrombin generation and are not in factual conflict.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Discuss the guidelines for prescribing drugs in pregnancy. Describe the common teratogenic drugs

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — A **teratogen** is a chemical, physical or infective agent that, acting during embryonic or fetal life, produces a permanent alteration of the structure or function of an organ; the same agent may cause death, malformation, growth restriction or a functional disorder depending on the dose and the gestational timing of exposure. Because almost every drug crosses the placenta (the exceptions being a few large organic ions such as heparin and insulin), prescribing in pregnancy always weighs a maternal

benefit against a fetal risk; only about 2–3% of birth defects are attributable to drugs, most being genetic or multifactorial/unknown.

Guidelines for prescribing drugs in pregnancy

- **Treat only when clearly indicated** — avoid all non-essential drugs; weigh the risk of the drug against the risk of leaving the maternal disease untreated (uncontrolled epilepsy, hypertension or depression can itself harm the fetus).
- **Know the critical period of exposure** — before day 31 post-LMP the effect is "all or none" (the conceptus either dies or survives unaffected); day 31–71 is the embryonic/organogenetic period and the time of greatest risk of structural malformation; after day 71 the fetus is chiefly susceptible to growth restriction and functional/CNS effects, since the brain continues developing throughout pregnancy.
- **Prefer old, well-tested drugs** at the lowest effective dose for the shortest duration; avoid newly launched agents with no human pregnancy data and avoid polytherapy — combining agents (e.g. two antiepileptics) roughly doubles the malformation risk of either drug alone.
- **Check the current drug-safety information before prescribing.** The historic FDA letter categories (A/B/C/D/X, 1979) were formally replaced in 2015 by the narrative **Pregnancy and Lactation Labeling Rule (PLLR)**, which gives a Fetal Risk Summary, Clinical Considerations and supporting Data for each drug instead of a single letter; current prescribing should reference PLLR-format labelling or a teratology information service rather than an old category alone.
- **Avoid confirmed major teratogens outright** — isotretinoin, methotrexate, warfarin, ACE inhibitors/ARBs, valproate, thalidomide, danazol and radioactive iodine — unless no safer alternative exists for a life-threatening maternal indication; women of reproductive age who need such drugs chronically should be switched to a safer alternative before conception is planned.
- **Counsel using absolute, not relative, risk** (e.g. "2 in 100 chance of a malformed baby" rather than "doubled risk"), since framing changes perceived risk; document the informed discussion.
- **After any teratogen exposure**, offer detailed/targeted sonography — with fetal echocardiography if a cardiac teratogen was involved — directed at the organ systems known to be at risk.
- **Favour drugs less likely to cross the placenta** when choosing an alternative — high molecular weight (>1000 Da), high protein binding, low lipid solubility and high ionisation all reduce transfer.
- **Avoid live-attenuated vaccines** in pregnancy and screen for alcohol, tobacco and recreational drug use at every antenatal visit; report significant exposures to a pregnancy-exposure registry where one exists.

Common teratogenic drugs and their fetal effects

Drug/agent	Principal fetal or neonatal effect
Thalidomide	*Phocomelia* (absence/underdevelopment of long bones) with exposure at menstrual day 34–50; also cardiac, ear, eye and GI defects; up to 40% neonatal mortality
Isotretinoin (vitamin A derivative)	*Retinoic acid embryopathy* — microtia/anotia, flat nasal bridge, hypertelorism, conotruncal cardiac defects, thymic hypoplasia/aplasia, CNS defects
Methotrexate	*Fetal methotrexate–aminopterin syndrome* — craniosynostosis ("clover-leaf" skull), wide nasal bridge, micrognathia, limb and CNS defects; greatest risk at 8–10 weeks postconception, dose ≥10 mg/week
Valproic acid	Highest-risk antiepileptic — neural tube defects (~4%), craniofacial anomalies, lower cognitive/IQ scores in exposed children
Carbamazepine / Phenytoin	*Fetal hydantoin syndrome* — hypertelorism, low nasal bridge, midface hypoplasia, hypoplastic distal phalanges/nails, growth impairment, intellectual disability; carbamazepine also raises neural tube defect risk
Lithium	*Ebstein anomaly* (apical displacement of the tricuspid valve); neonatal "floppy baby" toxicity if exposure continues close to delivery
Warfarin	*Warfarin embryopathy* — nasal hypoplasia, depressed nasal bridge, stippled epiphyses (chondrodysplasia punctata); CNS anomalies with 2nd/3rd-trimester exposure
ACE inhibitors / ARBs	*Fetopathy* on 2nd/3rd-trimester exposure — fetal renal hypoperfusion with oligohydramnios, renal tubular dysgenesis/anuria, calvarial hypoplasia, growth restriction, pulmonary hypoplasia
Tetracycline	Yellow-brown discolouration of deciduous teeth, inhibition of bone growth — risk after 25 weeks
Aminoglycosides (streptomycin, gentamicin)	8th cranial nerve (oto-)toxicity, nephrotoxicity, especially in preterm infants
Chloramphenicol	Neonatal "gray baby" syndrome (peripheral vascular collapse) — a fetotoxic, near-term effect

Drug/agent	Principal fetal or neonatal effect
Long-acting sulfonamides	Neonatal hemolysis in G6PD deficiency; displaces bilirubin from albumin, risking kernicterus if given near term
Androgens / Danazol	Virilization of the female fetus — clitoromegaly, labial fusion
Diethylstilbestrol (DES)	Vaginal adenosis, clear-cell vaginal/cervical adenocarcinoma, cervical hoods, uterine hypoplasia in female offspring
Alcohol (ethanol)	*Fetal alcohol syndrome* — pre/postnatal growth restriction, characteristic facies (short palpebral fissures, smooth philtrum, thin vermilion border), CNS/neurobehavioural impairment
Cocaine	Placental abruption, microcephaly, cardiac and CNS anomalies
Misoprostol (failed abortion, pregnancy continues)	Möbius sequence (facial/abducens palsy), limb-reduction defects
Radioactive iodine (^{131}I)	Fetal thyroid ablation and hypothyroidism, particularly after 10–12 weeks

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 34.3 — Gestational age and teratogenicity (DC Dutta's Obstetrics 9e, p.502)*

High-yield exam pointers

- Day 31–71 post-LMP (embryonic period) = window of maximum structural teratogenic risk; before day 31 = all-or-none.
- PLLR (2015) replaced the old FDA letter categories A/B/C/D/X with a narrative Fetal Risk Summary/Clinical Considerations/Data format.
- Classic "Category X" list to reproduce: alcohol, ACE inhibitors, lithium, methotrexate, valproic acid, mifepristone, danazol, isotretinoin, radioactive iodine.
- Only heparin and insulin (large polar molecules) essentially do not cross the placenta — first-choice for chronic disease control in pregnancy (e.g. insulin for diabetes, heparin for thromboprophylaxis instead of warfarin).
- Thalidomide window: day 34–50 → phocomelia. Methotrexate threshold: ≥10 mg/week, most vulnerable at 8–10 weeks.
- ACE inhibitors/ARBs are largely exonerated for 1st-trimester structural defects but are contraindicated in the 2nd/3rd trimester for renal fetopathy.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Obstetrics 9e still teaches the classic FDA A/B/C/D/X letter system; the US FDA formally retired it in 2015 in favour of the narrative Pregnancy and Lactation Labeling Rule, so current prescribing decisions should be checked against PLLR-format product labelling rather than the old letter alone.

SOURCE & COVERAGE

Williams Obstetrics 26e (Chapter 8, Teratology, Teratogens and Fetotoxic Agents); DC Dutta's Textbook of Obstetrics 9e (Chapter 34, Pharmacotherapeutics in Obstetrics); US FDA Pregnancy and Lactation Labeling Rule (2015).

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Discuss the inheritance of X-linked inheritance disorders

Asked in: Paper I 12-Nov-2019 — RGUHS MS Obstetrics & Gynaecology

Definition — X-linked inheritance disorders result from mutant genes carried on the X chromosome. Because a male is **hemizygous** (single X, paired with a Y) while a female carries two X chromosomes (one randomly inactivated in each cell — **lyonization**), the same mutant allele produces sex-different phenotypes. X-linked disorders are classified into **X-linked recessive** (the great majority) and **X-linked dominant** types.

Mechanism — why expression differs by sex

- **Males (XY, hemizygous)** — a single mutant allele on the only X is unmasked (no second X to carry a normal allele), so an X-linked recessive disease is fully expressed whenever the mutant gene is inherited.
- **Females (XX)** — a recessive mutant allele on one X is normally masked by the normal allele on the other X; the female is a **carrier**, disease-free but able to transmit the gene.
- **X-inactivation (Lyon hypothesis/*lyonization*) — early in embryogenesis one X in each somatic cell is randomly and permanently inactivated, creating a mosaic of two cell populations. When inactivation is skewed toward the* normal *X being silenced in most cells, an otherwise-asymptomatic carrier becomes a manifesting carrier — e.g., ~10% of* haemophilia *A carriers have factor VIII levels <30% of normal (similarly for factor IX in* haemophilia *B carriers), enough to raise bleeding risk at delivery;* Duchenne/Becker* muscular dystrophy carriers likewise carry an elevated cardiomyopathy risk and need periodic cardiac evaluation.

- **X-linked dominant** genes are expressed in heterozygous females as well as hemizygous males; several are so severe in males that the conception is non-viable, so affected individuals seen clinically are almost all female.

Pattern of transmission — recessive vs dominant

Feature	X-linked recessive	X-linked dominant
Who is usually affected	Males (fully); females rarely (only if homozygous or a manifesting carrier)	Females >> males; several forms lethal in the male fetus
Father-to-son transmission	**Never occurs** — a father gives his son a Y, not his X	Never occurs (same reason)
Daughters of an affected father	**All are obligate carriers** (each receives his single X)	All daughters affected (each receives the mutant X)
Sons of an affected father	All unaffected (receive his Y)	All unaffected
Offspring of a carrier/affected mother	50% of sons affected; 50% of daughters carriers	50% of children of either sex affected
Pedigree pattern	Trait "skips" generations, passing silently through carrier females	Trait appears every generation; no skipping
Consanguinity	Increases risk only if the partner is also a carrier (rare)	Not typically relevant

Recurrence risk by mating type

Mating	Risk to sons	Risk to daughters
Carrier mother × normal father (X-linked recessive)	50% affected, 50% normal	50% carriers, 50% normal
Affected father × normal mother (X-linked recessive)	0% affected (all normal)	100% obligate carriers
Affected father × carrier mother (rare, consanguinity)	50% affected	50% homozygous-affected, 50% carrier
Affected/heterozygous mother × normal father (X-linked dominant)	50% affected	50% affected
Affected father × normal mother (X-linked dominant)	0% affected	100% affected

Examples relevant to obstetrics & gynaecology

Type	Disorder	Basic defect
X-linked recessive	*Haemophilia* A / *Haemophilia* B	Factor VIII / factor IX deficiency; haemophilia A accounts for 80–85% of cases (~1:5000 male births)
X-linked recessive	*Duchenne*/*Becker* muscular dystrophy	Dystrophin gene mutation
X-linked recessive	Glucose-6-phosphate dehydrogenase (G6PD) deficiency	Variable enzyme activity due to lyonization; risk of haemolysis with oxidant drugs/infection
X-linked recessive	Red-green colour blindness	Opsin gene mutation
X-linked recessive	Androgen insensitivity syndrome	Androgen receptor gene defect (Xq11-12); 46,XY phenotypic female, primary amenorrhoea, blind vaginal pouch
X-linked recessive	*Fragile X* syndrome	CGG trinucleotide-repeat expansion at Xq27.3 (FMR1 gene); most common inherited intellectual disability
X-linked dominant	Vitamin D–resistant (hypophosphataemic) rickets	Renal phosphate wasting; mainly affects females
X-linked dominant	Incontinentia pigmenti	Lethal in most males; skin, dental, ocular and CNS anomalies in surviving females
X-linked dominant	*Rett* syndrome, *Aicardi* syndrome	Lethal in male conceptuses; only affected girls are born

Reproductive implications and prenatal diagnosis

- **Carrier detection** — factor VIII/IX assay (haemophilia), serum creatine kinase (DMD/BMD carriers), or direct mutation/DNA analysis in a known family.
- **Fetal sex determination** — transabdominal ultrasound or non-invasive cell-free fetal DNA (cffDNA) from maternal blood identifies fetal sex from ~9 weeks with >99% accuracy; since only male fetuses are at risk of an X-linked recessive disease, female fetuses can be reassured without an invasive procedure.
- **Confirmatory invasive testing** — chorionic villus sampling (10–13 weeks) or amniocentesis (15–20 weeks) for the specific familial mutation is offered only when the fetus is male (or, for X-linked dominant disease, regardless of sex).

- **Preimplantation genetic testing** (PGT-M) with in-vitro fertilisation allows selection of an unaffected embryo before transfer, avoiding a mid-trimester decision on pregnancy termination.
- **Genetic counselling** — construct a three-generation pedigree, calculate recurrence risk from the tables above, screen at-risk maternal female relatives (sisters, maternal aunts) for carrier status, and counsel on the reproductive options (prenatal diagnosis, PGT-M, or accepting the risk).

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 3.16 — X-linked recessive pedigree. Source: (By kind Permission (Arias High-Risk Pregnancy 5e, p.169)*

High-yield exam pointers

- **No male-to-male transmission** in any X-linked disorder — the single fact examiners test most.
- Affected father's **daughters are ALL obligate carriers**; his sons are all normal.
- Carrier mother: **50% sons affected, 50% daughters carriers.**
- *Lyon* hypothesis (lyonization) = random X-inactivation → explains **manifesting carriers** (e.g., haemophilia A carrier with factor VIII <30%).
- X-linked dominant conditions are often **lethal in males in utero** → disease seen almost exclusively in females (Rett, incontinentia pigmenti, Aicardi).
- Classic recessive list to write verbatim: haemophilia A/B, Duchenne/Becker muscular dystrophy, G6PD deficiency, colour blindness, androgen insensitivity syndrome, fragile X syndrome.
- Prenatal pathway: cffDNA/ultrasound sexing → CVS/amniocentesis (only if male) → mutation-specific diagnosis; PGT-M as an alternative.

SOURCE & COVERAGE

Williams Obstetrics 26e (Chapter 16, Genetics — X-linked and Y-linked inheritance, lyonization, fragile X); Arias' High-Risk Pregnancy & Delivery 5e (Chapter 3, Inheritance patterns — X-linked recessive/dominant pedigrees and examples); Berek & Novak's Gynecology 16e (androgen insensitivity syndrome).

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Discuss the management of intraoperative bleeding in pelvic surgery

Asked in: Paper I May 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — Surgical (intraoperative) haemorrhage is defined as blood loss exceeding 500 mL during a pelvic operation, or any blood loss that necessitates transfusion; it complicates approximately 2% of

gynaecological procedures. Its management rests on three pillars — preoperative anticipation, prompt stepwise surgical control of the bleeding source, and timely blood/product replacement.

Causes and risk factors

Category	Examples
Patient (coagulation) factors	Anticoagulant/antiplatelet therapy, inherited or acquired coagulopathy (von Willebrand disease, liver disease, disseminated intravascular coagulation (DIC)), pre-existing anaemia
Anatomical/procedural factors	Large fibroid uterus (myomectomy/hysterectomy), pelvic malignancy with tumour neovascularity, endometriosis obliterating surgical planes, pelvic lymphadenectomy (proximity to iliac vessels), dense adhesions from prior surgery or pelvic inflammatory disease, obstetric causes such as placenta accreta spectrum
Technical/human factors	Blind clamping or suturing into a pool of blood (risks ureteric injury), excessive monopolar electrosurgery causing delayed thermal-injury bleeding, poor exposure — particularly during minimally invasive surgery (MIS)

Immediate (first-line) surgical measures

- Apply direct pressure over the source with a finger or laparotomy sponge; use suction to clear the field and improve visualisation.
- Expose the bleeding pedicle by gentle blunt dissection and grasp it with DeBakey or right-angled forceps — never clamp blindly into a pool of blood (risks ureter/bladder/bowel injury).
- Secure the pedicle according to its size and location: electrocautery for a small bleeder, a surgical clip, or a figure-of-eight/interrupted suture ligature when close to the ureter, bladder, or bowel.
- If bleeding is persistent: maintain pressure, apply a topical haemostatic agent if suitable, inform anaesthesia/OR nursing, keep the patient warm, estimate blood loss, confirm IV access, send blood for cross-match, and activate the massive transfusion protocol (MTP) if indicated.
- Call for help early — extra suction/instruments, more nursing staff, and intraoperative consultation (gynaecologic oncologist, urologist, colorectal, general, or vascular surgeon) as the source dictates.

Surgical control of major or refractory pelvic haemorrhage

- **Venous bleeding**: sustained compression is first-line (low venous pressure favours stasis and clot formation); if unsuccessful, close the defect with clips or fine interrupted/figure-of-eight sutures, particularly in the parametrium, paracolpos, or deep pelvic sidewall.

- **Arterial bleeding**: if the vessel is expendable — uterine artery, ovarian artery, or the anterior division of the internal iliac artery — clamp and ligate or clip it. If the vessel must not be sacrificed — aorta, external iliac artery, or the posterior division of the internal iliac artery — repair the defect with a fine non-absorbable monofilament suture (e.g., 5-0 polypropylene), placed intima-to-intima and perpendicular to flow to avoid luminal narrowing; involve a vascular surgeon if grafting/bypass is required.
- **Stepwise pelvic devascularisation** (for diffuse pelvic/uterine bleeding such as atony, an extensive myomectomy bed, or postpartum haemorrhage): bilateral uterine artery ligation → ovarian vessel ligation at the infundibulopelvic ligament → bilateral internal iliac (hypogastric) artery ligation if bleeding continues.
  - *Internal iliac (hypogastric) artery ligation* — steps: open the retroperitoneum over the external iliac artery from the round ligament to the infundibulopelvic ligament; medialise the ureter with the reflected peritoneum; skeletonise the anterior division about 2 cm distal to the bifurcation (sparing the posterior division, which usually arises within 2 cm of it); pass a right-angled clamp lateral-to-medial (protects the vein); doubly ligate with delayed-absorbable suture (e.g., polyglactin) without dividing the vessel; check pedal pulses to exclude inadvertent external iliac ligation.
  - *Mechanism/complications*: reduces distal pulse pressure by ~85% (Burchell, 1968), converting flow to a low-pressure "venous-like" pattern favouring clot formation; collaterals preserve pelvic perfusion and fertility. Ligating the posterior division causes buttock claudication; ligating the external iliac artery causes limb ischaemia.
- **Pelvic packing** for uncontrollable haemorrhage: firm gauze/sponge packing (contained in a sterile bag, e.g., a Bogota bag) applied against the bleeding bed, with a "parachute pack" brought through an open vaginal cuff for pelvic-floor bleeding; the abdomen is closed loosely with the fascia left open (prevents abdominal compartment syndrome), or covered with a temporary negative-pressure dressing; the patient is resuscitated in the intensive care unit and returned to theatre at approximately 48 hours for pack removal and definitive repair.
- **Adjuncts**: hemoclips applied in a "V" configuration on vascular pedicles; bipolar (not monopolar) electrosurgery near the ureter/bowel, since monopolar current and its eschar conduct thermal injury to adjacent structures; topical haemostatic agents (oxidised regenerated cellulose, gelatin sponge, thrombin/fibrin sealants) for diffuse low-pressure oozing — reserved for persistent bleeding, not routine prophylaxis (risk of abscess/small-bowel obstruction with physical agents).
- **Non-surgical option**: selective angiographic embolisation (Gelfoam, coils, or particles via the hypogastric artery/its branches) when bleeding is diffuse or surgically inaccessible and the patient has been packed and haemodynamically stabilised.
- **In minimally invasive surgery**: if visualisation is lost or bleeding is uncontrolled, convert promptly to laparotomy through a vertical midline incision — do not wait to assemble

laparotomy trays before starting the skin incision; tamponade manually once the abdomen is entered.

Blood and blood-product replacement

Parameter	Value/action
Consider red-cell transfusion	Loss >15% of estimated blood volume (≈ weight in kg × 10 mL for 15% of volume)
Transfusion threshold	Restrictive: haemoglobin ≤7 g/dL (liberal transfusion at haemoglobin <9 g/dL is linked to worse perioperative outcomes)
Initial crystalloid resuscitation	Infused in a 3:1 ratio to estimated blood loss
Massive transfusion protocol (MTP) activation	When ≥4 units of packed red cells are given or anticipated over a short interval
Component replacement ratio	Packed red cells : platelets : fibrinogen products ≈ 2:1:1, or laboratory-guided replacement
Fresh frozen plasma	If prothrombin time (PT)/activated partial thromboplastin time (aPTT) >1.5× normal
Platelet transfusion	If platelet count <50–100 $\times 10^3/\mu L$
Cryoprecipitate	If fibrinogen <200 mg/dL; 20 units corrects fibrinogen <100 mg/dL
Intraoperative resuscitation goals	PT <14 s, aPTT <40 s, fibrinogen >100 mg/dL, platelets >80 $\times 10^3/\mu L$
Cell salvage (autologous transfusion)	Consider if anticipated loss >20% of blood volume; avoid in infected fields and relatively avoid in malignancy
Tranexamic acid (TXA)	1 g intravenous (WOMAN trial) — antifibrinolytic, reduces haemorrhage-related mortality; infuse slowly (rapid infusion can cause hypotension)
Recombinant activated factor VIIa	Reserved for catastrophic bleeding refractory to standard measures; given as boluses every 2 hours or as continuous infusion
Anticoagulant reversal	Protamine sulfate (heparin/low-molecular-weight heparin); vitamin K/prothrombin complex concentrate (warfarin); desmopressin (aspirin-related platelet dysfunction); idarucizumab or andexanet alfa (direct oral anticoagulants)

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 39.2 — Ligation of the right hypogastric artery. The clamp is passed from lateral to medial and the ligature is placed around the anterior division of the hypogastric artery; the ureter is reflected medially with the peritoneum. (Te Linde's Operative Gynecology 13e, p.2084)*

High-yield exam pointers

- Cut-off: >500 mL loss or need for transfusion; ~2% of gynaecological surgeries.
- Devascularisation order: uterine artery → ovarian vessel → bilateral internal iliac (hypogastric) artery.
- Internal iliac ligation: ~85% fall in pulse pressure (Burchell, 1968); anterior division only, 2 cm distal to bifurcation; check pedal pulses.
- Posterior-division ligation → buttock claudication; blind clamping → ureteric injury.
- MTP trigger ≥4 units packed red cells; ratio 2:1:1 (red cells:platelets:fibrinogen); restrictive transfusion trigger haemoglobin 7 g/dL.
- Tranexamic acid 1 g IV — WOMAN trial, reduced haemorrhage mortality.
- Pack → leave fascia open (abdominal compartment syndrome) → re-look at ~48 hours.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older texts present hypogastric artery ligation as first-line for pelvic haemorrhage, but it is technically demanding with modest, variable efficacy; compressive sutures and angiographic embolisation are now generally preferred where expertise allows.

SOURCE & COVERAGE

Te Linde's Operative Gynecology 13e (Chapter 39, Management of Surgical Hemorrhage); Williams Obstetrics 26e; DC Dutta's Obstetrics 9e.

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Discuss the pathophysiology and management of coagulation failure in obstetrics

Asked in: Paper I 06-Apr-2026 — RGUHS MS Obstetrics & Gynaecology

Definition — Coagulation failure (consumptive coagulopathy / disseminated intravascular coagulation, DIC) is a clinicopathological syndrome of widespread intravascular fibrin deposition and consumption of platelets and procoagulants, precipitated when an obstetric trigger overwhelms the normal haemostatic balance. It is always a **secondary** phenomenon — it never arises without an inciting

obstetric condition — and pregnancy's physiological hypercoagulable state (raised factors I, VII, VIII, IX, X; suppressed fibrinolysis until placental separation) makes gravidas especially prone to it.

Causes and pathophysiological mechanisms

DIC is triggered by one (or more) of three pathways, each releasing tissue factor/thromboplastin into the maternal circulation and activating the extrinsic coagulation cascade:

Mechanism	Obstetric trigger(s)
Endothelial injury	Pre-eclampsia, eclampsia, HELLP syndrome; septicaemia; septic abortion; chorioamnionitis; pyelonephritis; hypovolaemic shock
Release of thromboplastin (tissue factor)	Abruptio placentae; amniotic fluid embolism; retained dead fetus (>4 weeks); hydatidiform mole; caesarean section; intra-amniotic hypertonic saline
Release of phospholipids	Feto-maternal haemorrhage; incompatible blood transfusion; haemolysis; septicaemia

Cascade sequence: Tissue factor (an integral membrane glycoprotein exposed at the site of injury) complexes with factor VIIa to activate factors IX and X; thrombin so generated feeds back to activate factor XI, amplifying clot formation. This is counterbalanced by the fibrinolytic system (plasminogen → plasmin), which lyses fibrin to fibrin degradation products (FDP), including D-dimers. When consumption outstrips hepatic/marrow replacement, fibrinogen, platelets, and factors V/VIII fall critically — producing the paradox of simultaneous **microvascular thrombosis** and **haemorrhage** (from factor depletion plus secondary fibrinolysis).

- **Abruptio placentae** (commonest severe obstetric cause): the retroplacental clot consumes fibrinogen; clot retraction releases serum procoagulants back into circulation; thromboplastin from damaged decidua/myometrium enters the maternal circulation; accompanying shock impairs hepatic synthesis of clotting factors; raised FDP additionally inhibits myometrial contraction, worsening atony.
- **Amniotic fluid embolism:** thromboplastin-rich liquor amnii enters the circulation through a rent in membranes/placenta, occludes the pulmonary vascular tree, and triggers profound consumptive coagulopathy with secondary fibrinolysis.
- **Retained dead fetus:** gradual absorption of thromboplastin from placenta/decidua depletes fibrinogen, factor VIII and platelets over weeks; about one-quarter develop overt coagulopathy after 4 weeks of retention.
- **Endotoxaemia/sepsis:** endotoxin superimposed on the pregnancy hypercoagulable state produces a Shwartzman-like reaction with widespread fibrin deposition, including in the renal microvasculature.

Clinical features and diagnosis

Bleeding is disproportionate to trauma: prolonged oozing from venepuncture/injection sites, gum and gastrointestinal bleeding, and — classically — **postpartum haemorrhage despite a well-contracted uterus** (traumatic bleeding excluded), wound or episiotomy site bleeding, and haematoma formation.

Test	Finding in DIC
Platelet count	Falls; <50,000/μL in severe DIC (also thrombocytopenia, not seen in pure fibrinolysis)
PT / aPTT	Prolonged
Fibrinogen	<150 mg/dL is clinically significant; <100 mg/dL is the arbitrary critical level (Dutta); <50 mg/dL = severe hypofibrinogenaemia (Williams)
FDP / D-dimer	Markedly raised
Bedside clot observation test (Weiner)	Clot forms in 6–12 min normally; no clot by 30 min ⇒ fibrinogen <100 mg/dL
Peripheral smear	Fragmented/"helmet" red cells + thrombocytopenia (fibrinolysis alone shows normal morphology)

The **International Society on Thrombosis and Haemostasis (ISTH)** composite score (platelet count, fibrin-related marker, prolonged PT, fibrinogen) is applied once a DIC-triggering condition is identified: score <5 = non-overt DIC, ≥5 = overt DIC.

Management

Preventive: early delivery/uterine evacuation in abruption and dead fetus, effective control of severe pre-eclampsia/eclampsia/HELLP, avoiding intra-amniotic hypertonic saline, and prompt antibiotic control of sepsis have together reduced obstetric DIC.

Curative — stepwise:

- **Remove the trigger urgently** — expedite delivery (abruption), evacuate the uterus (dead fetus, molar pregnancy), or control sepsis; this alone resolves the coagulopathy in most cases.
- **Restore circulating volume** with crystalloids (Ringer lactate) via two large-bore IV lines; colloids (human albumin) may supplement; dextran is avoided as it impairs platelet function and cross-matching.
- **Blood component replacement**, targeting platelet count >50,000/μL and fibrinogen >100–150 mg/dL:

Component	Volume/unit	Effect per unit	Practical point
Fresh-frozen plasma (FFP)	~250 mL	Raises fibrinogen 5–10 mg/dL	Dose 10–15 mL/kg; give if fibrinogen <150 mg/dL or PT/aPTT prolonged; must be ABO/Rh compatible
Cryoprecipitate	~15 mL (200 mg fibrinogen)	Raises fibrinogen 5–10 mg/dL	15–20 units (3–4 g) needed to raise baseline to ~150 mg/dL; preferred when fibrinogen is critically low (less volume than FFP)
Platelet concentrate	~50 mL	Raises count 5,000–10,000/μL	Give if <50,000/μL with active bleeding; 6–10 units transfused rapidly (over ~10 min); ABO/Rh specific
Packed RBC (PRBC)	250–300 mL	Raises Hb ~1 g/dL, Hct 3–4%	Maintain Hb >8 g/dL
Whole blood	~500 mL	Raises fibrinogen ~12.5 mg/dL + 10,000–15,000 platelets	Rarely used in modern practice

- **Massive transfusion protocol (MTP):** activated once 4–5 units of PRBC have been given within ~2 hours, or ≥10 units are anticipated. Fixed-ratio protocols (e.g., PRBC:FFP alternating rounds, with a platelet 6-pack and 1 unit cryoprecipitate added at intervals) speed delivery and limit dilutional coagulopathy; survival is best when the plasma:RBC ratio approaches 1:1, and worst near 1:8.
- **Adjuncts:**
  - **Vitamin K** 5–10 mg IM replenishes the consumed vitamin K–dependent factors II, VII, IX, X.
  - **Recombinant activated factor VIIa (rFVIIa)** 60–100 μg/kg IV can reverse DIC within 10 minutes but is **ineffective if fibrinogen <50 mg/dL or platelets <30,000/μL**, carries an arterial thrombosis risk, and is **not recommended as first-line** therapy.
- **Surgical management** if haemorrhage persists despite correction — uterine balloon tamponade, uterine compression (B-Lynch) sutures, uterine/internal iliac artery ligation, and hysterectomy as the definitive last step.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 39.8 — Coagulation cascade and laboratory assessment of clotting factor deficiency (DC Dutta's Obstetrics 9e, p.610)*

High-yield exam pointers

- Three trigger mechanisms: **endothelial injury / thromboplastin release / phospholipid release** — map each to its obstetric causes.
- Fibrinogen critical level: **<100 mg/dL** (Dutta's arbitrary threshold); clinically actionable threshold **<150 mg/dL** (Williams).
- Weiner clot observation test: no clot by **30 minutes** ⇒ fibrinogen <100 mg/dL.
- Component doses: FFP 10–15 mL/kg; 1 unit cryoprecipitate → fibrinogen +5–10 mg/dL; 1 unit platelets → count +5,000–10,000/μL; Vitamin K 5–10 mg IM.
- rFVIIa dose **60–100 μg/kg IV**; fails if fibrinogen <50 mg/dL or platelets <30,000/μL.
- MTP triggered at 4–5 units PRBC/2 hours; survival best near a **1:1 plasma:RBC ratio**.
- Hallmark clinical clue: **PPH with a well-contracted uterus**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Obstetrics additionally recommends intravenous heparin (5,000 units every 4–6 hours) in amniotic-fluid-embolism-related DIC and fibrinolytic inhibitors for persistent post-abruption bleeding; the current (26th) edition of Williams Obstetrics states that unfractionated heparin has now been abandoned and that antifibrinolytics (tranexamic acid, epsilon-aminocaproic acid) are not recommended as first-line therapy for consumptive coagulopathy, since fibrinolysis is itself a protective mechanism — the current guidance should be followed in practice.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e (Chapter 39, "Blood Coagulation Disorders in Obstetrics," pp.583–587); Williams Obstetrics 26e (Chapter 44, "Obstetrical Coagulopathies," pp.776–779).

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Discuss the pharmacology of prostaglandins. Mention their clinical application

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Prostaglandins are membrane-derived lipid autacoids (eicosanoids) synthesized on demand from arachidonic acid via the cyclo-oxygenase (COX) pathway. Unlike hormones, they are not

stored, act locally in a paracrine/autocrine fashion close to their site of synthesis, and are rapidly inactivated — properties that explain both their short duration of action and their wide, tissue-specific clinical uses.

Biosynthesis & classification

Step	Enzyme/process	Product
Membrane phospholipids → arachidonic acid	Phospholipase A2	Free arachidonic acid
Arachidonic acid → PGG2 → PGH2 (endoperoxide)	Cyclo-oxygenase-1 (constitutive) and cyclo-oxygenase-2 (inducible)	Prostaglandin H2 (common precursor)
PGH2 → tissue-specific prostaglandin	Cell-specific synthases	PGE2, PGF2α, PGI2 (prostacyclin), thromboxane A2 (TXA2), PGD2

Prostaglandin	Principal source	Receptor	Key physiological role
PGE2	Myometrium, decidua, cervix	EP1–EP4	Uterine contraction, cervical ripening, vasodilation, gastric cytoprotection
PGF2α	Corpus luteum, myometrium, endometrium	FP	Uterine/bronchial/vascular smooth-muscle contraction; luteolysis
PGI2 (prostacyclin)	Vascular endothelium	IP	Vasodilation, inhibits platelet aggregation
TXA2	Platelets	TP	Vasoconstriction, promotes platelet aggregation
PGD2	Mast cells	DP	Bronchoconstriction, vasodilation

Mechanism of action

All prostaglandin receptors are G-protein-coupled receptors (GPCRs); the intracellular second messenger determines the smooth-muscle effect.

Receptor	G-protein/second messenger	Effect
EP2, EP4, IP, DP	Gs → increased cyclic AMP	Smooth-muscle relaxation, vasodilation, inhibition of platelet aggregation
EP1, FP, TP	Gq → increased inositol trisphosphate (IP3)/Ca2+	Smooth-muscle contraction, platelet aggregation
EP3	Gi → decreased cyclic AMP	Smooth-muscle contraction

Pharmacological actions

System	Effect
Uterus	PGE2 and PGF2α stimulate myometrial contraction at any gestational age and ripen the cervix by increasing collagenase activity and altering the glycosaminoglycan matrix
Cardiovascular	PGE2/PGI2 vasodilate; PGF2α/TXA2 vasoconstrict; TXA2 promotes and PGI2 inhibits platelet aggregation
Respiratory	PGE2 bronchodilates; PGF2α and TXA2 bronchoconstrict — hazardous in asthma
Gastrointestinal	PGE2 increases mucus/bicarbonate and decreases acid secretion (cytoprotective); increases intestinal motility, producing diarrhoea as a side effect
Renal	PGE2/PGI2 maintain glomerular afferent-arteriolar blood flow
Fetal	PGE2 maintains patency of the fetal ductus arteriosus in utero; cyclo-oxygenase inhibitors (indomethacin) risk premature constriction
Ocular	PGF2α analogues increase uveoscleral outflow, lowering intraocular pressure
Reproductive	PGF2α is the physiological luteolytic signal causing regression of the corpus luteum

Pharmacokinetics: Biological half-life is seconds to a few minutes; ~95% is inactivated in a single pass through the pulmonary circulation by 15-hydroxyprostaglandin dehydrogenase. Because they are synthesized on demand rather than stored, systemic (parenteral/oral) exposure is brief, favouring local (intracervical/vaginal/rectal) routes for sustained clinical effect.

Clinical applications in obstetrics & gynaecology

Agent	Preparation/dose	Indication
Dinoprostone (PGE2) gel — Prepidil	Intracervical 0.5 mg; repeat every 6 h, maximum 3 doses/24 h	Pre-induction cervical ripening
Dinoprostone (PGE2) vaginal insert — Cervidil	10 mg, releases ~0.3 mg/hr; single dose in posterior fornix, removed after 12 h or at labour onset, ≥30 min before oxytocin	Pre-induction cervical ripening
Dinoprostone 20-mg suppository	Per vaginam/per rectum	Mid-trimester termination (12–20 weeks) and evacuation after fetal demise up to 28 weeks; also used off-label for atony, 20 mg PR/PV every 2 h
Misoprostol (PGE1 analogue)	Vaginal 25 μg every 3–6 h, or oral 50–100 μg every 3–6 h (off-label)	Cervical ripening/labour induction
Misoprostol	600–1000 μg rectally, orally, or sublingually (single dose)	Second-line uterotonic for postpartum haemorrhage (ACOG)
Mifepristone + misoprostol	Mifepristone 200 mg orally; after 24 h, misoprostol 800 μg (buccal/vaginal) for ≤70 days' gestation, or 400 μg every 3 h up to 5 doses for later first-trimester use	Medical termination of pregnancy
Carboprost tromethamine (15-methyl PGF2α, Hemabate)	250 μg IM; repeat every 15–90 min, maximum 8 doses	Second-line uterotonic for atony refractory to oxytocin

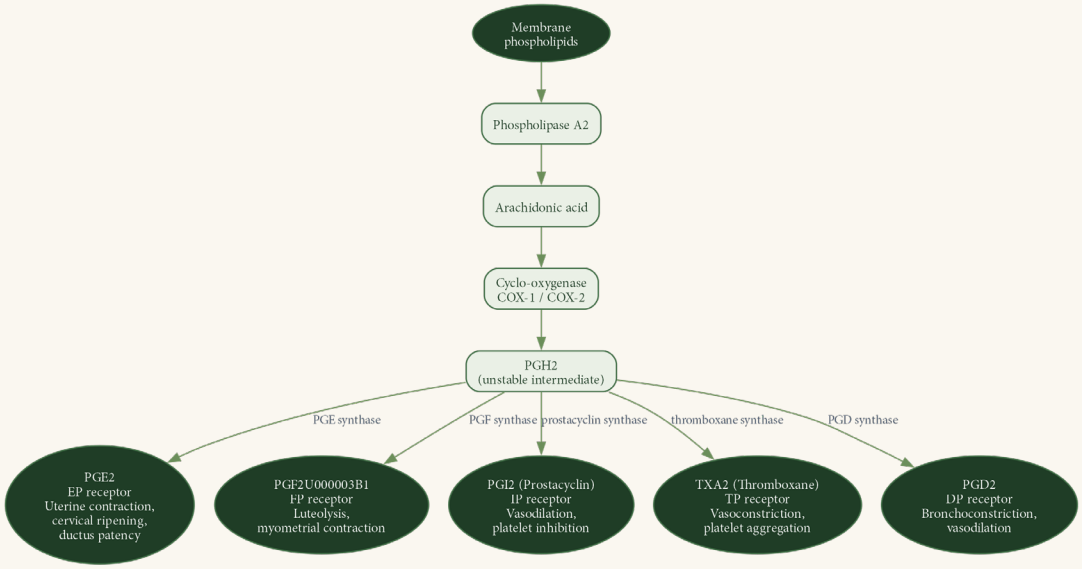
Clinical applications outside obstetrics & gynaecology

- **Misoprostol (PGE1)** — prevention of NSAID-induced peptic ulcer.
- **Alprostadil (PGE1)** — maintains ductus arteriosus patency in duct-dependent congenital cardiac disease in the neonate; also used intracavernosally for erectile dysfunction.
- **Epoprostenol/iloprost (PGI2 analogues)** — pulmonary arterial hypertension.
- **Latanoprost/travoprost (PGF2α analogues)** — first-line topical therapy for open-angle glaucoma.

Adverse effects & contraindications

Prostaglandin	Adverse effects	Contraindications
Dinoprostone (PGE2)	Uterine tachysystole (>5 contractions/10 min) with fetal heart rate change, diarrhoea, fever	Hypersensitivity, suspected fetal compromise or cephalopelvic disproportion, unexplained vaginal bleeding, six or more prior term pregnancies
Carboprost (PGF2α)	Diarrhoea, hypertension, vomiting, fever, flushing, tachycardia, arterial oxygen desaturation	Asthma, pulmonary hypertension, renal/hepatic/cardiac disease
Misoprostol (PGE1)	Diarrhoea, fever, shivering, tachysystole	Prior caesarean/uterine scar (avoid for induction)

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Prostaglandin biosynthesis pathway from membrane phospholipids to the five tissue-specific end products, each labelled with its receptor and principal action.

High-yield exam pointers

- Pathway mnemonic: **membrane phospholipid → arachidonic acid (phospholipase A2) → PGH2 (COX-1/COX-2) → PGE2/PGF2α/PGI2/TXA2 (specific synthases)**.
- **Carboprost** = 15-methyl PGF2α = Hemabate — 250 µg IM every 15–90 min, maximum 8 doses; avoid in **asthma**.
- **Misoprostol** for atony: 600–1000 µg PR/PO/sublingual (single dose).
- **Dinoprostone**: gel 0.5 mg intracervical (max 3 doses/24 h) vs insert 10 mg (0.3 mg/hr).

- **Mifepristone 200 mg + misoprostol 800 µg** — standard medical abortion regimen (≤70 days).
- **TXA2 clots, PGI2 flows** — opposite platelet/vascular effects from the same arachidonic acid precursor.
- **PGE2 keeps the ductus open**; NSAIDs/indomethacin close it.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Dosing above follows the American College of Obstetricians and Gynecologists (ACOG, 2019a) recommendations as printed in Williams Obstetrics 26th edition; DC Dutta's Gynaecology 7e covers the antiprostaglandin (cyclo-oxygenase-inhibitor) use in dysmenorrhoea but does not tabulate obstetric prostaglandin dosing to the same granularity, so the current guideline-based figures above should be used.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e (luteolysis); guideline: American College of Obstetricians and Gynecologists (ACOG 2019a, 2020b), World Health Organization (WHO 2012, 2018).

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Discuss the physiology of amniotic fluid. Describe clinical importance of Amniotic fluid abnormalities

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — Amniotic fluid (liquor amnii) is the clear fluid filling the amniotic cavity around the fetus, of mixed maternal-fetal origin in early pregnancy but derived predominantly from fetal urine and lung fluid in the third trimester. It cushions the fetus, permits growth and movement, and its volume is a key ultrasound marker of fetal well-being.

Physiology of amniotic fluid

Origin and circulation

- First half of pregnancy: the fluid is essentially a transudate across the amnion and the un-keratinised fetal skin (skin keratinises by ~20 weeks), so its composition resembles fetal/maternal plasma.
- Second half of pregnancy: fetal urination becomes the dominant source; fluid is contaminated by fetal urinary metabolites and its composition changes accordingly.
- Circulation is rapid — radioactive-sodium clearance studies show the water content is completely turned over roughly every **3 hours**.

Volume across gestation

Gestational age	Approximate amniotic fluid volume
12 weeks	~50 mL
20 weeks	~400 mL
36–38 weeks (peak)	~1000 mL
Term (40 weeks)	600–800 mL
43 weeks (post-term)	~200 mL

Production and resorption (late pregnancy, per 24-hour pathway)

Pathway	Effect	Approx. daily volume
Fetal urination	Production	1000 mL
Fetal lung fluid secretion	Production	350 mL
Fetal swallowing	Resorption	750 mL
Intramembranous flow (fetal placental-surface vessels)	Resorption	400 mL
Transmembranous flow (across amnion into uterine wall)	Resorption	Minimal

Physical and chemical properties

- Faintly alkaline reaction; low specific gravity of 1.010.
- Increasingly hypotonic to maternal serum as gestation advances (amniotic fluid ~250–260 mOsm/L vs maternal serum ~280 mOsm/L at term); an osmolarity of ~250 mOsm/L is a marker of fetal maturity.
- Composition — **water 98–99%**; solids 1–2%: *organic* (protein, non-protein nitrogen, glucose, urea, uric acid, creatinine, lipids, hormones such as prolactin, insulin, renin), *inorganic* (sodium, chloride, potassium close to maternal blood levels), and *suspended particles* (lanugo, desquamated fetal skin cells, vernix caseosa, cells shed from the fetal respiratory, urinary and genital tracts).
- Colour changes are diagnostically useful: colourless early in pregnancy → pale straw near term; **meconium-stained (green)** suggests fetal distress; **golden** colour with Rh-alloimmunisation (haemolysis/bilirubin); **greenish-yellow (saffron)** in post-maturity; **dark** discolouration with concealed haemorrhage; **dark brown ("tobacco juice")** with intrauterine fetal death.

Functions

- *During pregnancy*: shock-absorber protecting the fetus from trauma; maintains an even fetal temperature; distends the amniotic sac allowing free fetal growth and movement and preventing

adhesions between fetal parts and the sac; provides the fetus's water supply (nutritive value itself is negligible).

- *During labour*: the forewaters form a hydrostatic wedge that aids cervical dilatation; protects placental circulation from the pressure of uterine contractions while membranes are intact; guards against umbilical cord compression; flushes the birth canal at full dilatation and, through its bacteriostatic action, helps prevent ascending infection.

Clinical importance of amniotic fluid volume abnormalities

Assessment (ultrasound criteria) — the uterus is divided into four quadrants; the amniotic fluid index (AFI) is the sum of the single deepest vertical pocket in each quadrant, while the single/maximum deepest pocket (SDP) is measured in one sagittal plane (pocket must be ≥1 cm wide, free of cord/fetal parts).

Category	AFI	SDP
Oligohydramnios	<5 cm	<2 cm
Normal	5–24 cm	2–8 cm
Mild hydramnios	25–29.9 cm	8–9.9 cm
Moderate hydramnios	30–34.9 cm	10–11.9 cm
Severe hydramnios	≥35 cm	≥12 cm

Oligohydramnios

Category	Causes
Fetal	Chromosomal/structural anomalies, renal agenesis, obstructive uropathy (posterior urethral valves), fetal growth restriction, post-maturity, spontaneous rupture of membranes, intrauterine infection
Drug-related	Prostaglandin-synthetase inhibitors (NSAIDs), ACE inhibitors/angiotensin-receptor blockers
Maternal	Hypertensive disorders/pre-eclampsia, uteroplacental insufficiency, dehydration
Idiopathic	A substantial minority

Complications: (1) fetal — pulmonary hypoplasia, deformation syndrome (facial/limb contractures, clubfoot, Potter-type compression deformities), cord compression with variable decelerations, higher perinatal mortality, association with chromosomal abnormality when growth restriction coexists; (2) maternal — malpresentation, prolonged/obstructed labour, increased operative delivery.

Management (stepwise):

- Detailed anomaly scan with fetal renal tract survey and Doppler; exclude membrane rupture.

- Correct reversible causes — maternal oral hydration, stop offending drugs.
- Serial growth scans and umbilical artery Doppler if growth restriction/hypertension coexist.
- Amnioinfusion (transabdominal or intrapartum transcervical) to relieve cord compression and improve visualisation; evidence supports improved short-term AFI/reduced variable decelerations but not a consistent reduction in caesarean rate.
- Antenatal corticosteroids if preterm delivery anticipated.
- Time delivery on fetal status — isolated term oligohydramnios: induce; with growth restriction/abnormal Doppler/reduced fetal movement: expedite delivery.

Polyhydramnios (hydramnios)

Category	Causes
Fetal (~20%)	Anencephaly/open neural-tube defects (transudation from exposed meninges, absent swallowing reflex), oesophageal/duodenal atresia, facial clefts and neck masses (impaired swallowing), hydrops fetalis (Rh-alloimmunisation, non-immune, cardiothoracic anomaly, TORCH/parvovirus B19), aneuploidy
Placental	Chorioangioma
Multifetal gestation	Ten-fold more frequent; twin-to-twin transfusion syndrome — recipient twin develops polyhydramnios (donor develops oligohydramnios)
Maternal	Diabetes mellitus (maternal hyperglycaemia → fetal hyperglycaemia → fetal osmotic diuresis), cardiac/renal disease
Idiopathic	~50–60%

Complications: (1) maternal — pre-eclampsia, malpresentation with persistent floating head, preterm labour/premature rupture of membranes, placental abruption at membrane rupture, cord prolapse, uterine inertia, increased operative delivery, postpartum haemorrhage from uterine atony, subinvolution/puerperal sepsis; (2) fetal — perinatal mortality up to ~50% in severe/acute cases, chiefly from prematurity and congenital anomaly.

Management (stepwise):

- Detailed anomaly scan, glucose tolerance testing, Rh status/antibody screen, amniotic-fluid alpha-fetoprotein if neural-tube defect suspected.
- Mild, asymptomatic hydramnios (common in mid-trimester): expectant care only; volume often decreases as pregnancy advances.
- Symptomatic hydramnios: supportive bed rest; **sulindac (a COX-2-selective NSAID) 200 mg 12-hourly** reduces fetal urine output and is the most effective medical option for unexplained cases

— used under monitoring, with fetal echocardiographic surveillance for ductal constriction if given beyond early third trimester.

- Therapeutic amnioreduction for maternal distress: **slow decompression at ~500 mL/hour**, stopping once the AFI falls below 25 cm; may need repeating as fluid re-accumulates.
- Delivery: induce at term; perform controlled amniotomy with a stabilising oxytocin infusion after confirming a stable longitudinal lie, to avoid sudden decompression, cord prolapse or abruption; remain vigilant for cord prolapse, uterine inertia and postpartum haemorrhage.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 3.12 — Amniotic fluid volume is measured to determine AFI (DC Dutta's Obstetrics 9e, p.62)*

High-yield exam pointers

- AFI = sum of the deepest vertical pocket in each of 4 uterine quadrants; normal 5–24 cm.
- Oligohydramnios: AFI <5 cm or SDP <2 cm; anhydramnios = no measurable pocket.
- Hydramnios grading (AFI): mild 25–29.9, moderate 30–34.9, severe ≥35 cm.
- Production: fetal urine (1000 mL/day) + lung fluid (350 mL/day); resorption: fetal swallowing (750 mL/day) + intramembranous flow (400 mL/day).
- Complete fluid turnover every ~3 hours; osmolarity ~250 mOsm/L is a fetal maturity marker.
- Anencephaly associated with hydramnios in ~50%; diabetes in ~15–20% of hydramnios cases.
- Sulindac 200 mg 12-hourly for symptomatic hydramnios; amnioreduction at ~500 mL/hour.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Current practice (American College of Obstetricians and Gynecologists, 2020) increasingly favours the single deepest pocket over the AFI to diagnose oligohydramnios, since the AFI criterion labels more pregnancies as oligohydramnios without proven improvement in outcome — a nuance not always reflected in older textbook descriptions.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e; Williams Obstetrics 26e; American College of Obstetricians and Gynecologists (ACOG) practice guidance on amniotic fluid volume assessment.

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Discuss the uses of progesterone in Gynaecology

Asked in: Paper I 26-May-2025 — RGUHS MS Obstetrics & Gynaecology

Definition — Progesterone is a natural C-21 steroid secreted mainly by the theca-lutein cells of the corpus luteum, in trace amounts by the adrenal cortex, and by the placenta in pregnancy; it converts an oestrogen-primed proliferative endometrium into secretory endometrium. Natural progesterone is rapidly inactivated by first-pass hepatic metabolism when taken orally, so it is administered parenterally, vaginally, or as micronized/synthetic progestogens (progestins) that resist this breakdown.

Diagnostic use

Test	Dose	Interpretation
Progestin (progesterone) challenge test — used in the work-up of amenorrhoea	Medroxyprogesterone acetate (MPA) 10 mg orally daily for 5 days	Withdrawal bleeding within 2–7 days of stopping confirms (i) an intact hypothalamo-pituitary-ovarian axis, (ii) adequate endogenous oestrogen (>40 pg/mL), (iii) a responsive endometrium, and (iv) a patent utero-vaginal outflow tract — such patients respond to ovulation-induction agents. No bleeding suggests outflow-tract obstruction (e.g., Asherman syndrome) or a hypo-oestrogenic state (limitation: fluctuating oestrogen in hypothalamic amenorrhoea/early premature ovarian failure may still bleed).

Therapeutic uses

Indication	Agent(s)	Dose / regimen
Contraception	Progestin-only pill (minipill)	Norethisterone/desogestrel, continuous daily
	Depot medroxyprogesterone acetate (DMPA), IM	150 mg IM every 3 months (WHO: up to 4 months); Depo-subQ 104 mg subcutaneous every 3 months
	Norethisterone enanthate (NET-EN), IM	200 mg every 2 months
	Subdermal implant (etonogestrel, Implanon)	Effective for ~3 years
	Levonorgestrel intrauterine system (LNG-IUS)	Releases levonorgestrel intrauterine; effective ~5 years

Indication	Agent(s)	Dose / regimen
	Emergency contraception	Levonorgestrel 0.75 mg stat + 0.75 mg 12 h later, **or** 1.5 mg as a single dose — within 72 h (effective up to 120 h)
Abnormal uterine bleeding (ovulatory dysfunction, formerly "dysfunctional uterine bleeding")	Norethisterone or MPA	To arrest acute bleeding: 5 mg thrice daily till bleeding stops (usually 3–7 days), continued to complete 21 days. For cycle regulation: same agent from day 5–25 or day 15–25 for 3 cycles. More effective in anovulatory than ovulatory bleeding; ideal in adolescents and perimenopausal women
Endometriosis / adenomyosis	MPA, dydrogesterone, or 19-norethisterone derivatives	Norethisterone 5 mg or MPA 10 mg 2–3 times daily continuously for 6–9 months (induces amenorrhoea via decidualisation and atrophy of ectopic endometrium)
	Depot MPA, IM (family-complete women)	100 mg every 2 weeks × 4 doses, then 200 mg monthly × 4 doses
	LNG-IUS / etonogestrel implant	Alternative for pelvic pain and adenomyosis
Dysmenorrhoea	Dydrogesterone	5 mg from day 5 for 20 days; relieves pain by reducing uterine contractility without suppressing ovulation
Luteal phase defect	Progesterone in oil, IM	12.5 mg daily from 2–3 days after ovulation until menstruation, or until 10–12 weeks if conception occurs
	Micronized progesterone	100 mg thrice daily, oral or vaginal; or vaginal suppository 25 mg twice daily from 2–3 days after the basal-body-temperature rise

Indication	Agent(s)	Dose / regimen
Luteal-phase support in assisted reproduction (ART/IVF)	Vaginal micronized progesterone (gel/tablet), IM progesterone in oil, or oral dydrogesterone	Vaginal gel 90 mg once daily or tablet 100–200 mg twice daily; IM 25–50 mg daily; oral dydrogesterone 30 mg daily — started on the day of oocyte retrieval/embryo transfer, continued to 8–10 weeks' gestation if pregnancy occurs
Endometrial hyperplasia / endometrial intraepithelial neoplasia (EIN) and early well-differentiated endometrial carcinoma — fertility-sparing therapy or poor surgical candidates	17α-hydroxyprogesterone caproate, IM	1000 mg daily for 1 week, then weekly for 3 months, then every 2 weeks for 1 year
	MPA, IM (or oral)	400 mg IM weekly for 3 months then every 2 weeks for 1 year (oral MPA up to 150 mg/day, or megestrol acetate 160 mg/day, are alternatives)
	LNG-IUS	Alternative in poor surgical candidates, particularly early-stage (IA, grade 1) disease
	—	Response depends on tumour steroid-receptor density (highest in well-differentiated disease); repeat endometrial biopsy every 3 months to confirm regression
Premenstrual syndrome	Dydrogesterone (traditional use)	5 mg twice daily from day 5 for 20 days, for 3–6 cycles — *see coverage note below*
Postponement of menstruation	Norethisterone	5 mg thrice daily, started at least 3 days before the expected date and continued until postponement is no longer required; menses begin 48–72 h after stopping. No contraceptive protection during use
Hormone replacement therapy (HRT)	Any progestin (e.g., MPA, dydrogesterone, micronized progesterone), added to oestrogen in women with an intact uterus	Cyclic — for the last 12–14 days of each cycle; or continuous-combined daily — to oppose oestrogen-driven endometrial proliferation and prevent hyperplasia/carcinoma

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 8.8 — Endometrium in secretory and menstrual phase. Note the marked tortuosity of the glands (DC Dutta's Gynaecology 7e, p.93)*

High-yield exam pointers

- Progestin challenge test dose: **MPA 10 mg orally × 5 days**; positive withdrawal bleed = intact HPO axis + adequate oestrogen.
- Contraceptive depot doses: **DMPA 150 mg IM/3 months; NET-EN 200 mg IM/2 months.**
- Emergency contraception: **levonorgestrel 1.5 mg single dose (or 0.75 mg + 0.75 mg 12 h apart), within 72 h.**
- Endometriosis "pseudo-pregnancy" regimen: **norethisterone/MPA 5–10 mg 2–3 times daily × 6–9 months** → amenorrhoea.
- Fertility-sparing regimen for EIN/early endometrial cancer: **17-OHP caproate 1000 mg IM daily ×1 week → weekly ×3 months → 2-weekly ×1 year**, or **MPA 400 mg IM weekly ×3 months → 2-weekly ×1 year**, with 3-monthly biopsy.
- Luteal phase defect dose: **progesterone-in-oil 12.5 mg IM daily starting 2–3 days post-ovulation.**
- Remember: progesterone acts as an anti-oestrogen on the endometrium (↓ oestrogen receptors, induces oestradiol dehydrogenase, ↓ endometrial mitoses).

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Gynaecology (traditional teaching) lists dydrogesterone for premenstrual syndrome, but current evidence — large placebo-controlled trials and a Cochrane systematic review cited in Speroff's Clinical Gynecologic Endocrinology 9e — does not show progesterone/progestins superior to placebo for premenstrual syndrome; selective serotonin re-uptake inhibitors and lifestyle measures are now first-line. Also, the older term "atypical endometrial hyperplasia" has been replaced by "endometrial intraepithelial neoplasia (EIN)" per the 2015 ACOG/Society of Gynecologic Oncology reclassification (retained in Berek & Novak 16e), though many pathology reports still use the older WHO terminology.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e.

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Enumerate the hormones secreted by pituitary gland and its synthesis function of the hormones of pituitary gland

Asked in: Paper I 06-Apr-2026 — RGUHS MS Obstetrics & Gynaecology

Definition — The pituitary (hypophysis) lies in the sella turcica and has two embryologically distinct parts. The **anterior pituitary (adenohypophysis)** arises from oral ectoderm (Rathke pouch) and is controlled by hypothalamic releasing/inhibiting hormones carried via the hypophyseal portal venous system. The **posterior pituitary (neurohypophysis)** is a neuroectodermal downgrowth that only stores and releases hormones actually synthesized in the hypothalamus and delivered to it by axonal transport.

Hormones of the anterior pituitary

Hormone	Secretory cell	Chemical nature	Principal action
Growth hormone (GH/somatotropin)	Acidophil — somatotrope	Single-chain polypeptide (191 amino acids)	Skeletal/soft-tissue growth via hepatic insulin-like growth factor-1 (IGF-1); anti-insulin (diabetogenic) effect
Prolactin (PRL)	Acidophil — lactotrope	Polypeptide	Mammary ductal/lobular growth and lactogenesis
Thyroid-stimulating hormone (TSH)	Basophil — thyrotrope	Glycoprotein (α + β subunit)	Thyroid follicular growth; stimulates T3/T4 synthesis and release
Adrenocorticotropic hormone (ACTH)	Basophil — corticotrope	Polypeptide (39 amino acids), cleaved from POMC	Adrenal cortex (zona fasciculata/reticularis) — cortisol and androgen synthesis
Follicle-stimulating hormone (FSH)	Basophil — gonadotrope	Glycoprotein (α + β subunit)	Recruits/matures the Graafian follicle; induces granulosa aromatase (androgen → estrogen) and its own + LH receptors
Luteinizing hormone (LH)	Basophil — gonadotrope (same cell as FSH)	Glycoprotein (α + β subunit)	Theca-cell androgen synthesis; mid-cycle **LH surge** triggers oocyte meiotic resumption and ovulation; forms/maintains the corpus luteum

Hormone	Secretory cell	Chemical nature	Principal action
Melanocyte-stimulating hormone (MSH)	POMC by-product of the corticotrope	Peptide	Skin pigmentation (linea nigra, chloasma of pregnancy)

Synthesis & regulation — anterior pituitary

- The adenohypophysis differentiates into five secretory-cell types producing six major protein hormones (Williams Obstetrics 26e); by the 17th fetal week the pituitary synthesizes and stores all of them.
- Hypothalamic releasing hormones — gonadotropin-releasing hormone (GnRH), thyrotropin-releasing hormone (TRH), corticotropin-releasing hormone (CRH), growth-hormone-releasing hormone (GHRH) — and the inhibiting hormones (dopamine/prolactin-inhibiting factor for prolactin; somatostatin for GH) reach the gland via the hypophyseal portal vessels and act on cell-surface receptors, chiefly through cyclic AMP–protein kinase and Ca^{2+}/phosphokinase-C second-messenger cascades, to drive pulsatile gene transcription and hormone release (DC Dutta's Gynaecology 7e).
- FSH, LH and TSH are glycoproteins assembled from a common α-subunit (92 amino acids; single gene on chromosome 6p21.1–23, also shared with human chorionic gonadotropin) non-covalently linked to a hormone-specific β-subunit, which confers the hormone's biological and immunological specificity (Speroff 9e).
- GH and prolactin are non-glycosylated single-chain polypeptides synthesized independently by somatotropes and lactotropes; prolactin release is under tonic dopaminergic inhibition and is disinhibited by TRH and by suckling.
- ACTH, β-lipotropin, β-endorphin and MSH-related peptides are all cleaved post-translationally from one large precursor, pro-opiomelanocortin (POMC), synthesized by the corticotrope under CRH drive and suppressed by cortisol feedback (Speroff 9e).
- Finished hormones are packaged into secretory granules and released episodically by exocytosis; there is no direct neuronal connection between hypothalamus and adenohypophysis — control is entirely humoral, via the portal system.

Hormones of the posterior pituitary

Hormone	Hypothalamic nucleus of synthesis	Chemical nature	Principal action
Oxytocin	Paraventricular nucleus (predominant)	Nonapeptide	Myometrial contraction in labour (Ferguson reflex); milk-ejection reflex via myoepithelial contraction

Hormone	Hypothalamic nucleus of synthesis	Chemical nature	Principal action
Vasopressin / antidiuretic hormone (ADH, arginine vasopressin)	Supraoptic nucleus (predominant)	Nonapeptide (differs from oxytocin by 2 amino acids)	Renal free-water reabsorption via V2 receptors in the collecting duct; vasoconstriction via V1 receptors at high concentration

Synthesis & transport — posterior pituitary

- Oxytocin and vasopressin are synthesized as larger prohormones in the cell bodies of the magnocellular neurons of the supraoptic and paraventricular nuclei of the hypothalamus (Williams Obstetrics 26e; DC Dutta's Gynaecology 7e).
- Each prohormone is bound to its own carrier protein, **neurophysin**, and packaged into membrane-bound secretory vesicles within the neuron.
- The prohormone-neurophysin complex is carried by axonal flow down the hypothalamo-hypophyseal tract to nerve terminals in the posterior pituitary (pars nervosa/neural lobe); the prohormone is cleaved enzymatically to the mature nonapeptide plus neurophysin **during this axonal transport**, not at the site of synthesis (Williams Obstetrics 26e).
- The mature hormone is stored in the neural lobe and released into the systemic circulation by exocytosis on appropriate stimulation — cervical/vaginal stretch and suckling (Ferguson reflex) for oxytocin, and rising plasma osmolality or falling circulating blood volume for vasopressin.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 7.1 — Anatomy of the hypothalamus and pituitary. The hypothalamus, anterior pituitary and the portal system of blood supply is shown (DC Dutta's Gynaecology 7e, p.73)*

High-yield exam pointers

- 5 anterior pituitary cell types → 6 major hormones: GH, prolactin, ACTH, TSH, FSH, LH (gonadotropes make both FSH and LH).
- Common **α-subunit** (92 amino acids, chromosome 6p21.1–23) shared by FSH/LH/TSH/hCG; the **β-subunit** confers hormone specificity — a classic viva question.
- ACTH and MSH-related peptides share the same **POMC** precursor — explains hyperpigmentation in Addison disease and in pregnancy (chloasma, linea nigra).
- Posterior pituitary hormones are **stored and released, not synthesized, there** — synthesis is in the supraoptic (mainly ADH) and paraventricular (mainly oxytocin) hypothalamic nuclei, carried down by neurophysin.

- Oxytocin and vasopressin are both **nonapeptides** differing by only 2 amino acids.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> The pars intermedia and a discrete MSH-secreting cell population are well developed only in fetal life and largely regress in the adult human pituitary; most current teaching therefore treats MSH-related peptides as POMC by-products of the corticotrope rather than as output of a separate anatomical lobe.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e.

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Follow up of hydatiform mole

Asked in: Paper I 24-Sep-2025 — RGUHS MS Obstetrics & Gynaecology

Definition — Follow-up of hydatidiform mole is the mandatory period of surveillance after uterine evacuation, based chiefly on serial serum beta human chorionic gonadotropin (β-hCG) estimation, undertaken to detect persistent gestational trophoblastic neoplasia (GTN) at the earliest possible stage. Malignant sequelae follow **15–20% of complete moles and 1–5% of partial moles** (Williams Obstetrics 26e); since the disease can be clinically silent while remaining fully curable if caught early, follow-up must not be omitted even after hysterectomy.

Serum β-hCG surveillance protocol

Stage	Frequency	Target/duration
Baseline	Single estimation within 48 hours of evacuation	Reference value for the trend
Active phase	**Weekly serum β-hCG**	Until 3 consecutive weekly readings are normal/undetectable — usually achieved by **4–8 weeks** (median 6–7 weeks for complete mole, 6 weeks for partial mole)
Consolidation phase	**Monthly serum β-hCG**	For **6 consecutive months** after the first normal reading
If chemotherapy is required	Weekly β-hCG during treatment	Continue monthly follow-up for 1 year after hCG becomes normal post-chemotherapy

- The assay used must detect **all hCG iso-forms**, not merely the intact molecule measured by routine urine pregnancy kits.
- Early in follow-up, the less expensive immunological test may be used serially; once the titre falls low, it is replaced by a **more sensitive serum radioimmunoassay**.
- Hysterectomy at the time of evacuation reduces but does **not eliminate** the need for hCG follow-up — persistent GTN still occurs in 3–5% of cases after hysterectomy.

Clinical and radiological follow-up

- **History** at every visit — ask specifically for irregular vaginal bleeding, persistent cough, haemoptysis, or breathlessness (pointers to pulmonary metastasis).
- **Abdomino-vaginal examination** — assess uterine involution, regression of theca-lutein cysts (should resolve within ~2 months), and inspect the anterior vaginal wall for bluish, vascular metastatic deposits (never biopsy these — risk of severe haemorrhage).
- First pelvic examination is done about **1 week after evacuation**.
- **Chest X-ray** — repeated only if the baseline film was abnormal (every 4 weeks until remission is confirmed, then 3-monthly for the rest of follow-up) or if a normal baseline film's counterpart hCG titre later plateaus or rises.
- Cross-sectional imaging (ultrasound/CT/MRI) is reserved for cases in which hCG or clinical findings suggest metastatic disease — it is **not routine**.

Contraceptive advice during follow-up

Method	Advice during surveillance
Barrier methods	Safe throughout; first choice if compliance with follow-up is uncertain
Combined oral contraceptive pills	Safe once counselling is given; conventionally started once the β-hCG value is normal
Injectable progestin (depot medroxyprogesterone acetate)	Safe
Intrauterine device	**Contraindicated until β-hCG becomes undetectable** — risk of uterine perforation if invasive mole is present, and causes irregular bleeding that can mimic recurrent disease
Surgical sterilization	Option once family is complete; may be combined with the index hysterectomy

- **Rationale:** a rise in hCG from a fresh pregnancy is otherwise indistinguishable from a rise due to persistent trophoblastic disease.
- **Duration:** effective contraception is required for the entire hCG surveillance window. Classical teaching (DC Dutta) advises avoiding pregnancy for up to 1 year, but permits conception after a

minimum of **6 months once the hCG titre is confirmed negative** if the patient desires — the same practical duration given in Williams Obstetrics 26e and Berek & Novak's Gynecology 16e (effective contraception for the ~6-month monthly-surveillance interval, after which pregnancy is allowed).

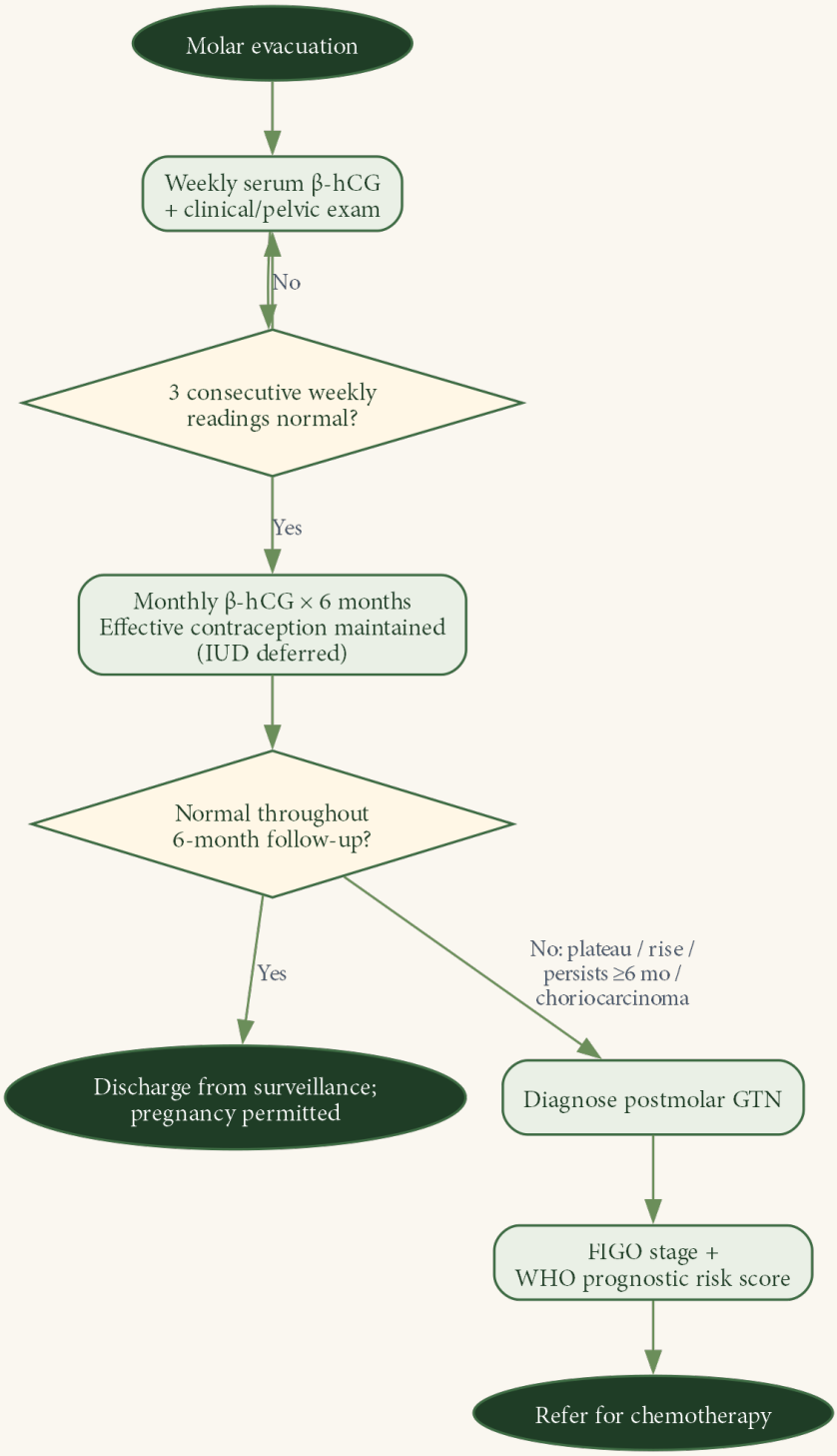
- If pregnancy occurs during surveillance, an hCG level should be checked **3 weeks after the end of that pregnancy** to exclude coexisting trophoblastic disease.

Criteria signalling failure of follow-up (postmolar GTN)

FIGO/WHO diagnostic criterion	Detail
Plateaued β-hCG	≤10% change over 4 weekly measurements across ≥3 weeks (days 1, 7, 14, 21)
Rising β-hCG	>10% rise over 3 consecutive weekly measurements across ≥2 weeks (days 1, 7, 14)
Persistently detectable β-hCG	Titre remains detectable at **6 months or more** after evacuation
Histology	Biopsy/curettage shows **choriocarcinoma**

Any one criterion diagnoses GTN. Supporting clinical "unfavourable" signs seen during follow-up: persistent ill health, continuing/irregular bleeding, respiratory symptoms, uterine subinvolution, vaginal metastasis, and a "cannon-ball" chest X-ray shadow. A confirmed diagnosis is staged anatomically (FIGO stage I–IV) and risk-scored by the modified WHO prognostic index (0–6 = low risk, ≥7 = high risk), and the patient is referred for chemotherapy (single-agent methotrexate or actinomycin-D for low risk; multi-agent EMA-CO for high risk) rather than being managed within the follow-up protocol itself.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Follow-up algorithm for hydatidiform mole, from molar evacuation through hCG surveillance to discharge or diagnosis of postmolar GTN.

High-yield exam pointers

- **"Weekly till negative (4–8 wk), then monthly × 6 months"** — the protocol to write verbatim.

- Malignant sequelae: **complete mole 15–20%, partial mole 1–5%**; persists in 3–5% even after hysterectomy.
- **IUD contraindicated** until hCG undetectable; barrier/COC/DMPA all safe.
- Avoid pregnancy through the surveillance window — classically **1 year**, or a minimum of **6 months** after a negative titre if desired.
- FIGO/WHO criteria for postmolar GTN: **plateau ×4 over 3 weeks; rise ×3 over 2 weeks; hCG detectable ≥6 months; choriocarcinoma on histology.**
- WHO prognostic score **0–6 = low risk (single-agent chemo), ≥7 = high risk (EMA-CO)**.
- Theca-lutein cysts regress by ~2 months; vaginal metastatic nodules must **never be biopsied**.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> DC Dutta's Obstetrics 9e is the classical Indian-exam source for the follow-up intervals and contraceptive advice above; the diagnostic criteria for postmolar gestational trophoblastic neoplasia and the FIGO anatomical staging with modified WHO prognostic scoring are taken from Williams Obstetrics 26e, which both DC Dutta's Obstetrics and Berek & Novak's Gynecology 16e concur with in substance.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Obstetrics 9e; Williams Obstetrics 26e; Berek & Novak's Gynecology 16e; FIGO (2009) staging and diagnostic scoring system for gestational trophoblastic neoplasia.

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Genetics of recurrent pregnancy loss

Asked in: Paper I 06-Apr-2026 — RGUHS MS Obstetrics & Gynaecology

Definition — Recurrent pregnancy loss (RPL) is two or more (American Society for Reproductive Medicine, ASRM-2013) or, by the older Royal College of Obstetricians and Gynaecologists (RCOG)/European Society of Human Reproduction and Embryology (ESHRE) criterion, three or more spontaneous losses confirmed by ultrasound or histopathology, before 20-24 weeks. **Primary RPL** occurs in a woman with no prior live birth; **secondary RPL** follows one (Williams). Genetic

abnormalities are the largest identifiable contributor — either a **fetal/embryonic** chance aneuploidy or a recurring **parental** structural rearrangement.

Classification of genetic causes

Category	Examples	Approximate contribution
Fetal/embryonic numerical abnormality (aneuploidy)	Autosomal trisomy (13, 16, 18, 21, 22 commonest), monosomy X (45,X), triploidy/polyploidy	Cause of 50-75% of *all* first-trimester miscarriages; in RPL couples, euploid (chromosomally normal) abortuses are relatively *more* frequent than in sporadic loss, especially under age 35
Parental structural chromosomal rearrangement	Balanced reciprocal translocation, balanced Robertsonian translocation, pericentric/paracentric inversion, sex-chromosome mosaicism	2-5% of couples with RPL (Williams: 2-4%; Speroff: ~5%)
Submicroscopic/molecular factors	Copy-number variants below karyotype resolution (picked up only on chromosomal microarray/next-generation sequencing), skewed X-chromosome inactivation (>90% preferential inactivation of one X), gonadal/germline mosaicism, single-gene defects	Emerging category; clinically relevant copy-number variants found in ~1.6% of losses labelled "euploid" by conventional karyotype
Gametic (sperm) aneuploidy	Abnormal sperm morphology, DNA fragmentation, chromosome non-disjunction	Minor; sperm aneuploidy rarely exceeds 1-2% and contributes far less than oocyte aneuploidy

Mechanisms of fetal aneuploidy

- Over 90% of miscarriage-associated chromosomal abnormalities are **numerical** (aneuploidy/polyploidy); the remainder are structural rearrangements or mosaicism.
- Most trisomies arise from **maternal meiotic non-disjunction**; oocyte aneuploidy is <10% before age 35 but rises steeply, approaching 100% by age 45 — the chief reason miscarriage risk climbs with maternal age.
- **Monosomy X (45,X)** is the single most frequent specific chromosomal abnormality among abortuses.
- **Triploidy** (69 chromosomes) follows fertilisation of a normal ovum by two sperm (diandric, → partial mole) or a diploid ovum by one sperm (digynic); triploid conceptuses almost always abort early.

- A normal 46,XX karyotype on products of conception (POC) does **not** exclude a genetic cause — it may reflect maternal cell contamination of the specimen, or a submicroscopic defect undetectable by conventional karyotyping.

Parental chromosomal rearrangements — mechanism and offspring risk

Type	Mechanism	Population prevalence	Risk of an abnormal (unbalanced) pregnancy
Balanced **reciprocal translocation**	Segment exchange between two non-homologous chromosomes; carrier is phenotypically normal	~1 in 600 births	5-30% if ascertained after the birth of an abnormal child; ~5% if ascertained incidentally (e.g., infertility work-up)
Balanced **Robertsonian translocation**	Fusion of the long (q) arms of two acrocentric chromosomes (13, 14, 15, 21, 22) at one centromere; carrier has 45 chromosomes	~1 in 1000 individuals	~15% if the mother is the carrier, ~2% if the father is; a **homologous** Robertsonian translocation (both copies of the same chromosome) yields no normal gametes at all
Pericentric inversion	Breaks in both p and q arms spanning the centromere → duplication-deletion gametes	inv(9)(p11q12) is a normal variant in ~1% of the population	5-10% if ascertained after an abnormal child; 1-3% if ascertained otherwise
Paracentric inversion	Break confined to one arm; centromere not included	—	Gametes are either balanced or so grossly abnormal that fertilisation fails; risk of a *liveborn* abnormal child is very low, though infertility can result

Robertsonian translocations are found in fewer than 5% of couples evaluated for RPL and are **not** a major cause of miscarriage in isolation, but any fetus/child found to carry an unbalanced translocation warrants karyotyping of both parents.

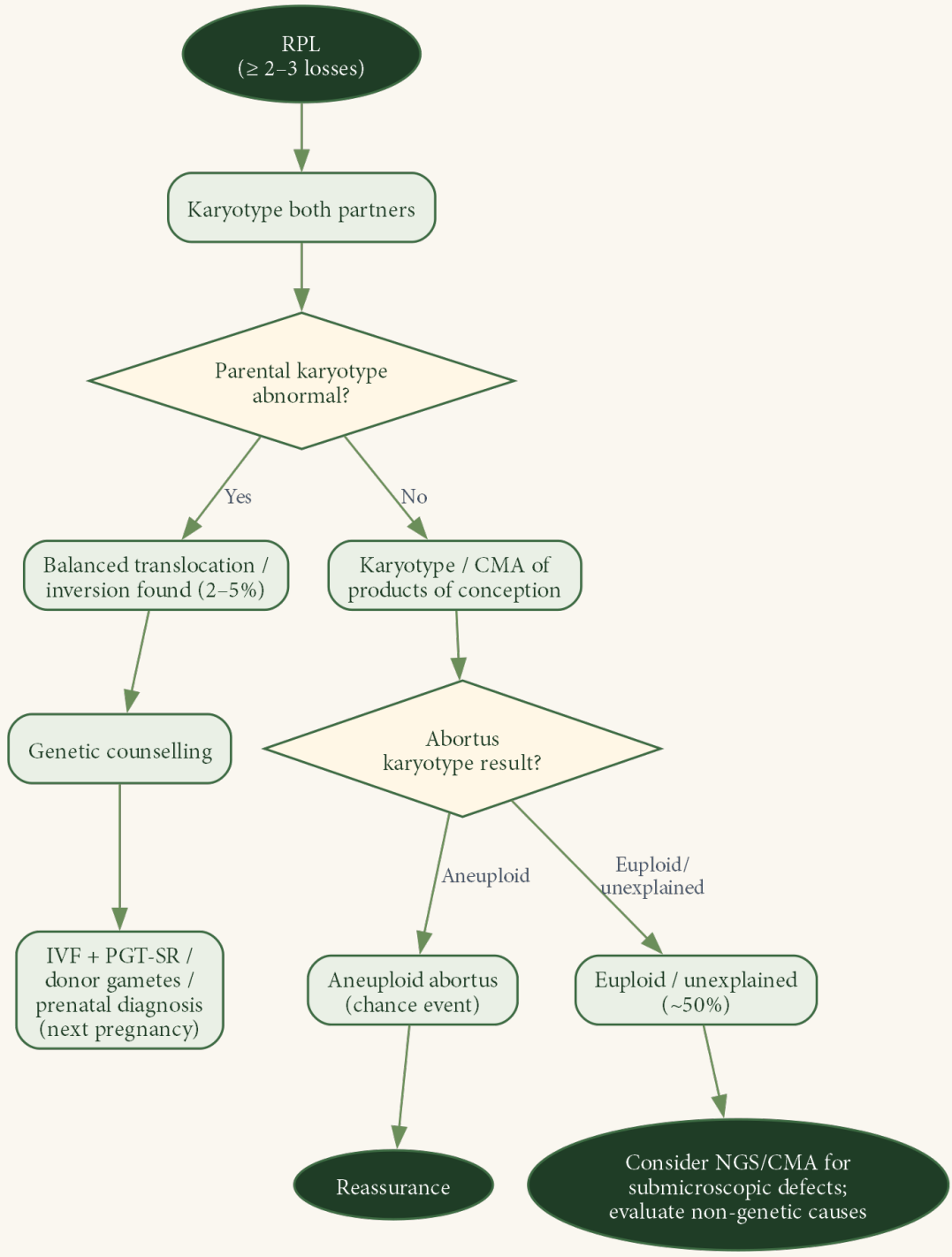
Genetic evaluation of the couple

Test	What it detects/purpose
Peripheral blood karyotype — **both partners**	Balanced reciprocal/Robertsonian translocation, inversion, or mosaicism (2-5% yield); cornerstone investigation recommended by ASRM
Karyotype of products of conception (current/most recent loss)	Distinguishes a one-off chance aneuploid loss (no added recurrence risk) from an unbalanced-translocation loss (→ prompts parental karyotyping)
Chromosomal microarray (CMA)/array-CGH on POC	Detects submicroscopic copy-number variants; works on non-viable or degraded tissue where cell culture fails, so more sensitive than conventional karyotyping
Next-generation sequencing (NGS)	Identifies mosaicism, triploidy, and copy-number variants missed by karyotype/CMA
Sperm fluorescence in-situ hybridisation (FISH)	If the male partner carries a translocation, quantifies the proportion of chromosomally unbalanced sperm and helps predict success with in-vitro fertilisation (IVF) plus preimplantation genetic testing (PGT)

Genetic-specific management

- **Genetic counselling** for any couple with an abnormal karyotype — explain the segregation mechanism and the offspring-risk figures above, and consider karyotyping the carrier's own parents/siblings if the rearrangement may be familial.
- **IVF with preimplantation genetic testing for structural rearrangements (PGT-SR)** — trophectoderm biopsy at the blastocyst stage (day 5); only chromosomally normal/balanced embryos are transferred. This substantially lowers the miscarriage rate per pregnancy in translocation carriers, but overall live-birth rate with IVF+PGT is **not** superior to expectant management for RPL as a whole (ASRM data cited in Williams).
- **PGT for aneuploidy (PGT-A)** in advanced maternal age or unexplained RPL improves implantation and lowers miscarriage rate per transfer but has **not** been shown to raise the cumulative live-birth rate; it is not recommended solely for the indication of RPL when the parental karyotype is normal.
- **Donor gametes** (oocyte or sperm) — an option when carrier risk is high, especially for female translocation carriers, for whom (unlike sperm-FISH in men) there is no way to directly quantify the proportion of abnormal gametes.
- **Prenatal diagnosis in a subsequent spontaneous pregnancy** — chorionic villus sampling or amniocentesis with karyotype/CMA, offered regardless of maternal age once a parental rearrangement is confirmed.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Genetic evaluation pathway in recurrent pregnancy loss.

High-yield exam pointers

- Genetic (parental) causes account for only **2-5%** of RPL couples, even though aneuploidy causes **50-75%** of *all* miscarriages (a chance event, not a recurring parental defect).

- Commonest parental rearrangement = **balanced reciprocal translocation**; the recurring t(11;22)(q23;q11) is the most frequently reported specific reciprocal translocation in humans. Commonest Robertsonian = der(13;14).
- Memorise the risk figures: reciprocal translocation 5-30% (after an abnormal child) / ~5% (incidental); Robertsonian ~15% maternal / ~2% paternal carrier.
- Karyotype **both partners** + karyotype/CMA of the abortus = cornerstone genetic work-up.
- **PGT-SR**, not PGT-A, is the evidence-based IVF option for translocation carriers; PGT-A does not raise live-birth rate in unexplained RPL.
- **Skewed X-inactivation** (>90%) is a reported (though inconsistently confirmed) marker in unexplained RPL.
- inv(9)(p11q12) is a normal population variant — do not over-call it as pathogenic.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Definitions vary across bodies: Dutta cites ASRM-2013 (two or more losses) while the older RCOG/ESHRE convention required three or more before 24 weeks — either is acceptable to quote, but state the source when you do.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e (Chapter 11 "Recurrent Miscarriage" and Chapter 16 "Genetics"); Speroff's Clinical Gynecologic Endocrinology & Infertility 9e (Chapter 30 "Recurrent Early Pregnancy Loss"); DC Dutta's Textbook of Obstetrics 9e; American Society for Reproductive Medicine (ASRM) Practice Committee guidance on RPL evaluation, as cited in Williams 26e.

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Gonadal dysgenesis

Asked in: Paper I 06-Apr-2026 — RGUHS MS Obstetrics & Gynaecology

Definition — Gonadal dysgenesis is the incomplete or defective development of the gonads resulting from disturbed germ-cell migration or organisation, most often due to a structural or numerical sex-chromosome abnormality (occasionally a single-gene mutation) affecting the bipotential gonad and urogenital ridge. The gonads fail to differentiate and are replaced by fibrous **"streak" gonads** that lack germ cells and secrete neither steroid hormones nor inhibin, producing hypergonadotropic

hypogonadism; it is one of the commonest causes of primary amenorrhoea (approximately 30–40% of cases).

Classification and karyotypes

Four clinically distinct patterns are recognised, distinguished chiefly by karyotype and by whether Y-chromosome material is present (which dictates malignancy risk):

Type	Karyotype	Gonads	Key clinical features
Turner syndrome (classic)	45,X (or structural X defect — deletion, ring, isochromosome)	Bilateral streak gonads	Short stature (<150 cm), webbed neck, low posterior hairline, shield chest with widely spaced nipples, *cubitus valgus*, short 4th metacarpal, primary amenorrhoea with absent secondary sexual characters
Mosaic Turner syndrome	45,X/46,XX (or other cell line)	Variable — may retain functioning ovarian cortex	Milder or absent stigmata; ~15% begin but do not complete puberty, ~5% menstruate and rarely conceive
Pure gonadal dysgenesis, 46,XX	46,XX	Bilateral streak gonads	Average height, no somatic stigmata, delayed puberty, primary amenorrhoea; may coexist with sensorineural deafness (**Perrault syndrome**, autosomal recessive)
**Pure gonadal dysgenesis, 46,XY* (Swyer syndrome)*	46,XY (SRY gene mutation in 10–15%)	Bilateral streak gonads — no anti-Müllerian hormone or androgen secretion	Average height, normal Müllerian development (uterus and vagina present), delayed puberty, primary amenorrhoea, normal pubic/axillary hair (excludes androgen insensitivity)

Type	Karyotype	Gonads	Key clinical features
Mixed gonadal dysgenesis	45,X/46,XY mosaic	Testis on one side, streak/rudimentary gonad on the other	Ambiguous genitalia at birth; virilization with amenorrhoea at puberty; asymmetric (often unilateral) Müllerian development

Investigations

Test	Purpose / expected finding
Karyotype (peripheral lymphocytes)	Confirms diagnosis and defines the type; mandatory in every case
FISH for Y-chromosome material	Detects occult Y-derived material not seen on standard karyotype (identifies a further ~5% of Turner syndrome cases); governs the decision for gonadectomy
Serum FSH and LH	Markedly raised — hallmark of hypergonadotropic hypogonadism
Serum estradiol	Low
Pelvic ultrasonography	Confirms Müllerian structures (uterus present in Turner, mosaic, 46,XX and Swyer forms; its absence points instead to androgen insensitivity) and detects a gonadal mass
Echocardiography	At diagnosis, once between 12–15 years, then every 5 years if normal — screens for bicuspid aortic valve, coarctation, aortic dilatation
Renal ultrasonography	Once if normal, every 3–5 years if abnormal — horseshoe kidney, renal agenesis
TSH/free T4 and anti-endomysial antibody	At diagnosis (autoimmune thyroiditis, coeliac disease); TSH repeated every 1–2 years
Audiometry	At diagnosis, once in the teens/young adulthood, every 10 years if normal
CBC, fasting glucose, lipid profile, renal and liver function	Every 2 years

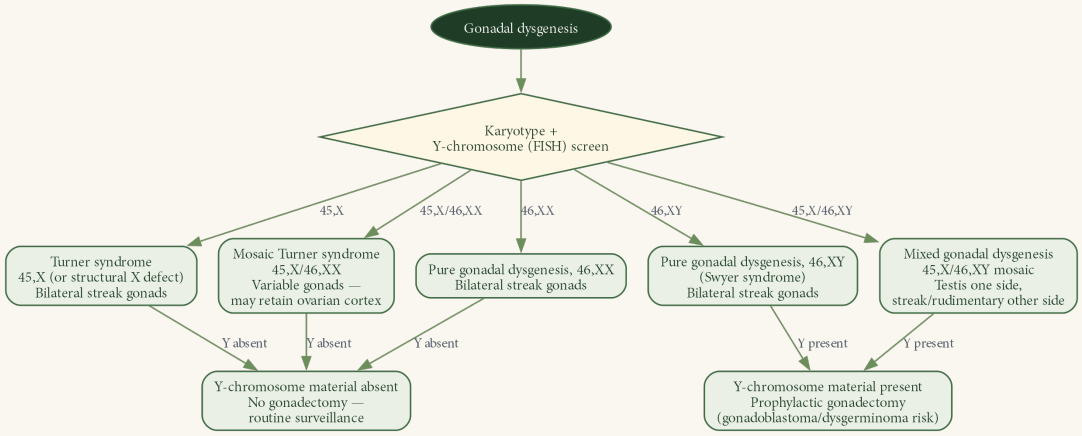
Management

- **Karyotype plus Y-chromosome screen (FISH) in every patient** — presence of Y-chromosome material mandates **prophylactic gonadectomy**, since the dysgenetic gonad carries a 20–30% risk

of gonadoblastoma/dysgerminoma (risk is lower, 5–10%, in Turner syndrome specifically); gonadectomy is done soon after diagnosis in Swyer syndrome and mixed gonadal dysgenesis.

- **Growth-hormone (GH) therapy** for short stature (Turner and mosaic forms) — start as soon as the growth curve falls below the 5th percentile, ideally by 4–5 years of age, and continue to near-final height; dose is individualised to response, and oxandrolone may be added in girls older than 8 years with marked short stature.
- **Induction of puberty with sex-steroid replacement** — start low-dose oestrogen (micronised estradiol 0.25–0.5 mg/day, or a transdermal estradiol patch) around 12–14 years of age (no later than 15, and not before 12 unless height is already maximised); increase every 3–6 months guided by Tanner stage and bone age, completing maturation over 2–3 years; add a progestin (e.g., medroxyprogesterone acetate) once withdrawal bleeding occurs or after 12–24 months of oestrogen alone, to protect the endometrium and produce cyclic bleeds.
- **Long-term cyclic hormone replacement** until the average age of natural menopause, for bone, cardiovascular and vaginal health, with awareness of an increased venous thromboembolism risk in Turner syndrome.
- **Systemic surveillance** in Turner syndrome — cardiac, renal, thyroid, metabolic, coeliac and hearing screening at the intervals listed above.
- **Fertility** — donor-oocyte in vitro fertilisation with a gestational carrier is the realistic option in both Turner and Swyer syndrome; in Turner syndrome, pregnancy is a **relative contraindication** (American Society for Reproductive Medicine, 2012) because of up to a 100-fold increased risk of maternal death from aortic dissection/rupture, so cardiac evaluation is mandatory before any pregnancy attempt.
- **Counselling** of the patient and family at diagnosis and at disclosure, particularly in 46,XY gonadal dysgenesis, reinforcing the patient's female gender identity.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Classification flowchart of gonadal dysgenesis by karyotype, with Y-chromosome status as the branch point deciding prophylactic gonadectomy.

High-yield exam pointers

- Turner syndrome (45,X) is the commonest cause of gonadal dysgenesis and of primary amenorrhoea; gonads are bilateral fibrous streaks.
- Rule of thumb — "any Y, gonads must go": 20–30% gonadoblastoma risk with Y-chromosome material (5–10% specifically in Turner syndrome) drives prophylactic gonadectomy.
- Swyer syndrome = 46,XY + female phenotype + normal uterus present (streak gonad makes neither anti-Müllerian hormone nor androgen) + primary amenorrhoea.
- Mixed gonadal dysgenesis = 45,X/46,XY + ambiguous genitalia at birth + virilization at puberty.
- Hormone sequence to write: low-dose oestrogen alone first → add progestin after withdrawal bleed or 12–24 months → continue cyclic HRT till menopausal age.
- GH before oestrogen — early GH (by age 4–5) and delayed oestrogen protect final adult height.
- Turner syndrome plus pregnancy = relative contraindication (ASRM 2012) — aortic dissection risk.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's classical teaching regimen (conjugated oestrogen 0.625 mg with medroxyprogesterone acetate, started after 13 years) remains an acceptable exam answer, but current sources (Speroff, Berek & Novak) favour a lower starting dose titrated upward over 2–3 years to better protect final height and lower thromboembolism risk.

SOURCE & COVERAGE

Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e; American Society for Reproductive Medicine Practice Committee guidance (2012), as cited in Berek & Novak 16e.

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Gonadotropin Releasing Hormone (GnRH)

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — Gonadotropin releasing hormone (GnRH), also called luteinizing hormone releasing hormone (LHRH), is a hypothalamic decapeptide (10 amino acids) synthesised by neurons of the arcuate nucleus and secreted in a pulsatile fashion into the hypothalamo-hypophyseal portal circulation. It reaches the anterior pituitary gonadotrophs, where it stimulates the synthesis, storage and pulsatile release of both follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

SOURCE & COVERAGE

Feature	Detail
Chemical nature	Decapeptide; very short half-life of 2–4 minutes due to rapid cleavage of peptide bonds at amino acid positions 5–6, 6–7 and 9–10
Site of synthesis	Neurons of the arcuate nucleus (medial-basal hypothalamus); 1,000–3,000 GnRH neurons in the human
Embryological origin	GnRH neurons arise in the medial olfactory placode and migrate along the nervus terminalis into the septal-preoptic/arcuate region; failure of this migration (with failure of olfactory axon migration) causes **Kallmann syndrome** — anosmia/hyposmia with hypogonadotropic hypogonadism (X-linked, autosomal-dominant or autosomal-recessive; genes include *KAL1* (anosmin-1), *FGFR1*, *PROKR2*)
Transport	Axonal (tuberoinfundibular tract) to the median eminence, then via the hypothalamo-hypophyseal **portal vessels** to the anterior pituitary — the arcuate nucleus + median eminence together form the key locus for GnRH release into the portal system

Secretion pattern & control

- **Nature of secretion** — tonic, cyclic and pulsatile centres in the hypothalamus regulate output; the tonic centre reflects negative feedback of gonadal steroids, the cyclic centre responds to the

sustained pre-ovulatory estradiol rise, and pulsatile secretion is governed by neurotransmitters/neuromodulators.

- **Pulse frequency and amplitude vary across the cycle:**

Cycle phase	Pulse frequency	Pulse amplitude
Follicular phase	Rapid — about 1 pulse/60–90 minutes	Low
Luteal phase	Slow — about 1 pulse/2–3 hours	High

- **Kisspeptin–GPR54 system** — kisspeptin, from *KISS1* neurons in the arcuate nucleus, is the obligatory upstream activator of the GnRH pulse generator and the key trigger for pubertal onset; loss-of-function mutation of the kisspeptin receptor (*KISS1R*/GPR54) causes failure of puberty.
- **Neurotransmitter/neuromodulator control:**

Agent	Effect on GnRH pulsatility
Norepinephrine	Stimulatory
Dopamine, serotonin	Inhibitory
Endogenous opioids (endorphins, enkephalins, dynorphins)	Inhibitory — implicated in stress/exercise-related hypothalamic amenorrhoea
Prostaglandin E, neuropeptide Y	Stimulatory

- **Feedback loops** — *ultrashort* (GnRH autoregulates its own synthesis and its own pituitary receptor number), *short* (FSH/LH exert negative feedback on hypothalamic GnRH), *long* (gonadal steroids are inhibitory throughout the cycle except in the late follicular phase, when sustained high estradiol, via catechol-oestrogens, exerts positive feedback to trigger the mid-cycle GnRH/LH surge).

Mechanism of action on the gonadotroph

- GnRH binds a **7-transmembrane G-protein-coupled receptor** on the gonadotroph, coupled via Gq/11 to **phospholipase C**.
- Phospholipase C hydrolyses membrane phosphoinositide to generate two second messengers — **inositol 1,4,5-trisphosphate (IP3)**, which mobilises intracellular calcium, and **1,2-diacylglycerol (DAG)**, which activates **protein kinase C**.
- Rising intracellular calcium plus activated protein kinase C together trigger exocytotic release of stored FSH/LH and stimulate their ongoing biosynthesis.
- Gonadotropins exist in two pools — a readily releasable **primary pool** and a **reserve pool**; repeated GnRH pulses progressively transfer the reserve pool into the releasable pool, termed "**self-priming**", which is maximal when estrogen levels are high (e.g., late follicular phase).

- **Pulse-frequency dependence** — low GnRH pulse frequency favours FSH release/synthesis, while higher frequency favours LH.
- **Receptor regulation** — intermittent, physiological GnRH pulses **up-regulate** receptor number and maintain pituitary sensitivity; continuous, non-pulsatile GnRH exposure causes receptor internalisation and uncoupling from its effector system — **desensitisation/down-regulation** — the pharmacological basis of GnRH agonist therapy.

Clinical & diagnostic significance

- **Puberty (gonadarche)** — kisspeptin-mediated disinhibition increases the amplitude and frequency of pulsatile GnRH (nocturnal first, then diurnal), driving the rise in FSH/LH that initiates gonadal steroidogenesis.
- **GnRH stimulation test** — 100 μg GnRH given subcutaneously with serum LH measured; a rise in LH >15 mIU/mL indicates gonadotropin-dependent (central/true) precocious puberty.
- **Pulsatile GnRH pump therapy** — used for ovulation induction in women with hypogonadotropic hypogonadism (WHO Group I anovulation). The intravenous route (2.5–5 μg/pulse every 60–90 minutes, increased to 10–20 μg/pulse if unresponsive) mimics the physiological pulse generator, restores normal follicular recruitment and feedback, and carries low risk of multiple pregnancy/ovarian hyperstimulation compared with exogenous gonadotropins.

GnRH agonists & antagonists — clinical applications

Class	Mechanism	Representative agents & dose	Clinical uses
Agonists (amino acid substitution at position 6 and/or C-terminal modification resists degradation)	Initial "flare" (transient rise in FSH/LH), then after 1–3 weeks of continuous exposure — desensitisation and down-regulation → reversible hypogonadotropic, hypo-estrogenic state	Leuprolide 3.75–7.5 mg IM monthly or 11.25 mg 3-monthly; goserelin 3.6 mg SC monthly; triptorelin 3.75 mg monthly or 11.25 mg 3-monthly; buserelin/nafarelin (nasal)	Endometriosis, uterine leiomyoma (pre-operative shrinkage), central precocious puberty, long-protocol controlled ovarian stimulation for IVF; "add-back" steroid therapy limits hypo-estrogenic bone loss/vasomotor side effects

Class	Mechanism	Representative agents & dose	Clinical uses
Antagonists (multiple amino acid substitutions)	Immediate competitive blockade of the GnRH receptor — no flare, gonadotropin suppression within 24–72 hours	Ganirelix/cetrorelix 0.25 mg SC daily (fixed or flexible-onset protocol) or cetrorelix 3.0 mg single dose (covers ~96 hours); elagolix — oral, non-peptide antagonist	Antagonist protocol for controlled ovarian stimulation in IVF (now used more widely than the long agonist protocol); elagolix for endometriosis-associated pain and fibroid-related heavy menstrual bleeding

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 7.1 — Anatomy of the hypothalamus and pituitary, showing the arcuate nucleus, median eminence, tanycytes and hypothalamo-hypophyseal portal vessels (DC Dutta's Gynaecology 7e, p.73)*

High-yield exam pointers

- GnRH = decapeptide, arcuate nucleus, half-life 2–4 minutes (cleavage at amino acid positions 5–6, 6–7, 9–10).
- Receptor mechanism: GPCR → phospholipase C → IP3/DAG → protein kinase C + Ca^{2+} (not cAMP).
- Pulse pattern: follicular phase fast/low-amplitude (~q60–90 min); luteal phase slow/high-amplitude (~q2–3h).
- Kisspeptin–GPR54 = obligatory trigger of the GnRH pulse generator and of puberty.
- Kallmann syndrome = anosmia + hypogonadotropic hypogonadism (GnRH neuron migration defect).
- Agonist → flare then down-regulation (continuous exposure); Antagonist → immediate competitive block (no flare).
- GnRH pump: 2.5–5 µg/pulse IV every 60–90 minutes for ovulation induction in hypogonadotropic hypogonadism.
- GnRH stimulation test: LH >15 mIU/mL after 100 µg GnRH = central (true) precocious puberty.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Some older texts describe the pituitary second-messenger pathway for GnRH as adenylate cyclase–cyclic AMP; current evidence establishes the GnRH receptor as Gq-coupled, signalling through phospholipase C-generated IP3/diacylglycerol and protein kinase C/calcium, which is the pathway followed here.

SOURCE & COVERAGE

Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; DC Dutta's Textbook of Gynaecology 7e.

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Gonadotropins

Asked in: Paper I 15-Nov-2022 — RGUHS MS Obstetrics & Gynaecology

Definition — Gonadotropins are glycoprotein hormones that regulate gonadal function: **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)**, secreted by anterior pituitary gonadotrope cells under hypothalamic control, and **human chorionic gonadotropin (hCG)**, secreted by the placental syncytiotrophoblast. All three share a common alpha-subunit with thyroid-stimulating hormone (TSH); hormone specificity is conferred by the beta-subunit.

Chemistry and structure

Feature	FSH	LH	hCG (placental)
Subunits	α (92 amino acids, common) + β (118 aa, specific)	α (92 aa, common) + β (121 aa, specific)	α (92 aa, common) + β (145 aa — largest, unique 29-amino-acid carboxyl-terminal tail)
Gene for α-subunit	Single gene, chromosome 6 — shared by FSH, LH, hCG, TSH	same	same
Carbohydrate side chains	4 (2 per subunit)	3 (single glycosylation site on β)	4 sites on β — most heavily glycosylated/sialylated
Sialic acid content (determines biologic half-life)	Moderate–high	Lowest	Highest
Circulating half-life	3–4 hours	~20–50 minutes (biphasic clearance)	Whole hCG ~24 hours; free α-subunit 6–8 minutes

- The α- and β-subunits are non-covalently linked heterodimers stabilised by internal disulfide bonds; the carbohydrate moiety (chiefly **sialic acid**) determines metabolic clearance, while the protein core determines receptor binding.
- The hCG β-gene transcription site lacks a hormone-response element, so hCG secretion **escapes steroid feedback regulation**, unlike FSH/LH.

- Rate-limiting step in synthesis is availability of the **β-subunit** (excess free α-subunit circulates normally).

Synthesis, secretion and regulation

- **Hypothalamic drive** — gonadotropin-releasing hormone (GnRH), a decapeptide from the arcuate nucleus (half-life 2–4 minutes), is released in a **pulsatile** fashion into the hypophyseal-portal circulation and stimulates gonadotrope synthesis, storage (readily-releasable + reserve pools) and release of FSH/LH.
- **Pulse-frequency coding** — lower GnRH pulse frequency favours **FSH** secretion; higher frequency favours **LH** secretion (varies through the cycle — slow in luteal phase, fast in late follicular phase).
- **Continuous (non-pulsatile) GnRH exposure** causes receptor **down-regulation/desensitisation** — the pharmacological basis of GnRH-agonist pituitary suppression; intermittent pulses cause **up-regulation** (self-priming).
- **Feedback loops** —
  - *Long loop*: gonadal steroids (estrogen, inhibin) act on hypothalamus/pituitary.
  - *Short loop*: FSH/LH themselves negatively feedback on hypothalamic GnRH.
  - Estrogen is **negative feedback** on both FSH and LH at low/moderate levels; when estradiol exceeds **~200 pg/mL and is sustained for ≈50 hours** (achieved when the dominant follicle reaches ~15 mm), it switches to **positive feedback**, producing the mid-cycle **LH surge**.
  - **Inhibin B** (granulosa cells) selectively suppresses FSH.
- **Neuromodulators** — norepinephrine stimulates GnRH release; dopamine, serotonin and endogenous opioids (endorphins, enkephalins, dynorphins) inhibit it.

Mechanism of action

- FSH and LH act via **G-protein-coupled, 7-transmembrane receptors** on target cells — FSH-receptor exclusively on **granulosa cells**; LH-receptor on **theca cells** throughout the cycle, and on granulosa cells only after FSH induces LH-receptor expression on the dominant follicle.
- Receptor binding activates **adenylate cyclase → cyclic AMP → protein kinase A**, which phosphorylates steroidogenic enzymes (including StAR protein and aromatase) to drive steroid synthesis.
- hCG binds the **same LH/hCG receptor** as LH (structurally near-identical action), which is why hCG can substitute for the LH surge to trigger ovulation and support the corpus luteum.

Physiological actions — Two-cell, two-gonadotropin concept

Phase/site	LH	FSH
Follicular phase — ovary	Stimulates **theca cells** to synthesise androgens (androstenedione) from cholesterol	Stimulates **granulosa cells** — proliferation, follicular growth/recruitment/selection of the dominant follicle, and **aromatase** activity converting theca-derived androgen to estradiol
Mid-cycle	**LH surge** triggers final oocyte maturation (resumption of meiosis), follicular rupture/ovulation ~36 hours later, and luteinisation of granulosa cells	FSH surge co-occurs, contributing to plasminogen-activator–mediated follicular rupture and inducing LH receptors
Luteal phase	Maintains the **corpus luteum**; in luteinised granulosa-theca cells drives a one-gonadotropin (LH-only) system for progesterone/estradiol synthesis	Minimal role
Testis	Stimulates **Leydig cells** — testosterone synthesis	Stimulates **Sertoli cells** — spermatogenesis support, inhibin and androgen-binding protein secretion

Clinical applications

Application	Detail
Assay	Serum FSH/LH by immunoassay (chemiluminescence/ELISA); serum/urine β-hCG for pregnancy diagnosis and gestational trophoblastic disease follow-up
Ovarian reserve	Day-3 serum **FSH > 10 IU/L** suggests diminished ovarian reserve
Indications for exogenous gonadotropin therapy	Hypogonadotropic hypogonadism (WHO Group I), clomiphene-resistant PCOS (WHO Group II), unexplained infertility, ovulation induction/superovulation for assisted reproduction
Agents	Human menopausal gonadotropin (hMG — FSH+LH mixture), purified/highly-purified urinary FSH, recombinant FSH

Application	Detail
Regimen	Start low-dose (e.g., 75 IU IM/day) from cycle day 2–5, continued 7–10 days; monitor with serial transvaginal sonography and serum estradiol; optimum when lead follicle 18–20 mm and estradiol 500–1500 pg/mL; **trigger ovulation with hCG 5000–10,000 IU IM** — ovulation follows in ~36 hours
Pulsatile GnRH	For hypothalamic amenorrhoea — 5 μg IV every 90 minutes via infusion pump
GnRH agonists/antagonists	Agonists (buserelin, nafarelin) cause an initial "flare" (2–3 weeks) then pituitary down-regulation; antagonists (cetrorelix) block the LH surge immediately, without a flare — both used to prevent premature LH surge in controlled ovarian stimulation
Contraindications	Primary ovarian failure (high FSH), uncontrolled thyroid/adrenal disease, sex-hormone-dependent tumour, pituitary tumour, ovarian cysts
Key risks	Multiple pregnancy, ovarian hyperstimulation syndrome (OHSS), miscarriage

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 7.4 — Fluctuations of levels of different gonadotropins (above) and steroid hormones (below) during a normal ovulatory menstrual cycle (DC Dutta's Gynaecology 7e, p.77)*

High-yield exam pointers

- Common **α-subunit (92 aa)** shared by FSH, LH, hCG, TSH; **β-subunit** confers specificity — hCG β is largest (145 aa, unique 29-aa tail).
- Half-life ranking (∝ sialic acid content): **hCG (~24 h) > FSH (3–4 h) > LH (20–50 min)**.
- GnRH pulse frequency rule: **low frequency → FSH; high frequency → LH**.
- **Two-cell, two-gonadotropin concept**: LH → theca-cell androgens; FSH → granulosa-cell aromatisation to estrogen.
- Estrogen **positive feedback** trigger for the LH surge: **>200 pg/mL sustained ~50 hours**.
- Day-3 **FSH > 10 IU/L** = diminished ovarian reserve.
- Ovulation-trigger dose: **hCG 5000–10,000 IU IM**, ovulation at **~36 hours**.
- GnRH agonist = flare then down-regulation; GnRH antagonist = immediate block, no flare.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Brand-name gonadotropin preparations and step-up dosing schedules quoted in older textbook editions are illustrative of the classical protocol; contemporary assisted-reproduction practice more often uses recombinant FSH/LH with antagonist protocols, but the underlying gonadotropin physiology tested in this question is unchanged.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Williams Obstetrics 26e.

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Graffian follicle

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — The Graafian follicle (correctly spelled thus, after the Dutch anatomist **Regnier de Graaf, 1641–1673**; commonly written "Graffian") is the **fully mature, preovulatory antral follicle** of the ovary — the end point of folliculogenesis. It measures about **20 mm** (Berek & Novak: >20 mm) just before ovulation, is filled with liquor folliculi, and houses the oocyte ready to complete its first meiotic division and be expelled at ovulation.

Structure of the mature Graafian follicle

From outside inward, the wall and contents comprise the following layers.

Layer (outside → inside)	Description
Theca externa	Outermost fibrous connective-tissue capsule, continuous with ovarian stroma; contains the smooth-muscle-like myoid cells whose contraction contributes to rupture
Theca interna	Vascular, steroidogenic layer; cells bear **LH receptors** and convert cholesterol to androgens (two-cell, two-gonadotropin concept)
Membrana granulosa (limitans)	Basement membrane separating theca interna from granulosa cells; avascular until just before ovulation, when LH depolymerises it to allow vascularisation of the granulosa

Layer (outside → inside)	Description
Granulosa cell layer (membrana granulosa cells)	Multilayered, avascular, oestrogen- and FSH-receptor–rich cells lining the antral cavity; some are recruited as **LH receptors** develop under FSH/oestrogen synergy
Discus proligerus (cumulus oophorus)	A mound of granulosa cells anchoring the oocyte to the follicular wall
Corona radiata	Innermost, radially arranged granulosa cells immediately surrounding the oocyte and its zona pellucida
Oocyte	Primary oocyte (~130 µm), arrested in prophase of meiosis I until the LH surge; surrounded by the glycoprotein **zona pellucida**
Antrum	Fluid-filled cavity containing **liquor folliculi** — oestrogen, FSH, a trace of androgen, prolactin, oocyte maturation inhibitor (OMI), luteinisation inhibitor, inhibin, and proteolytic enzymes/plasmin

Folliculogenesis — stages leading to the Graafian follicle

Stage	Size / timing	Hormone dependence	Key event
Primordial follicle	0.03–0.05 mm; oocyte ~18–24 µm	Gonadotropin-**independent**	Single layer of flattened pregranulosa cells around an arrested oocyte; the resting pool present from fetal life
Preantral (primary/secondary) follicle	Grows to 2–5 mm	Gonadotropin-independent until 2–5 mm, then **FSH-dependent (rescue)**; unrescued follicles undergo atresia	Pregranulosa cells become cuboidal and multilayer; zona pellucida forms; theca interna begins to differentiate; whole cohort of ~5–10 follicles/ovary recruited over **~85 days spanning 3 ovarian cycles**

Stage	Size / timing	Hormone dependence	Key event
Antral (secondary/vesicular) follicle	Reaches ~1 mm by ~2 months, ~5 mm by a further 2 weeks	**FSH**-driven fluid secretion; granulosa cells acquire **LH receptors** under FSH + oestrogen synergy	Fluid spaces coalesce into an antrum; by **day 5–7** the follicle with the highest intrafollicular oestrogen: androgen ratio and maximal FSH receptors is selected as the **dominant follicle**; the rest become atretic by day 8
Graafian (preovulatory) follicle	~20 mm, reached in the final ~2 weeks before ovulation	Combined **FSH + LH** action	Fully differentiated layers as above; primary oocyte completes meiosis I just before ovulation

Hormonal regulation and the ovulatory trigger

- **Two-cell, two-gonadotropin concept — LH** acts on **theca cells** to produce androgens; these diffuse into the granulosa cells, where **FSH**-induced aromatase converts them to **oestrogens** (oestradiol). This is the basis of steroidogenesis in the developing and Graafian follicle.
- Rising oestradiol from the dominant follicle exerts **negative feedback** on FSH (suppressing rival follicles) but, once it exceeds a **critical threshold of ~200 pg/mL sustained for ≥ 48 hours**, switches to **positive feedback** on the anterior pituitary, producing the **midcycle LH surge**.
- FSH-and-oestrogen synergy induces **LH receptors on granulosa cells** of the dominant follicle — a prerequisite for the LH surge to trigger luteinisation, progesterone synthesis, and ovulation.
- The **LH surge** (i) resumes and completes the first meiotic division of the oocyte (secondary oocyte + first polar body), (ii) initiates luteinisation of granulosa cells with progesterone/prostaglandin synthesis, and (iii) triggers a secondary FSH surge that activates the plasminogen activator–plasmin cascade, weakening the follicular wall.
- **Ovulation timing**: approximately **10–12 hours after the LH peak**, or **32–36 hours after the onset of the LH surge** (Berek & Novak's Gynecology 16e: 34–36 hours after the initial LH rise); the effective LH surge itself lasts about 24 hours.
- Local **prostaglandins** (from theca-externa micromuscle contraction) and passive stretching of the thinned follicular wall (intrafollicular pressure stays low, ~10–15 mmHg) complete rupture at the **stigma**, a conical, avascular projection on the ovarian surface.

Fate of the Graafian follicle

- At ovulation the cumulus detaches, and the oocyte with its corona radiata is extruded with follicular fluid through the stigma over 30–120 seconds; it is picked up by the fallopian tube fimbriae.
- The **collapsed, ruptured Graafian follicle luteinises into the corpus luteum**, passing through proliferation → vascularisation → maturation (peak secretory activity by day 7–8, ~1–2 cm) → regression (from day 22–23, becoming the corpus albicans) if fertilisation does not occur; if pregnancy occurs it becomes the **corpus luteum of pregnancy**, sustained by hCG until the **luteal–placental shift (7–10 weeks)**.
- **Clinical correlations**: an unruptured, distended Graafian follicle can persist as a **follicular cyst** (usually < 5 cm, lined by granulosa cells); on transvaginal ultrasound "folliculometry," a follicle reaching ≥ **18–20 mm** mean diameter is used as the criterion for triggering ovulation (hCG trigger) in ovulation-induction and assisted reproduction cycles, directly reflecting the mature Graafian follicle's size.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 8.5 — A mature Graafian follicle (DC Dutta's Gynaecology 7e, p.89)*
>
> Label from outside inward: theca externa → theca interna → membrana granulosa → granulosa cell layer → antrum (liquor folliculi) → discus proligerus/cumulus oophorus → corona radiata → zona pellucida → oocyte.

High-yield exam pointers

- Eponym: **Regnier de Graaf**, Dutch anatomist — mature preovulatory follicle named after him.
- **Size ~20 mm** (Berek & Novak: >20 mm) just before ovulation; total folliculogenesis from primordial to Graafian spans **~85 days (3 ovarian cycles)**.
- Layers outside-in mnemonic: **T**heca externa → **T**heca interna → **M**embrana granulosa → **G**ranulosa cells → **A**ntrum → **C**umulus/corona → **O**ocyte ("TT-MGACO").
- **Two-cell, two-gonadotropin theory**: LH → theca → androgens; FSH → granulosa → aromatisation → oestrogen.
- Ovulation trigger numbers: oestradiol **>200 pg/mL for ≥48 h** → LH surge → ovulation **10–12 h after LH peak / 32–36 h after LH surge onset**.
- Fate: ruptured Graafian follicle → corpus luteum (regresses day 22–23) → corpus albicans, or corpus luteum of pregnancy if fertilisation occurs.
- Applied point: **≥18–20 mm follicle on folliculometry** = the ultrasound correlate of the mature Graafian follicle, used to time the hCG ovulation trigger in ART.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Minor discrepancy across sources on exact post-surge ovulation timing (Dutta: 32–36 hours; Berek & Novak: 34–36 hours after LH surge onset) — both agree on 10–12 hours after the LH peak, which is the figure worth reproducing in the exam.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Williams Obstetrics 26e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e.

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Group B Streptococcus infection in pregnancy

Asked in: Paper I 06-Apr-2026 — RGUHS MS Obstetrics & Gynaecology

Definition — *Streptococcus agalactiae* (Group B Streptococcus, GBS) is a gram-positive, facultative anaerobic coccus that colonizes the lower gastrointestinal and genitourinary tract in 10–25% of pregnant women, transiently, intermittently, or chronically. It is the leading cause of neonatal early-onset sepsis and an important cause of maternal peripartum infection, transmitted to the fetus mainly by ascending or intrapartum exposure to colonized genital secretions.

Maternal and neonatal effects

System	Effects
Maternal	Asymptomatic bacteriuria/UTI, acute pyelonephritis, ascending intra-amniotic infection (chorioamnionitis), preterm labour and preterm prelabour rupture of membranes (PPROM), postpartum endometritis, wound infection, rarely osteomyelitis
Neonatal	Early- and late-onset invasive disease — respiratory distress, apnoea, hypotension, sepsis, pneumonia, meningitis; survivors of meningitis may have neurological sequelae

Early- vs late-onset neonatal GBS disease

Feature	Early-onset disease	Late-onset disease
Onset	Birth to 7 days (most within 12–24 hr)	7 days to 3 months

Feature	Early-onset disease	Late-onset disease
Source	Vertical transmission from maternal colonization during labour	Vertical + nosocomial/community acquisition
Predominant presentation	Sepsis, pneumonia, respiratory distress	Meningitis
Preventable by intrapartum prophylaxis	Yes — the target of screening/IAP	No
Mortality	~4% at term, higher if preterm	Lower than early-onset, but neurological sequelae common in survivors

Screening for GBS colonization

- **Universal vaginal–rectal culture screening** of all pregnant women at **36–38 weeks' gestation** (American College of Obstetricians and Gynecologists, 2020), unless intrapartum antibiotic prophylaxis (IAP) is already indicated on other grounds.
- **Technique** — a single swab of the lower vagina then the rectum (through the anal sphincter); selective enrichment broth improves yield of GBS on subculture.
- **Nucleic acid amplification testing (NAAT)/PCR** — available in some centres for rapid intrapartum identification when antenatal status is unknown; more expensive and cannot give antibiotic susceptibilities.
- **GBS bacteriuria of any colony count** detected on a routine prenatal urine culture during the current pregnancy is itself an indication for intrapartum prophylaxis (repeat screening culture is not required); counts $\geq 10^5$ CFU/mL additionally require treatment of the bacteriuria to reduce the risk of pyelonephritis.

Indications for intrapartum antibiotic prophylaxis (IAP)

IAP indicated	IAP not indicated
GBS bacteriuria in current pregnancy (any colony count)	Negative vaginal–rectal culture at ≥36 weeks in current pregnancy, regardless of intrapartum risk factors
Previous infant with invasive GBS disease	Caesarean delivery before labour onset, with intact membranes, regardless of GBS status or gestational age
Positive GBS screening culture in current pregnancy	Unknown GBS status with a negative intrapartum NAAT and no risk factors

IAP indicated	IAP not indicated
Unknown GBS status at labour onset **with** any of: birth <$37^0/_7$ weeks; membrane rupture ≥18 hr; intrapartum temperature ≥100.4°F (38.0°C); intrapartum NAAT positive; GBS-positive in a prior pregnancy	—

Intrapartum antimicrobial prophylaxis regimens

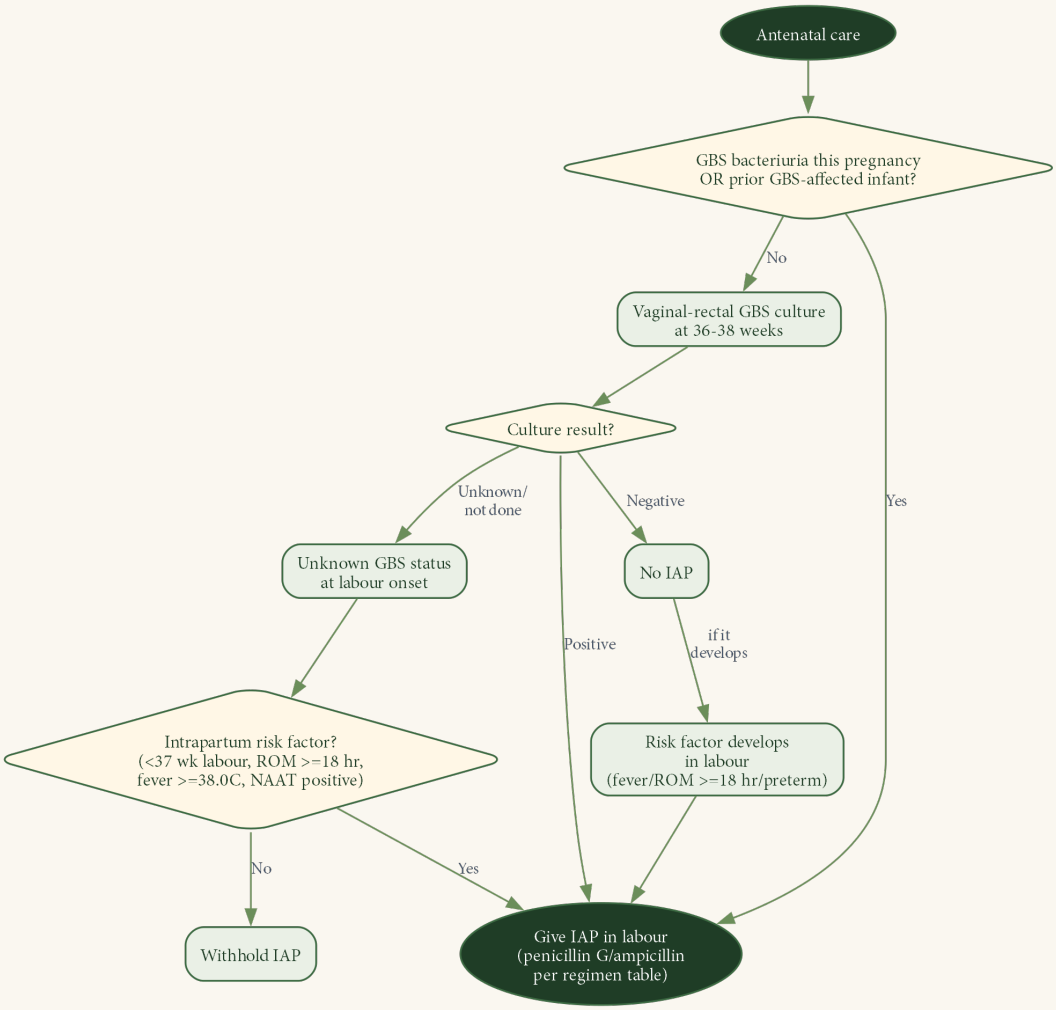
Regimen	Drug and dose
Recommended	Penicillin G 5 million units IV initial dose, then **2.5–3.0 million units IV every 4 hr** until delivery
Alternative	Ampicillin **2 g IV initial dose, then 1 g IV every 4 hr** (or 2 g every 6 hr)
Penicillin-allergic, **not** high risk of anaphylaxis	Cefazolin 2 g IV initial dose, then **1 g IV every 8 hr**
Penicillin-allergic, **high risk of anaphylaxis**, GBS clindamycin-susceptible	Clindamycin **900 mg IV every 8 hr** until delivery
Penicillin-allergic, **high risk of anaphylaxis**, clindamycin-resistant/susceptibility unknown	Vancomycin **1 g IV every 12 hr**, or 20 mg/kg IV every 8 hr (max 2 g/dose)

Isolates from penicillin-allergic women should be tested for clindamycin and erythromycin susceptibility, with inducible clindamycin resistance testing if erythromycin-resistant but clindamycin-susceptible; erythromycin itself is no longer used for prophylaxis.

Management in special situations

- **Threatened/established preterm labour or PPROM <37 weeks** — obtain a GBS culture at admission; start IAP empirically and continue until the culture result is known or delivery occurs.
- **Planned caesarean delivery before labour onset with intact membranes** — GBS chemoprophylaxis is **not** required regardless of colonization status.
- **Rupture of membranes ≥18 hours or intrapartum fever** — start IAP even if GBS status is unknown.
- **Penicillin-allergy risk stratification** — consider antenatal penicillin-allergy testing in GBS-colonized women at high risk of anaphylaxis to allow first-line penicillin/ampicillin use where safe.
- Continue the chosen agent at the stated interval **until delivery**.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

GBS screening and intrapartum prophylaxis algorithm, from the 36–38-week culture (or bypass for bacteriuria/prior affected infant) through to the IAP decision at labour.

High-yield exam pointers

- Universal culture screening window: **36–38 weeks** gestation (vaginal + rectal swab).
- First-line: **Penicillin G 5 million units IV load, then 2.5–3.0 million units IV q4h**; alternative **Ampicillin 2 g IV load, then 1 g IV q4h**.
- Penicillin allergy pathway: low anaphylaxis risk → **cefazolin**; high risk + clindamycin-sensitive → **clindamycin**; high risk + resistant/unknown → **vancomycin**.
- **No IAP** needed for elective caesarean before labour with intact membranes, whatever the GBS status.
- **GBS bacteriuria (any count) or a prior GBS-affected baby** = automatic IAP indication — no need to wait for the 36–38-week culture.

- Early-onset disease (<7 days) = sepsis/pneumonia and is what IAP prevents; late-onset (7 days–3 months) = meningitis and is **not** prevented by IAP.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> DC Dutta's text still cites the CDC-2002 universal-culture recommendation and an ampicillin regimen of 1 g 6-hourly; the screening window (now 36–38 weeks) and dosing intervals above follow the current ACOG (2020) guidance, which supersedes the older textbook figures.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e (Chapter 67 — Group B Streptococcus, Tables 67-2 and 67-3); DC Dutta's Textbook of Obstetrics 9e; American College of Obstetricians and Gynecologists (2020) guidance as cited in Williams Obstetrics 26e.

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Describe hematological changes in pregnancy

Asked in: Paper I 16-Dec-2023 — RGUHS MS Obstetrics & Gynaecology

Definition — Normal pregnancy produces coordinated adaptations in blood volume, the cellular and coagulation-fibrinolytic components of blood, and iron metabolism, driven mainly by oestrogen/progesterone-mediated vasodilatation and activation of the renin-angiotensin-aldosterone system. These changes meet the metabolic demands of the fetoplacental unit, protect the mother against impaired venous return in the supine/erect posture, and prepare her for the blood loss of delivery.

1. Blood volume & erythropoiesis

Parameter	Non-pregnant	Pregnancy (term)	Change	Onset / peak
Blood volume	4000 mL	5500 mL	+30–45%	begins ~6th week; rises fastest in the second trimester; plateaus at 30–34 weeks
Plasma volume	2500 mL	3750 mL (+1.25 L)	+40–50%	begins ~6 weeks; plateaus ~30 weeks
Red cell volume	1400 mL	1750–1850 mL	+20–30% (350–450 mL)	begins ~10 weeks; rises steadily to term, no plateau

Parameter	Non-pregnant	Pregnancy (term)	Change	Onset / peak
Total Hb mass	475 g	560 g	+18–20%	parallels red cell mass
Haematocrit	38%	32–33%	falls	disproportionate plasma rise

The disproportionate rise in plasma volume relative to red cell mass produces **physiological (dilutional) anaemia** — haemoglobin concentration falls by roughly 2 g/dL despite a rising *total* Hb mass; reticulocyte count and erythropoietin level rise mildly (mild erythroid hyperplasia in the marrow). A haemoglobin below 11.0 g/dL, particularly late in pregnancy, is abnormal and usually reflects true iron-deficiency anaemia rather than dilution.

Advantages of the hemodilution:

- Reduced blood viscosity improves uteroplacental perfusion and materno-fetal gas exchange.
- Protects against the adverse effects of impaired venous return in the supine and erect postures.
- Buffers the mother against the blood loss of delivery.

2. Iron metabolism

Iron economy of pregnancy	Amount
Total iron requirement of pregnancy	≈1000 mg
— transferred to fetus & placenta	300 mg
— expanded maternal red cell mass	400–500 mg
— obligatory losses (gastrointestinal, skin, urine)	200 mg
Daily requirement, second half of pregnancy	6–7 mg/day (vs 1 mg/day non-pregnant)
Recommended daily supplementation (WHO, 2016)	30–60 mg elemental iron + 400 µg folic acid
Therapeutic dose for established iron-deficiency anaemia	~200 mg elemental iron/day

Demand is concentrated in the second half of pregnancy. Without supplementation, serum iron and ferritin fall after mid-pregnancy even though placental iron transfer to the fetus continues despite maternal deficiency — maternal and fetal haemoglobin concentrations do not correlate.

3. White cells & inflammatory markers

- Total leucocyte count rises physiologically; upper normal limit ~15,000/µL; during labour and the early puerperium it may reach ≥25,000/µL (mechanism unclear; a similar rise follows strenuous exercise).

- Absolute T-lymphocyte numbers increase (relative lymphocytosis); B-cell numbers are unchanged; CD4:CD8 ratio is unaltered.
- Erythrocyte sedimentation rate (ESR) rises markedly (elevated fibrinogen and globulins) — it therefore has little diagnostic value in pregnancy.
- C-reactive protein is mildly higher through pregnancy and labour; complement factors C3 and C4 rise significantly in the second and third trimesters.
- Procalcitonin stays low in mid-pregnancy but rises near term and in the early puerperium.

4. Coagulation & fibrinolysis — a procoagulant state

Factor	Non-pregnant	Change across pregnancy
Fibrinogen (Factor I)	200–400 mg/dL	+50% (300–600 mg/dL; ~450 mg/dL average at term)
Factors VII, VIII, IX, X	baseline	Progressively increased
Factors XI, XIII	baseline	Decreased
Free protein S	baseline	Progressively decreased → acquired resistance to activated protein C
Antithrombin	baseline	Falls ~13% from mid-pregnancy to term; falls further (~30%) until 12 h post-delivery; back to baseline by 72 h postpartum
D-dimer	baseline	Rises with each trimester (ongoing fibrin turnover)
Clotting time	baseline	Unaffected

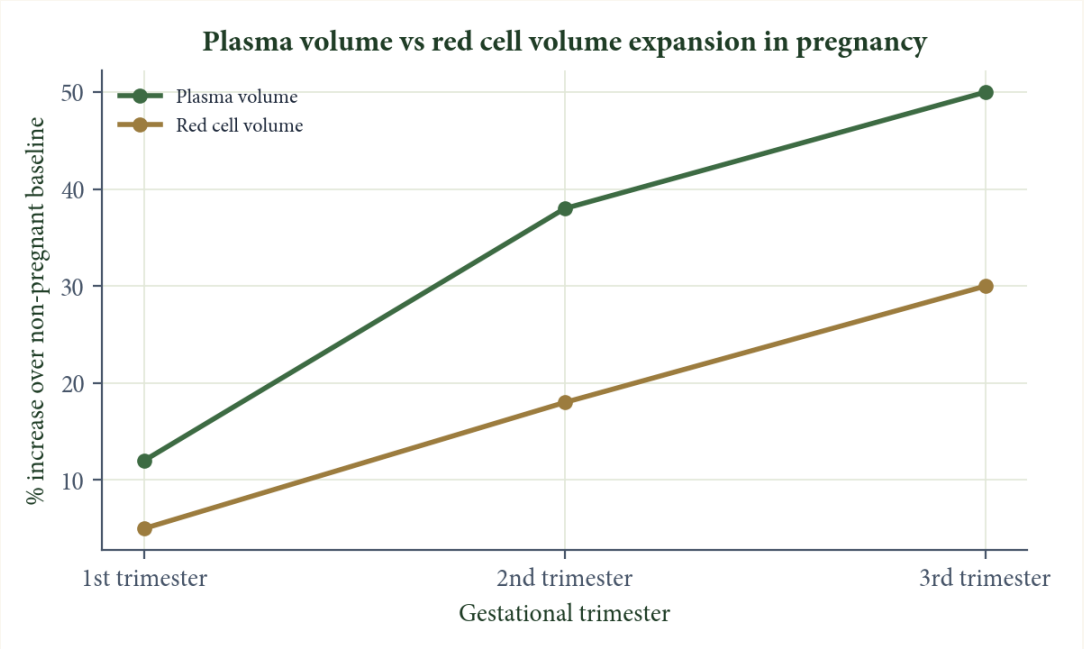
Increased thrombin generation together with reduced natural anticoagulants (protein S, antithrombin) tilts haemostasis toward clot formation; fibrinolytic activity, though ultimately net-increased (rising D-dimer), remains relatively suppressed until placental separation. This procoagulant state limits blood loss at delivery but underlies the raised risk of venous thromboembolism in pregnancy and the puerperium.

5. Platelets & spleen

- Platelet count declines mildly across gestation from haemodilution plus increased peripheral consumption. Thrombocytopenia (platelet count <150,000/μL) is found in ~10% of gravidas; 75% of this is benign **gestational thrombocytopenia** — nadir typically in the third trimester, rarely below 70,000–100,000/μL, with no maternal or fetal complication. Counts return to non-pregnant values by 4–12 weeks postpartum.

- Spleen size increases up to 50% by term compared with the first trimester (mechanism uncertain; possibly related to the expanded blood volume).

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Plasma volume rises steeply and plateaus near +50% by the third trimester, while red cell volume rises more slowly and near-linearly to ~+30% at term; the widening gap between the two curves is the basis of physiological (dilutional) anaemia.

High-yield exam pointers

- Blood volume +30–45%, peaks 32–34 weeks; plasma volume (+40–50%) rises more than red cell volume (+20–30%) → dilutional anaemia.
- Haemoglobin <11.0 g/dL, especially late in pregnancy, is pathological (iron deficiency), not physiological.
- Total iron requirement of pregnancy ≈1000 mg; second-half daily need 6–7 mg/day; WHO supplementation = 30–60 mg elemental iron + 400 µg folic acid.
- Leucocytosis: up to 15,000/µL normally, ≥25,000/µL in labour/early puerperium.
- Fibrinogen rises 50% (200–400 → 300–600 mg/dL); Factors XI and XIII fall; pregnancy = procoagulant state.
- Platelets fall mildly (gestational thrombocytopenia, ~75% of pregnancy thrombocytopenia); ESR rises up to four-fold but is not diagnostic in pregnancy.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Exact percentage figures for blood/plasma/red-cell volume expansion vary slightly by textbook edition (e.g., blood volume peak quoted as +40–45% at 32–34 weeks in one spine text versus +30–45% at 30–34 weeks in another); both describe the same physiological pattern, and either figure is acceptable in the exam.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e (Chapter 5, "Hematological Changes," Tables 5.1–5.3); Williams Obstetrics 26e (Chapter 4, "Hematological Changes," Table 4-4, Figure 4-7); World Health Organization (2016) antenatal iron and folic acid supplementation recommendation.

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Hormones of Anterior Pituitary

Asked in: Paper I 29-Jul-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — The anterior pituitary (**adenohypophysis**) develops from oral ectoderm (Rathke pouch) and lies in the sella turcica. It comprises **five secretory-cell types** that produce **six major hormones**, entirely under humoral control of hypothalamic releasing/inhibiting hormones delivered through the **hypophyseal portal venous system** — there is no direct neural connection between hypothalamus and adenohypophysis.

Cell types, chemical nature & hypothalamic control

Hormone	Secretory cell	Chemical nature	Hypothalamic control
Growth hormone (GH/somatotropin)	Acidophil — somatotrope	Single-chain polypeptide, 191 amino acids, ~22 kDa	Stimulated by **GHRH**; inhibited by **somatostatin**
Prolactin (PRL)	Acidophil — lactotrope	Single-chain polypeptide (structurally related to GH)	Tonically **inhibited by dopamine** (prolactin-inhibiting factor); disinhibited/stimulated by **TRH** and suckling
Thyroid-stimulating hormone (TSH)	Basophil — thyrotrope	Glycoprotein, common α + specific β subunit	Stimulated by **TRH**; inhibited by somatostatin/dopamine and by thyroid hormone feedback

Hormone	Secretory cell	Chemical nature	Hypothalamic control
Adrenocorticotropic hormone (ACTH)	Basophil — corticotrope	39-amino-acid peptide cleaved from **pro-opiomelanocortin (POMC)**	Stimulated by **CRH**; inhibited by cortisol feedback
Follicle-stimulating hormone (FSH)	Basophil — gonadotrope	Glycoprotein, common α + specific β subunit	Stimulated by pulsatile **GnRH**; selectively inhibited by ovarian **inhibin**
Luteinizing hormone (LH)	Basophil — gonadotrope (same cell as FSH)	Glycoprotein, common α + specific β subunit	Stimulated by pulsatile **GnRH** (high-frequency pulses favour LH)

The **α-subunit** of FSH, LH, TSH (and placental hCG) is identical (chromosome 6p21); the unique **β-subunit** confers each hormone's biological and immunological specificity — GnRH binding activates the cAMP–protein kinase C–Ca^{2+} cascade to trigger gonadotropin release and biosynthesis.

Physiological actions

- **GH** — drives skeletal and soft-tissue growth chiefly via hepatic **insulin-like growth factor-1 (IGF-1)**; also has a direct **anti-insulin (diabetogenic)** effect, promotes lipolysis and protein anabolism; secretion is pulsatile, peaking with slow-wave sleep.
- **Prolactin** — promotes mammary ductal and lobulo-alveolar development in pregnancy (synergising with oestrogen/progesterone) and initiates **lactogenesis** once oestrogen/progesterone fall after delivery; suppresses hypothalamic GnRH pulsatility, which underlies **lactational amenorrhoea**; it is the only anterior pituitary hormone under predominant tonic **inhibitory** control.
- **TSH** — stimulates thyroid follicular-cell growth and T3/T4 synthesis and release; abnormal secretion causes menstrual and ovulatory dysfunction.
- **ACTH** — stimulates the adrenal **zona fasciculata and reticularis** to synthesise cortisol and adrenal androgens; shows a diurnal rhythm (peak on waking); its POMC precursor also yields β-lipotropin and β-endorphin (β-melanocyte-stimulating hormone [MSH] is a POMC by-product but has no established function in the adult human).
- **FSH** (morphogenic, acts on granulosa cells):
  - Rescues antral follicles from atresia and drives granulosa-cell proliferation and follicular-fluid (antrum) formation.
  - Induces **aromatase**, converting theca-derived androgen to oestrogen in granulosa cells.
  - Induces its own and LH receptors on granulosa cells, and stimulates granulosa production of **activin/inhibin**.

- Stimulates plasminogen activator needed for follicular rupture.
- Rises early in the cycle, peaks around day 12 (pre-ovulatory), and declines to baseline by about day 18.

- **LH** (steroidogenic, acts on theca cells; **two-cell, two-gonadotropin** system):
  - LH drives theca-cell androgen synthesis, which diffuses to granulosa cells for FSH-induced aromatisation to oestrogen.
  - A sustained oestradiol peak for ~24 hours triggers the mid-cycle **LH surge** by positive feedback; the surge lasts about 24 hours.
  - **Ovulation occurs ~32–36 hours after the onset of the LH surge (10–12 hours after the LH peak)**; the surge triggers resumption of oocyte meiosis I, follicular rupture, and luteinisation of granulosa cells with progesterone and prostaglandin synthesis.
  - LH maintains the **corpus luteum** in the luteal phase.

Clinical correlation in Obstetrics & Gynaecology

- **Hyperprolactinaemia** disrupts GnRH pulsatility, causing anovulation, oligo/amenorrhoea ± galactorrhoea; treated with dopamine agonists — **bromocriptine** or **cabergoline**.
- **Sheehan syndrome** — pituitary ischaemic necrosis following severe postpartum haemorrhagic shock, causing panhypopituitarism; lactation failure is typically the earliest clue, followed by amenorrhoea and features of hypothyroidism/hypoadrenalism.
- **GnRH agonist "flare" effect** — initial FSH/LH up-regulation, then profound down-regulation from pituitary GnRH-receptor loss (a reversible "medical hypophysectomy"), exploited in endometriosis/fibroid therapy.
- **Prolactinoma** is the commonest functioning pituitary adenoma causing infertility/menstrual disturbance in reproductive-age women and needs monitoring through pregnancy.
- **Elevated FSH** is the key biochemical marker of ovarian failure/menopause and of diminished ovarian reserve; exogenous **FSH/hMG/hCG** underlie gonadotropin ovulation-induction protocols.
- **Cushing disease** — a basophil (corticotrope) microadenoma hypersecreting ACTH causes adrenal hyperplasia with hirsutism, menstrual irregularity and centripetal obesity.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 7.1 — Anatomy of the hypothalamus and pituitary. The hypothalamus, anterior pituitary and the portal system of blood supply is shown (DC Dutta's Gynaecology 7e, p.73)*

High-yield exam pointers

- **5 cell types → 6 hormones**: somatotrope-GH, lactotrope-PRL, thyrotrope-TSH, corticotrope-ACTH, gonadotrope-FSH & LH (same cell secretes both gonadotropins).

- Common **α-subunit** (FSH, LH, TSH, hCG) vs hormone-specific **β-subunit** — classic viva point.
- **Prolactin** is the only hormone under predominant **inhibitory** hypothalamic control (dopamine); TRH stimulates it.
- **LH surge → ovulation in 32–36 h** (10–12 h after the LH peak) — write these numbers exactly.
- **POMC** → ACTH + β-lipotropin + β-endorphin (± vestigial MSH) — links Cushing disease/Addison pigmentation logic.
- **Sheehan syndrome**: postpartum haemorrhagic shock → pituitary necrosis → panhypopituitarism; failure to lactate is the earliest sign.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> MSH-related peptides are functionally vestigial in the adult human anterior pituitary — a discrete pars intermedia/MSH-secreting population is prominent only in fetal life — so most current teaching lists GH, prolactin, TSH, ACTH, FSH and LH as the six clinically relevant anterior pituitary hormones.

> **SOURCE & COVERAGE**
> Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; DC Dutta's Textbook of Gynaecology 7e; Williams Obstetrics 26e.

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HPO axis

Asked in: Paper I Nov 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — The hypothalamic-pituitary-ovarian (HPO) axis is the integrated neuroendocrine system linking the hypothalamus (pulsatile gonadotropin-releasing hormone, GnRH), the anterior pituitary gonadotrophs (follicle-stimulating hormone, FSH, and luteinizing hormone, LH) and the ovary

(folliculogenesis, steroidogenesis and ovulation), coordinated by negative and positive feedback of ovarian steroids and peptides. It is the physiological basis of the normal ~28-day menstrual cycle.

Components and their secretions

Level	Structure	Hormone secreted	Key feature
Hypothalamus	Arcuate nucleus (+ preoptic area) neurons; axons end on hypophyseal portal vessels at the median eminence	GnRH (also called luteinizing hormone–releasing hormone, LHRH)	Decapeptide (10 amino acids); encoded by a 92-amino-acid preprohormone that also yields GnRH-associated peptide (GAP, a prolactin inhibitor); half-life only 2–4 minutes; must be secreted in **pulses**, not continuously
Anterior pituitary	Gonadotroph (basophilic) cells	FSH and LH (glycoprotein hormones, common α-subunit + hormone-specific β-subunit)	A single GnRH pulse drives both FSH and LH; the ratio secreted depends on GnRH pulse **frequency**
Ovary	Granulosa cells (FSH receptors), theca cells (LH receptors), corpus luteum	Estradiol, progesterone, inhibin, activin, anti-Müllerian hormone (AMH)	Two-cell, two-gonadotropin theory: LH drives theca-cell androgen synthesis; FSH drives granulosa aromatization of androgen to estradiol

Pulsatile GnRH secretion — the pacemaker of the axis

- GnRH is released from the arcuate nucleus into the portal circulation as discrete pulses; continuous (non-pulsatile) GnRH exposure **down-regulates** pituitary GnRH receptors and switches off gonadotropin secretion — the physiological basis of GnRH-agonist therapy.
- A critical range of pulse frequency and amplitude is required for normal gonadotropin output; in monkey studies, 1 pulse/hour reproduced physiological portal GnRH levels, while increasing frequency to 2–5 pulses/hour paradoxically suppressed gonadotropin secretion.
- **Decreasing** GnRH pulse frequency favours **FSH** secretion; **increasing** frequency favours **LH** secretion.
- Cycle-phase variation in LH pulse frequency/amplitude (a surrogate marker for GnRH pulses, since the long half-life of FSH precludes its use for this purpose):

Cycle phase	LH pulse frequency (interval)	LH pulse amplitude
Early follicular	~90 min	6.5 IU/L
Late follicular	60–70 min	7.2 IU/L
Early luteal	~100 min	15.0 IU/L
Late luteal	~200 min	8.0 IU/L

- The slowing of GnRH pulse frequency in the late luteal phase favours FSH synthesis over LH, driving the FSH rise that recruits the next cohort of follicles.

Feedback loops that regulate the axis

Feedback type	Mechanism
Long-loop feedback	Circulating ovarian steroids (estradiol, progesterone) act on both hypothalamus and pituitary
Short-loop feedback	Pituitary gonadotropins (FSH/LH) feed back negatively on their own secretion via hypothalamic GnRH
Ultrashort-loop feedback	GnRH inhibits its own synthesis/release
Negative feedback (low/early estrogen)	Low-level estradiol suppresses FSH (very sensitive) and LH via the hypothalamus
Negative feedback (estrogen + inhibin)	Rising estradiol combined with inhibin B from the dominant follicle produces profound, sustained FSH suppression — atresia of the non-dominant cohort
Positive feedback (peak estrogen — the LH surge trigger)	Sustained estradiol >200 pg/mL for approximately 50 hours (reached when the dominant follicle is ~15–18 mm) switches estrogen's action on LH from inhibitory to stimulatory, triggering the mid-cycle **LH surge** that causes ovulation ~36 hours later
Progesterone action	Negative feedback at the hypothalamus (slows GnRH pulses); positive/permissive action directly on the pituitary, amplifying the LH surge
Inhibin/activin (gonadal peptides)	Inhibin selectively suppresses FSH; activin stimulates FSH — a paracrine/endocrine fine-tuning loop independent of steroids

Physiological phases of the cycle driven by the axis

- **Follicular phase** — rising FSH (from luteal-phase withdrawal of estradiol/progesterone/inhibin A) recruits a cohort of follicles; the dominant follicle is selected as it acquires FSH-independent

LH responsiveness and produces rising estradiol + inhibin B, which suppress FSH to atretic levels in the remaining cohort.

- **Mid-cycle** — sustained high estradiol flips negative to positive feedback → LH surge (+ smaller FSH surge) → resumption of oocyte meiosis, follicular rupture, luteinization; ovulation occurs about 34–36 hours after the LH surge onset.
- **Luteal phase** — the corpus luteum (LH-dependent) secretes progesterone and estradiol, which negatively feed back to suppress FSH/LH; luteolysis at 14 days (if no conception) withdraws steroid/inhibin-A support, releasing FSH to rise and start the next cycle.

Clinical relevance of the HPO axis (why it is examined)

Disorder	HPO axis defect
Hypothalamic amenorrhea (stress, weight loss, exercise)	Reduced GnRH pulse frequency/amplitude → low FSH/LH, low estradiol
Polycystic ovary syndrome	Increased GnRH pulse frequency → LH:FSH ratio favouring LH → theca hyperandrogenism
Kallmann syndrome	Failure of GnRH neuron migration from olfactory placode → hypogonadotropic hypogonadism with anosmia
GnRH agonist therapy (endometriosis, fibroids, precocious puberty, IVF down-regulation)	Continuous receptor occupancy → gonadotroph down-regulation → medical "castrate" state
Menopause	Ovarian follicular depletion removes negative feedback → persistently high FSH/LH

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 7.8 — Interplay of hormones along the hypothalamo-pituitary-ovarian axis through feedback mechanism (DC Dutta's Gynaecology 7e, p.83)*

High-yield exam pointers

- GnRH: decapeptide, arcuate nucleus, half-life 2–4 minutes, must be **pulsatile** — continuous exposure down-regulates receptors (basis of GnRH-agonist "flare then suppress" action).
- Slow GnRH pulses → more **FSH**; fast GnRH pulses → more **LH** ("Slow=FSH, Fast=LH").
- Positive feedback trigger for the LH surge: estradiol **>200 pg/mL sustained ~50 hours**, dominant follicle ~15–18 mm.
- Three feedback loops: **long** (steroid → hypothalamus/pituitary), **short** (gonadotropin → hypothalamus), **ultrashort** (GnRH → itself).
- Inhibin suppresses FSH; activin stimulates FSH — remember "In-hibin Inhibits."

- Two-cell, two-gonadotropin theory: **theca + LH → androgens; granulosa + FSH → aromatization to estradiol.**

> **SOURCE & COVERAGE**
> Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Gynaecology 7e.

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Immunological control of fertility

Asked in: Paper IV 04-Aug-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — Immunological control of fertility refers to the use, or spontaneous occurrence, of an antibody response directed against reproduction-specific antigens to interrupt fertility. It has two faces: (1) deliberate **immunocontraceptive vaccines** raised against antigens unique to gametes/early pregnancy (human chorionic gonadotropin (hCG), sperm antigens, zona pellucida (ZP)), intended as a reversible, non-hormonal method of contraception; and (2) naturally occurring **antibody-mediated (immunological) infertility**, where antisperm or anti-ZP antibodies impair fertilization.

Why reproductive antigens are vaccine targets

- Gamete- and trophoblast-restricted antigens (hCG beta-subunit, sperm-surface antigens, ZP glycoproteins) are not expressed on vital organs, so an induced antibody response is contraceptive without systemic autoimmune injury.
- The antibody titre declines over months, so the effect is **reversible** — unlike surgical sterilization.
- No daily compliance is needed, unlike hormonal contraceptives.

Target antigens used for immunocontraceptive vaccines

Target antigen	Basis of selection	Vaccine strategy	Effect	Current status
hCG (beta-subunit)	The beta-subunit is structurally distinct from luteinizing hormone (LH)/thyroid-stimulating hormone (TSH)/follicle-stimulating hormone (FSH) but is weakly immunogenic alone, so it is coupled to a carrier (hapten) to raise antibody	**Anti-hCG vaccine**, most effective form directed against the **C-terminal peptide of the beta-subunit of hCG**	Neutralises hCG after fertilisation (a post-fertilisation, pre-implantation acting agent); antibody does **not** cross-react with LH; effect lasts up to **12 months**	Research/trial stage; not a licensed clinical product
Sperm antigen (LDH-X, sperm-specific lactate dehydrogenase isoenzyme)	Sperm-restricted enzyme	Anti-LDH-X antibody	Significant reduction in viable sperm and defective implantation shown in experimental animals	Experimental
Zona pellucida (ZP)	Oocyte glycoprotein coat; most extensively studied oocyte target antigen	Antisera to ZP coat the zona surface	Blocks sperm penetration of the zona; sera from infertile women with anti-ZP antibodies can block fertilisation *in vitro*	Experimental in humans (autoimmune oophoritis risk); zona-based vaccines are an established tool for **wildlife population control**

Naturally occurring antibody-mediated (immunological) infertility

Antibody	Isotype & site	Mechanism	Effect on fertility
Antisperm antibodies	**IgG** — cervical mucus, serum, semen; **IgA** — cervical mucus and seminal plasma (agglutinating); **IgM** — serum only (large molecule, does not cross into secretions)	Bind sperm surface antigens on the head, body, or tail	Immobilise or agglutinate sperm, impair penetration of cervical mucus, and prevent fertilisation; may arise in either partner after genital infection, trauma, torsion, or vaso-vasostomy (breach of the blood–testis barrier)
Anti-zona pellucida antibodies	Present in serum of some infertile women	Coat the zona surface	Block sperm–zona binding/penetration; demonstrable defect *in vitro* fertilisation

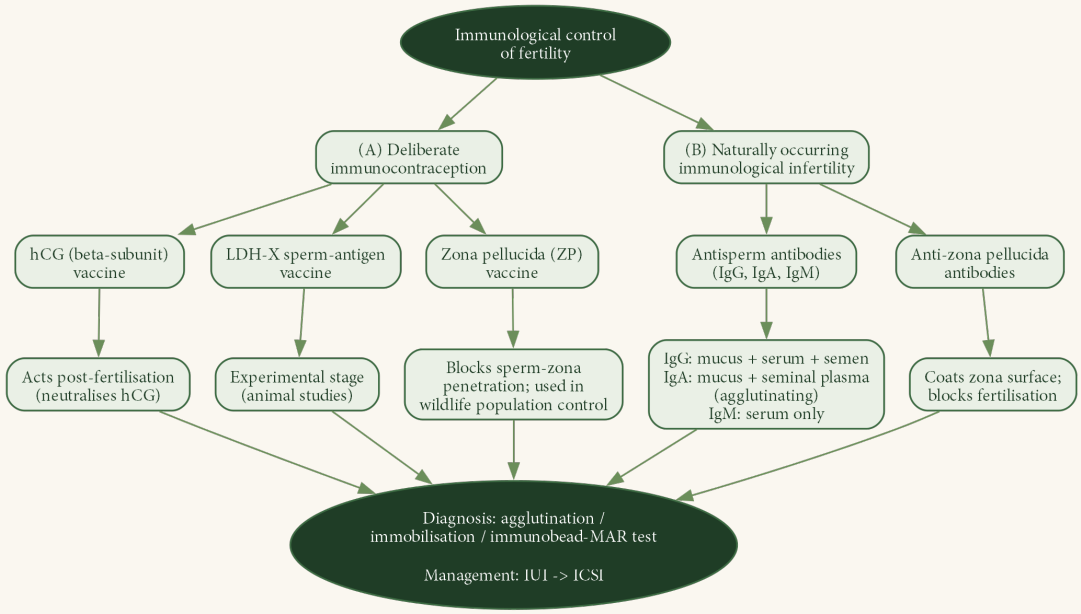
Diagnosis of immunological (antibody-mediated) infertility

- **Sperm agglutination test** and **sperm immobilisation test** — historical serological tests for antisperm antibody following infection, trauma, or vasectomy.
- **Postcoital test** — historically suggested if a poor result was obtained; **no longer performed routinely** as it has no proven value in guiding treatment.
- **Immunobead/mixed antiglobulin reaction (MAR) test** — beads or latex particles coated with anti-human-immunoglobulin bind antibody already present on the sperm surface; considered clinically significant when **more than 50% of sperm are antibody-coated**.
- Routine antisperm antibody testing is **rarely performed today** — detection has not been shown to change management or improve pregnancy outcome, especially once intrauterine insemination (IUI), in vitro fertilisation (IVF), or intracytoplasmic sperm injection (ICSI) are available.

Clinical management once immunological infertility is suspected

- **Intrauterine insemination (IUI)** — historically the most effective treatment strategy for antisperm-antibody-related and unexplained infertility.
- **Intracytoplasmic sperm injection (ICSI)** — used when IUI fails or IVF is otherwise indicated; effectively bypasses any adverse effect of antisperm antibodies on fertilisation.
- Condom therapy to reduce antigen exposure has been described historically but lacks proven benefit and is largely abandoned.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Classification flowchart: immunocontraceptive vaccine targets (arm A) and naturally occurring antibody-mediated infertility (arm B) converging on shared diagnosis/management.

Recent advances [RA]

- **Anti-hCG conjugate vaccines**: recombinant beta-hCG (or its C-terminal peptide) coupled to tetanus/diphtheria toxoid carriers has been carried through Phase I/II human trials in India (National Institute of Immunology, New Delhi) demonstrating reversible, antibody-titre-dependent contraception; no anti-hCG vaccine has yet been licensed for clinical use.
- **Zona-pellucida-based immunocontraception**: porcine zona pellucida (PZP) vaccines are an established, reversible tool for **wildlife population control** (feral horses, deer); human application remains experimental because of the risk of vaccine-induced autoimmune oophoritis.
- **Sperm-antigen vaccine research**: recombinant sperm-restricted proteins (e.g., epididymal protease inhibitor, sperm-specific ion channel proteins) are under preclinical evaluation as candidate contraceptive antigens for unisex vaccines; none has reached human trials.
- **Anti-GnRH (immunocastration) vaccines** are an established veterinary tool (e.g., livestock immunocastration) but induce hypogonadism and are not used for human contraception.
- Standardisation of antisperm-antibody testing (immunobead/MAR test thresholds) is now referenced to the current **WHO laboratory manual for the examination and processing of human semen**; contemporary infertility-society guidance (in line with Speroff) advises **against routine antisperm-antibody testing**, since IUI/ICSI make the result rarely actionable.

- To date, **no immunocontraceptive vaccine (anti-hCG, anti-sperm, or anti-ZP) is approved for routine human use** anywhere in the world; all remain investigational.

High-yield exam pointers

- 4 antigen targets to recall: **hCG (beta, C-terminal peptide) — LDH-X (sperm) — Zona pellucida (ZP) — antisperm surface antigens.**
- Anti-hCG vaccine acts **after fertilisation** (does not prevent conception, causes early loss of the fertilised ovum); does **not** cross-react with LH.
- Antisperm antibody isotypes: **IgG** (mucus + serum + semen), **IgA** (mucus + seminal plasma, agglutinating), **IgM** (serum only).
- Immunobead/MAR test positivity threshold: **>50% sperm coated**.
- Antisperm antibody testing is now **rarely done** — IUI then ICSI bypass its clinical relevance.
- No immunocontraceptive vaccine is currently licensed for human use — all are investigational/experimental.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> For reference only — the porcine zona pellucida wildlife vaccine and livestock anti-GnRH immunocastration vaccine are well-established veterinary/wildlife tools, cited here only to illustrate that the underlying immunological principle is proven, not because either is used in human contraception.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Obstetrics 9e (Chapter 39, "Immunological control of fertility"); DC Dutta's Textbook of Gynaecology 7e (Immunological factor in infertility); Speroff's Clinical Gynecologic Endocrinology & Infertility 9e (sperm autoantibodies, immunobead testing, IUI/ICSI). Coverage note: the on-disk corpus does not carry a dedicated "recent advances" subsection for this niche topic; the Recent Advances points above draw on well-established, widely cited research (Talwar et al. anti-hCG vaccine programme, porcine zona pellucida wildlife vaccination, WHO semen-analysis manual) rather than a single indexed corpus page.

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Imperforate hymen

Asked in: Paper I Nov 2018 · Paper III Oct 2008 · Paper I Sep 2007 (3×) — RGUHS MS Obstetrics & Gynaecology

Definition — Imperforate hymen is the commonest congenital obstructive anomaly of the female genital outflow tract, in which the hymenal membrane fails to perforate because the central cells of the **Müllerian eminence** (where the fused paramesonephric ducts meet the urogenital sinus) fail to

disintegrate. The uterus, cervix and vagina proximal to the membrane are normally formed and ovarian function is entirely normal, so once cyclical endometrial shedding begins, menstrual blood is retained behind the obstruction — **cryptomenorrhea**.

Clinical presentation

Age group	Mechanism	Presentation
Neonate (first weeks of life)	Maternal/placental **estrogen** stimulates cervical and vaginal gland secretion, and desquamation, behind the imperforate membrane	**Mucocolpos** ± hydrocolpos — a bulging bluish introital membrane, a lower abdominal/pelvic mass, occasionally urinary retention or respiratory distress from mass effect
Peripubertal girl, typically **14–16 years** (DC Dutta)	Onset of cyclical menstruation with no outflow	Cryptomenorrhea → **hematocolpos** → **hematometra** → **hematosalpinx** if the fimbrial ends seal and the condition is neglected

Adolescent clinical features (the classic exam presentation):

- **Primary amenorrhea with normal secondary sexual characteristics** — breast and pubic/axillary hair development are normal because ovarian function is unaffected.
- Periodic, and later continuous, **lower abdominal pain**.
- **Acute retention of urine** — often the presenting complaint; caused by elongation and posterior compression of the urethra by the distended, blood-filled vagina.
- **Suprapubic swelling** — may be the distended bladder, the hematocolpos/hematometra, or both; catheterisation clarifies which.
- Constipation/tenesmus from rectal compression by the distended vagina.
- **Vulval inspection**: a tense, bulging, bluish membrane at the introitus (blood visible through the translucent hymen).
- **Per-rectal examination**: the vagina bulges anteriorly; a **perirectal mass that protrudes with Valsalva** is the key finding that confirms the obstruction is at the introital level rather than higher up (Berek & Novak).
- Rarely, retrograde spill through the tubes causes **hemoperitoneum and pelvic endometriosis**, or ascending infection produces pyocolpos/pyometra.

Diagnosis and investigations

Test	Finding / purpose
Vulval inspection	Tense, bulging, bluish membrane at the introitus

Test	Finding / purpose
Per-rectal examination	Bulging vagina anteriorly; perirectal bulge with Valsalva localises the obstruction to the introitus
Pelvic ultrasonography (transabdominal)	Confirms **hematocolpos ± hematometra ± hematosalpinx**; confirms a normally formed uterus and cervix above the obstruction
MRI pelvis	Reserved for equivocal cases — delineates the level/thickness of the obstructing membrane and separates a true imperforate hymen from a higher transverse vaginal septum
Renal ultrasound / IVP	To exclude a coexisting urinary-tract anomaly when other Müllerian anomalies are suspected
Karyotype	Only if virilisation or ambiguous genitalia raises suspicion of androgen insensitivity — not needed for a straightforward imperforate hymen

Differential diagnosis of outflow obstruction

Feature	Imperforate hymen	Transverse vaginal septum	Vaginal agenesis (MRKH)	Complete androgen insensitivity
Hymen on inspection	Bulging, bluish membrane visible at introitus	Normal hymenal ring; septum lies higher (≈45% upper, 40% mid, 15% lower vagina — DC Dutta)	Normal hymenal ring; short/blind vaginal pouch	Normal hymenal ring; blind vaginal pouch
Perirectal bulge with Valsalva	Present	Often absent if septum is high	Absent	Absent
Uterus	Present and functioning	Present and functioning	Absent/rudimentary	Absent (regressed by anti-Müllerian hormone)
Pubic/axillary hair	Normal	Normal	Normal	Sparse or absent
Karyotype	46,XX	46,XX	46,XX	46,XY

Management

- Confirm the diagnosis clinically, supported by pelvic ultrasonography, before any intervention.
- Definitive treatment is a **cruciate (X-shaped) incision** of the hymen under aseptic technique; the four resulting quadrants of hymenal tissue are trimmed back — not flush with the vaginal

mucosa — to prevent reclosure, and the pooled dark, tarry, altered blood is allowed to **drain spontaneously** (DC Dutta).

- **Do not** apply pressure from above during drainage, and **do not** perform an internal (vaginal/bimanual) examination at the same sitting.
- **Do not** attempt simple needle aspiration of a hematocolpos without complete surgical deroofing of the membrane — incomplete drainage predisposes to secondary infection and **pyocolpos** (Berek & Novak).
- Post-operatively, nurse the patient propped up with the head end raised and cover with antibiotics; a full internal examination for residual pathology (a partial septum or an associated anomaly) is deferred until after the next menstrual period.
- Symptomatic neonatal mucocolpos/hydrocolpos is treated the same way — hymenotomy — if it produces a mass effect, urinary retention, or respiratory compromise.
- Long-term reproductive outcome is excellent, as the uterus, tubes and ovaries are normal.

Complications if undiagnosed or untreated

- Progressive hematometra and hematosalpinx, occasionally becoming irreversible if longstanding.
- Secondary infection — pyocolpos, pyometra, pelvic sepsis.
- Endometriosis secondary to retrograde menstruation through the tubes.
- Acute urinary retention and recurrent urinary tract infection; rarely upper-tract compromise from chronic compression.
- Subfertility if diagnosis and treatment are delayed with resultant tubal damage.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 4.1 — Hematocolpos, hematometra and hematosalpinx resulting from an imperforate hymen (DC Dutta's Gynaecology 6e, p.58)*

High-yield exam pointers

- Embryology one-liner: failure of disintegration of the central cells of the **Müllerian eminence** at the urogenital sinus.
- Peak age of adolescent presentation: **14–16 years** (DC Dutta).
- Classic triad: primary amenorrhea + cyclical/continuous lower abdominal pain + acute retention of urine, with **normal secondary sexual characteristics** — this is cryptomenorrhea.
- Cause of urinary retention: **elongation and posterior compression of the urethra** by the distended vagina.
- Distinguishing sign versus a higher transverse septum or vaginal agenesis: **perirectal bulge on Valsalva** and a visible bulging bluish membrane at the introitus.

- Never needle-aspirate a hematocolpos and never do an internal exam at first sitting — risk of **pyocolpos**.
- Treatment = **cruciate incision with trimming of the quadrants**, not a simple stab incision, followed by spontaneous drainage.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Routine gentle inspection of the introitus in every female neonate (checking hymenal patency) is recommended in the newborn nursery so that an imperforate hymen is picked up before a hematocolpos develops years later; this is a practice point from Berek & Novak rather than a graded society guideline.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e (and 6e for the labelled figure); Berek & Novak's Gynecology 16e.

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Intrauterine insemination

Asked in: Paper I Nov 2016 · Paper III Oct 2008 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — Intrauterine insemination (IUI) is an assisted reproductive technique in which a washed, concentrated suspension of motile spermatozoa — from the husband (artificial insemination husband, **AIH**) or a donor (artificial insemination donor, **AID**) — is deposited directly into the uterine cavity through a transcervical catheter, timed to coincide with ovulation. It bypasses an abnormal or hostile endocervical canal and delivers a higher concentration of motile, processed sperm closer to the fallopian tubes than natural intercourse or intracervical insemination (ICI).

Indications and prerequisites

Category	Examples
Cervical factor	Hostile/abnormal cervical mucus, cervical stenosis or surgery (e.g., post-cone biopsy) — best results obtained here
Male factor	Mild oligozoospermia or asthenozoospermia with an adequate processed count; ejaculatory dysfunction/impotence or an anatomical defect (e.g., hypospadias) but normal ejaculate obtainable
Immunological factor	Antisperm antibodies, male or female

Category	Examples
Unexplained infertility	Combined with controlled ovarian stimulation (COS) — best results obtained here
Mild endometriosis	Combined with COS
No male partner / same-sex female couple	Donor IUI (AID), e.g., partner azoospermia or social indication

Prerequisites before offering IUI:

- At least one patent fallopian tube, confirmed by hysterosalpingography or laparoscopy
- Normal uterine cavity (hysteroscopy/saline sonography if suspected polyp/septum)
- Processed total motile sperm count (**TMSC**) adequate — minimum ~1 million, but best results when it exceeds 10 million
- Reasonable ovarian reserve and ovulatory potential

Technique

- **Semen collection** — by masturbation after a *short* abstinence of 2–3 days; longer abstinence (older recommendations of up to 5–7 days) lowers motile count and increases sperm DNA fragmentation and is no longer advised.
- **Sperm processing** — semen is washed in culture medium to remove seminal plasma proteins and prostaglandins that would otherwise cause uterine cramping or an anaphylactoid reaction if placed intrauterine unprocessed. Methods: simple **wash**, **swim-up** (motile sperm swim into the supernatant, free of dead cells/debris), and **density-gradient centrifugation** (recovers the most motile, morphologically normal fraction — preferred technique).
- **Timing** — decided by the chosen ovulation-monitoring protocol (see table below).
- **Positioning** — patient in the lithotomy position; a bivalve speculum exposes the cervix; excess cervical mucus is gently wiped from the external os.
- **Insemination** — about 0.3–0.5 mL of the processed sperm concentrate is loaded into a soft, flexible catheter and passed gently through the internal os into the mid-uterine cavity (avoiding fundal trauma) under aseptic precautions; the suspension is injected slowly and the catheter withdrawn.
- **Post-procedure rest** — the patient remains supine for about 15 minutes.
- **Luteal support** — vaginal progesterone may be added after stimulated cycles.
- **Repeat cycles** — 3–6 cycles are usually offered (up to 12 for donor IUI); no proven benefit of a double insemination per cycle over a single, well-timed insemination.

Timing of IUI

Monitoring method	Timing
Natural cycle — cervical mucus/basal body temperature/urinary LH kit	IUI ×2, traditionally on day 12 and day 14
Clomiphene citrate–induced cycle	IUI timed to the LH surge/hCG trigger after completing the clomiphene course
Urinary LH surge detection	IUI ~24 hours after the colour change (positive kit)
hCG trigger + follicular sonography (current preferred method)	hCG given when the leading follicle reaches ~18 mm; single IUI performed 24–36 hours later (ovulation itself follows 34–46 hours after hCG)

Success rate and factors affecting it

- Per-cycle pregnancy (fecundity) rate: clomiphene + IUI ≈ 7–8%; gonadotropin + IUI ≈ 10–12%; natural-cycle donor IUI ≈ 10% — all substantially lower than IVF (≈ 30% per cycle).
- Cumulative pregnancy rate: 20–40% over 3–6 stimulated cycles; up to 90% by 12 cycles of donor IUI with frozen sperm in women under 30 years with no other infertility factor.
- Favourable factors: processed TMSC > 10 million; ≥2 follicles ≥15 mm at trigger; age < 35 years; short (2–3 day) abstinence; treatment for cervical-factor or unexplained infertility (the two best-responding indications).
- Couples who fail to conceive after 3–6 IUI cycles (or 6–12 for donor IUI) should be reassessed for missed female/male factors and counselled to proceed to in vitro fertilisation (IVF)/intracytoplasmic sperm injection (ICSI).

Complications

- Uterine cramping or, rarely, an anaphylactoid-type reaction from inadequately washed seminal plasma
- Pelvic infection (uncommon; minimised by strict asepsis)
- Spotting from catheter trauma to the cervix/endometrium
- Multiple pregnancy and ovarian hyperstimulation syndrome (OHSS) — risk arises from the concomitant controlled ovarian stimulation, not from the insemination itself, and is highest with gonadotropin-stimulated cycles
- Psychological and financial burden of repeated failed cycles

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

No dedicated procedure figure was found in the indexed textbook figure set (closest matches were unrelated catheter illustrations), so describe a labelled schematic instead: a sagittal view showing a bivalve speculum exposing the cervix, a soft IUI catheter passed through the external and internal os into the mid-uterine cavity (tip kept clear of the fundus), the 0.3–0.5 mL sperm suspension being deposited, and both fallopian tube ostia labelled at the cornua.

High-yield exam pointers

- Volume inseminated: **0.3–0.5 mL** of processed sperm.
- Minimum processed TMSC ~1 million; **best results above 10 million**.
- Preferred sperm-prep method: **density-gradient centrifugation**.
- Current timing: single IUI **24–36 hours after hCG trigger** (given at ~18 mm follicle).
- Best indications: **cervical factor** and **unexplained infertility**.
- Per-cycle success ~10% (IUI) vs ~30% (IVF); cumulative 20–40% by 3–6 cycles.
- Short (2–3 day) abstinence beats the old 5–7 day rule.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's description of routine *double* insemination on cycle day 12 and 14 (or 34–40 hours after hCG) reflects an older protocol; current evidence (Berek & Novak's Gynecology 16e) shows a single, well-timed insemination 24–36 hours after hCG trigger is equally effective, so single IUI is now preferred.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e.

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Iron metabolism and mention the different iron preparations used in pregnancy

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Iron is the essential trace element for haemoglobin and myoglobin synthesis and for oxidative enzyme function. Pregnancy imposes a large, non-uniform increase in iron requirement — driven by expansion of the maternal red cell mass and fetoplacental transfer — that dietary intake and

existing stores usually cannot meet alone, making supplementation with oral or parenteral iron preparations a routine part of antenatal care.

Iron metabolism

- **Body iron content and distribution** — Total body iron in a normal adult woman is 2.0–2.5 g (about half that of men). Most is incorporated into haemoglobin (about 75%) and myoglobin; the rest is held as storage iron (ferritin and haemosiderin). Storage iron in a normal young woman is only about 300 mg — a slender reserve even before pregnancy adds demand.
- **Absorption** — Dietary iron is absorbed in the **ferrous (Fe^{2+}) form** from the **duodenum and proximal jejunum**; only about **10%** of ingested iron is normally absorbed, though gut absorption efficiency rises through pregnancy.
- **Transport** — Absorbed iron is released into the circulation bound to the plasma transport protein **transferrin**, which delivers it to erythroid precursors in the bone marrow and to other iron-requiring tissues.
- **Storage** — Iron not immediately used for haemoglobin synthesis is stored as **ferritin** (readily mobilisable) or **haemosiderin** (a more stable form), chiefly in the liver, spleen and bone marrow. Serum ferritin parallels total body iron stores and is the single most reliable laboratory indicator of iron status.
- **Regulation — the hepcidin–ferroportin axis** — **Hepcidin**, a peptide hormone, is the master regulator of systemic iron homeostasis. It suppresses **ferroportin**, the sole transmembrane channel that exports iron from enterocytes (and macrophages) into plasma; high hepcidin blocks iron release, low hepcidin permits it. Hepcidin concentration falls progressively through pregnancy, de-repressing ferroportin and thereby increasing both intestinal iron absorption and iron release from stores.
- **Placental transfer** — Iron crosses the placenta by **active, unidirectional transport**, exported from the syncytiotrophoblast via ferroportin (also favoured by the pregnancy fall in hepcidin) and delivered to fetal transferrin. This transfer is autonomous and protected: it continues even against severe maternal iron depletion, so the fetus is not anaemic at birth even when the mother's haemoglobin is markedly low.

Iron requirement in pregnancy

Because the requirement is not spread evenly across gestation, both the total amount needed and its trimester-wise distribution are commonly tested.

Component of the ~1000 mg total requirement	Approximate amount
Fetus and placenta (fetoplacental transfer)	300 mg

Component of the ~1000 mg total requirement	Approximate amount
Expansion of maternal red cell mass (≈450–500 mL increase × 1.1 mg elemental iron/mL)	≈500 mg
Obligatory losses (gastrointestinal tract, skin, urine)	200 mg
Total	**≈1000 mg**

Period	Daily iron requirement
First trimester	≈1 mg/day (near the basal non-pregnant loss)
Second half of pregnancy (after mid-pregnancy)	6–7 mg/day — far exceeds what diet/stores alone supply
Lactation	≈1 mg/day

Because dietary intake and endogenous stores are almost never sufficient to cover this late-pregnancy surge, routine supplementation with a therapeutic iron preparation — oral first-line, parenteral when indicated — is advised for essentially all pregnant women.

Oral iron preparations

Oral ferrous salts are first-line; the elemental iron content (the pharmacologically active fraction) differs by salt, which is the detail most often tested.

Iron salt	Usual tablet/capsule strength	Elemental iron per unit
Ferrous sulphate	300 mg	60 mg
Ferrous sulphate (dried)	200 mg	65 mg
Ferrous fumarate	200 mg	65 mg
Ferrous gluconate	300 mg	35 mg
Iron polymaltose complex (ferric form)	100 mg tablet	100 mg — soluble at neutral pH, fewer gastrointestinal side effects, better absorbed with food

- The standard prophylactic tablet is **ferrous sulfate 200 mg (60 mg elemental iron) with folic acid 1 mg, once daily**, started once early-pregnancy nausea has settled.
- If intolerance (epigastric pain, nausea, vomiting, diarrhoea or constipation) develops, start with one tablet daily and escalate gradually to a maximum of three tablets a day, or switch to an alternative salt.
- Tea should be avoided within 1 hour of the dose, as tannins impair absorption.

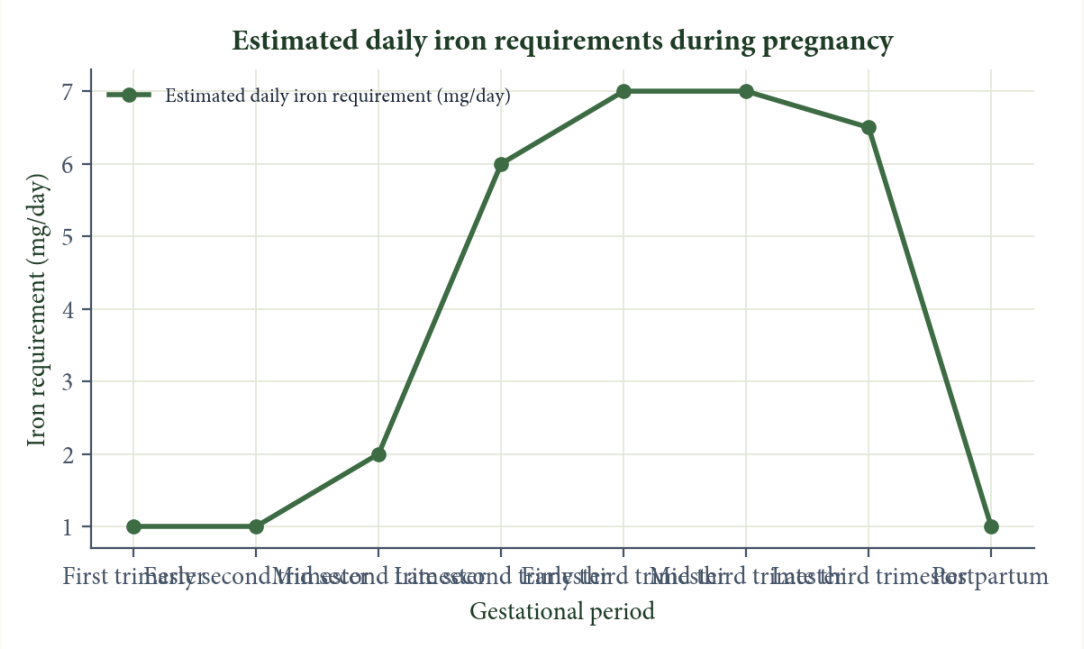
Parenteral iron preparations

Parenteral therapy is reserved for women who are (a) intolerant of oral iron, (b) unwilling to continue daily oral therapy, or (c) in an advanced stage of pregnancy (beyond 32 weeks) where oral treatment cannot raise haemoglobin adequately before delivery. It requires confirmed iron-deficiency anaemia, adequate supervision, and facilities to manage an anaphylactic reaction.

Route	Preparation	Elemental iron content	Usual regimen
Intramuscular (deep, Z-track)	Iron dextran (Imferon)	50 mg/mL	Calculated total dose divided into deep IM injections — largely superseded due to pain, skin staining, abscess formation and anaphylaxis risk
Intravenous	Iron (ferrous) sucrose	20 mg/mL	100 mg/dose, usually once daily, up to about 10 doses (or as a total dose infusion)
Intravenous	Sodium ferric gluconate complex	12.5 mg/mL	125 mg/dose, usually once daily, about 8 doses needed
Intravenous	Iron carboxymaltose / iron isomaltose	Manufacturer-specific	Similar efficacy to iron sucrose but needs fewer injections and a shorter infusion time per sitting

- **Total dose infusion (TDI)** — the total iron deficit is first calculated (from body weight and the haemoglobin deficit, per the manufacturer's dosing table) and given as a single intravenous infusion, avoiding repeated visits.
- Iron sucrose is regarded as safe with fewer side effects than iron dextran, though it needs multiple sittings; iron dextran can be completed in a single dose but carries the higher anaphylaxis risk.
- Parenteral iron therapy is generally deferred beyond the first trimester.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Daily iron need stays near basal (~1 mg/day) through the first trimester, rises steeply after mid-pregnancy to a peak of 6–7 mg/day through the second half, then falls sharply after delivery (after Williams Obstetrics Fig. 4-6).

High-yield exam pointers

- Total iron requirement of pregnancy ≈ **1000 mg** = 300 mg (fetus + placenta) + ≈500 mg (expanded red cell mass) + 200 mg (obligatory losses).
- Daily requirement rises from ≈1 mg/day (first trimester) to **6–7 mg/day** after mid-pregnancy (Pritchard, 1970).
- Only about **10%** of dietary iron is absorbed, from the **duodenum and jejunum**, in the **ferrous** form.
- **Hepcidin ↓ in pregnancy → ferroportin de-repressed → ↑ enterocyte absorption + ↑ placental transfer.**
- Elemental iron to write from memory: ferrous sulfate 300 mg → 60 mg; ferrous fumarate 200 mg → 65 mg; ferrous gluconate 300 mg → 35 mg; iron polymaltose 100 mg tablet → 100 mg elemental.
- Parenteral iron indicated for oral intolerance, non-compliance, or pregnancy beyond 32 weeks; iron sucrose (20 mg/mL) and iron dextran (50 mg/mL) are the classic intravenous/intramuscular agents.
- Fetal iron transfer across the placenta is active and autonomous — the baby is not anaemic at birth even with severe maternal iron-deficiency anaemia.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Iron metabolism in pregnancy

Asked in: Paper I May 2019 · Paper I May 2015 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — Iron metabolism in pregnancy denotes the physiological adaptations in intestinal absorption, plasma transport, storage and placental transfer that allow the mother to meet an additional iron requirement of roughly **1000 mg** over gestation. This is achieved chiefly by a pregnancy-induced fall in **hepcidin**, which raises intestinal iron absorption and drives active, unidirectional transfer of iron to the fetus.

Total iron requirement and its distribution

- Total iron content of a normal adult woman is **2.0–2.5 g** (about half that of men); pre-pregnancy iron stores in a healthy young woman approximate only **300 mg** (Pritchard).
- The additional ~1000 mg required by a normal singleton pregnancy is distributed as follows:

Component of iron requirement	Approximate amount	Basis
Actively transferred to fetus + placenta	~300 mg	Active transplacental transport
Incorporated into expanded maternal red-cell mass	~500 mg	~450 mL rise in circulating RBC volume × 1.1 mg iron/mL RBC
Obligatory losses (GI tract, skin, urine)	~200 mg	Occur even if the mother is iron-deficient
Total	**~1000 mg**	Williams Obstetrics 26e

- Distribution over time is markedly uneven: requirement is low in the first trimester (no menstrual loss, minimal fetal demand) and rises steeply after mid-pregnancy, when the daily requirement imposed by pregnancy plus maternal excretion averages **6–7 mg/day** (Pritchard, 1970) — most of the 1000 mg is used in the **latter half** of pregnancy.
- Few women have sufficient dietary intake or stores to supply this; if a non-anaemic pregnant woman is not given supplemental iron, serum iron and ferritin decline after mid-pregnancy and the optimal rise in maternal red-cell volume fails to develop, so haemoglobin and haematocrit fall further as plasma volume expands.

Recommended daily iron allowance	Non-pregnant	Pregnancy	Lactation
ICMR (India; DC Dutta's Obstetrics 9e)	18 mg	40 mg (2nd half)	30 mg
IOM/National Academy of Sciences, endorsed by AAP–ACOG 2017 (Williams Obstetrics 26e)	—	27 mg elemental	9 mg

Absorption and transport

- Dietary iron is absorbed almost entirely in the **duodenum and jejunum**, in the reduced **ferrous** (**Fe^{2+}**) form; only about **10%** of ingested iron is normally absorbed.
- Absorption requires an **acid duodenal milieu** — antacids, H2-blockers and proton-pump inhibitors impair it.
- Absorbed iron is released into plasma bound to **transferrin**.
- Circulating transferrin-bound iron is then either:
  - incorporated into **haemoglobin** (~75%) and myoglobin, or
  - stored as **ferritin** or **hemosiderin** (reticuloendothelial stores).
- Pregnancy increases the fractional absorption of dietary iron above the non-pregnant baseline, driven by falling hepcidin (below).

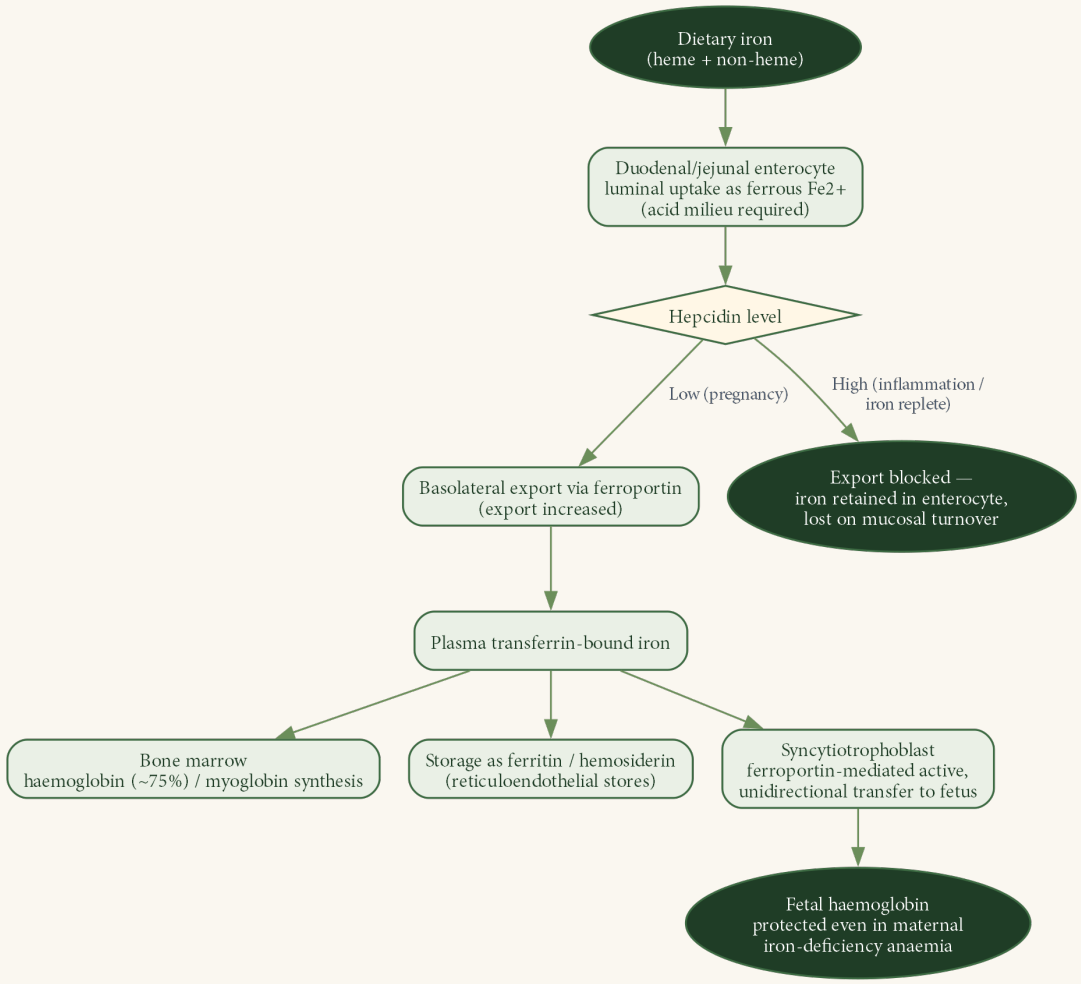
Regulation — the hepcidin–ferroportin axis

- **Hepcidin**, a hepatic peptide hormone, is the master homeostatic regulator of systemic iron metabolism.
- Hepcidin levels **fall early in pregnancy**. Lower hepcidin:
  - increases iron **absorption** by permitting export via **ferroportin** on the basolateral membrane of duodenal enterocytes;
  - increases iron **transfer to the fetus** by augmenting ferroportin-mediated export from the **syncytiotrophoblast**.
- Hepcidin **rises** with inflammation, and **falls** with iron deficiency and with rising levels of testosterone, oestrogen, vitamin D and possibly prolactin.
- Serum ferritin normally declines through pregnancy; a level **<10–15 µg/L confirms iron-deficiency anaemia**.

Placental transfer, fetal iron economy and postpartum balance

- Placental iron transport is **active and unidirectional** (maternal → fetal), so fetal plasma iron concentration is kept **higher than maternal** plasma iron.
- Because transfer is placenta-driven rather than passively dependent on maternal supply, **fetal red-cell production is not impaired even when the mother has marked iron-deficiency anaemia** — maternal haemoglobin as low as 3 g/dL has been documented with a normal fetal haemoglobin of 16 g/dL at the same time.
- With a normal vaginal delivery, blood loss of **500–600 mL** is typical; not all of the iron laid down as maternal haemoglobin is thereby spent, and the surplus haemoglobin-iron released postpartum is reconverted to **stored iron**.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Fig: Iron absorption, hepcidin-regulated transport, and placental transfer in pregnancy.

High-yield exam pointers

- Total pregnancy iron requirement ~**1000 mg** = 300 mg (fetoplacental) + 500 mg (maternal red-cell mass expansion) + 200 mg (obligatory losses).
- Total body iron in an adult woman **2.0–2.5 g**; pre-pregnancy stores only ~**300 mg** — usually inadequate without supplementation.
- Daily requirement climbs to **6–7 mg/day after mid-pregnancy** — most of the 1000 mg is used in the second half.
- **Hepcidin falls in pregnancy** → more enterocyte absorption + more syncytiotrophoblast transfer to fetus (via ferroportin at both sites).
- Iron transfer to the fetus is **active and unidirectional** — fetal Hb stays normal even with severe maternal iron-deficiency anaemia.

- RDA to quote: **ICMR (India) 40 mg elemental iron/day** in the second half of pregnancy vs **IOM/ACOG (US) 27 mg elemental iron/day**.
- Iron is absorbed as **ferrous (Fe^{2+})** form in the duodenum/jejunum; antacids/H2-blockers/PPIs impair absorption.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> The ICMR recommended dietary allowance for iron in pregnancy (40 mg elemental iron/day, second half) is higher than the US IOM/AAP–ACOG figure (27 mg/day) because it corrects for the lower bioavailability of iron in a predominantly cereal/vegetable-based Indian diet; both are physiological requirement figures, not the therapeutic dose used to treat established iron-deficiency anaemia.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Lymphatic drainage of cervix

Asked in: Paper I 12-Nov-2021 · Paper I May 2009 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — The cervix drains through a **subepithelial (mucosal) plexus** that communicates freely across the midline and with a deeper **stromal (intramural) plexus** running with the cervical branches of the uterine vessels. From this stromal plexus, collecting trunks leave the cervix in three directions within the parametrium and along the uterosacral ligaments to reach the pelvic lymph nodes, which in turn drain to the common iliac and para-aortic chains. The lower uterine body and the upper two-thirds of the vagina are contiguous with the cervix and share this identical nodal pattern. This stepwise pattern is the anatomical basis of spread in carcinoma cervix and dictates the extent of lymphadenectomy in radical hysterectomy.

Course of the collecting lymphatic trunks

Route	Course	Node(s) reached
Lateral (main) route	Along the base of the broad ligament/parametrium, alongside the uterine vessels, crossing above the ureter	**Parametrial node → obturator**, **internal iliac (hypogastric)**, **external iliac** (medial & middle groups)
Postero-lateral route	Along the **uterosacral ligaments**	**Sacral group** (lateral sacral + presacral nodes)

Route	Course	Node(s) reached
Minor/inconsistent route	Occasionally along the anterior vaginal wall/bladder base	**Vesical nodes** → external iliac group

Groups of lymph nodes draining the cervix

Tier	Node group	Location / afferents	Note
Primary	**Parametrial**	In the parametrium, near the crossing of the ureter and uterine artery	Small, **inconsistently present** (first station when present)
Primary	**Obturator**	In the obturator fossa, along obturator vessels/nerve	Most consistent first station; commonest **sentinel node** site
Primary	**Internal iliac (hypogastric)**	Along internal iliac vessels	Also receives afferents from obturator and sacral groups
Primary	**External iliac**	Anterior (middle) and medial groups along external iliac vessels	**Medial and middle groups classically involved in carcinoma cervix**
Primary	**Sacral** (lateral sacral + presacral)	Lateral to rectum / in front of sacral promontory	Reached via the uterosacral-ligament route
Secondary	**Common iliac**	Receives efferents from all primary groups	Arranged in lateral, intermediate, medial subgroups
Tertiary	**Para-aortic (lumbar)**	Below and near origin of the ovarian artery	→ cisterna chyli → thoracic duct → left venous angle (left subclavian–jugular junction)

Pattern of spread and clinical significance

- **Stepwise spread**: carcinoma cervix disseminates in the same sequence as normal drainage — parametrial → obturator/internal iliac/external iliac/sacral (primary) → common iliac → para-aortic (secondary/tertiary) — before haematogenous or distant spread; rarely, spread along the round ligament reaches the superficial inguinal nodes.
- **Staging correlate**: the **FIGO 2018 revised staging of carcinoma cervix** (Bhatla et al., FIGO Committee Report, *Int J Gynecol Obstet* 2019) incorporates nodal status directly into staging — **Stage IIIC1** (pelvic lymph node metastasis only) and **Stage IIIC2** (para-aortic lymph node

metastasis), with an **r** (imaging) or **p** (pathology) suffix recording how the metastasis was confirmed; earlier FIGO staging was purely clinical and ignored nodal status.

- **Surgical correlate**: radical (Wertheim's, type III) hysterectomy for early-stage cervical cancer includes thorough bilateral **pelvic lymphadenectomy** — external iliac, internal iliac, obturator and common iliac nodes — with **para-aortic node sampling** if pelvic nodes are positive on frozen section.
- **Sentinel lymph node mapping**: dye (indocyanine green) or radiocolloid (technetium-99) is injected directly into the cervix, usually at the **3 and 9 o'clock positions**; sentinel nodes are typically found **medial to the external iliac, ventral to the internal iliac (hypogastric)**, or in the **upper obturator space** — the technique is endorsed by the National Comprehensive Cancer Network (NCCN) for tumours **<2 cm**.
- **Imaging**: contrast-enhanced CT, MRI and PET can detect pelvic/para-aortic nodal and parametrial disease, but per Dutta's Gynaecology these imaging findings do not by themselves change the clinically assigned FIGO stage unless confirmed as above.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 2.3 — Schematic representation of the lymphatic drainage of the cervix (DC Dutta's Gynaecology 7e, p.43)*
>
> Label: subepithelial plexus in the cervical wall → parametrial node (inconsistent, dotted) → obturator, external iliac, internal iliac nodes on each side → common iliac and presacral nodes.

High-yield exam pointers

- **Two intrinsic plexuses**: subepithelial (mucosal) + stromal, freely crossing the midline.
- **Three routes**: lateral (parametrial → obturator/iliac), postero-lateral (uterosacral → sacral), minor anterior (vesical).
- **Five primary node groups — mnemonic "POIES"**: **P**arametrial, **O**bturator, **I**nternal iliac, **E**xternal iliac, **S**acral.
- Secondary → **common iliac**; tertiary → **para-aortic** → cisterna chyli → thoracic duct → left venous angle.
- **Obturator node = commonest sentinel node** in carcinoma cervix; mapping dye injected at **3 and 9 o'clock** of the cervix.
- **FIGO 2018**: node-positive disease = **Stage IIIC** (IIIC1 pelvic, IIIC2 para-aortic; r = radiologic, p = pathologic).
- Radical (Wertheim's) hysterectomy lymphadenectomy = **external iliac + internal iliac + obturator + common iliac** ± para-aortic sampling.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older textbook descriptions, and the pre-2018 FIGO scheme still printed in some editions, treat carcinoma cervix as a purely clinically staged disease; the current FIGO 2018 revision (Bhatla et al. 2019) allows imaging- and pathology-confirmed nodal status to directly assign Stage IIIC.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e (including FIGO Committee Report: Bhatla N, Berek JS, Cuello Fredes M, et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynecol Obstet* 2019).

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Lymphatic drainage of the reproductive organs

Asked in: Paper III 26-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — The lymphatics of the female genital tract begin as intrinsic mucosal/subserosal plexuses within each organ and drain, via named collecting trunks, to a fixed sequence of pelvic and inguinal **node groups** before finally emptying through the **para-aortic (lumbar) chain**, cisterna chyli and thoracic duct into the left subclavian vein. Because malignancy spreads along these same channels, the pattern of drainage of the ovary, fallopian tube, uterus, cervix, vagina and vulva is the anatomical basis for staging and the extent of lymphadenectomy in gynaecological cancer surgery.

Groups of pelvic and inguinal lymph nodes

Node group	Location	Chief afferents
Superficial inguinal (horizontal + vertical chains)	Along the inguinal ligament and long saphenous vein	Vulva, perineum, lower vagina (below hymen), anal canal (below Hilton's line), gluteal region, anterior abdominal wall below umbilicus, uterine **cornu** (via round ligament)
Deep inguinal (femoral), incl. **gland of Cloquet/Rosenmüller**	Medial to femoral vein, in femoral canal; 5–6 nodes	Glans clitoris, deep femoral vessels, efferents from superficial inguinal group
External iliac (lateral, middle/anterior, medial subgroups)	Along external iliac vessels	Cervix, upper vagina, bladder, inguinal nodes
Internal iliac (hypogastric) + inconsistent **parametrial** node	Along internal iliac vessels; parametrial near the ureter–uterine artery crossing	All pelvic viscera, deep perineum, obturator and sacral groups

Node group	Location	Chief afferents
Obturator	Obturator fossa	Cervix, bladder
Sacral (lateral + presacral)	Lateral to rectum / front of sacral promontory	Cervix (posterior route, along uterosacral ligaments), rectum
Common iliac (lateral, intermediate, medial)	Above the iliac bifurcation	External + internal iliac groups
Para-aortic (lumbar) — inferior group near origin of inferior mesenteric artery; superior group near origin of ovarian artery	Along the aorta	Ovary, fallopian tube, uterine fundus (**direct**), sacral and common iliac groups

Efferents from the para-aortic nodes ascend as lumbar trunks to the **cisterna chyli**, and thence via the **thoracic duct** to open into the **left subclavian vein** at its junction with the left internal jugular vein.

Organ-wise pattern of drainage

Organ / region	Primary node(s)	Onward drainage
Ovary & fallopian tube	**Para-aortic (lumbar) nodes directly**, along the ovarian vessels/infundibulopelvic ligament	Free cross-anastomosis with the opposite side across the uterosacral fold and the subperitoneal plexus of the fundus
Uterine fundus (with adnexal lymphatics)	Para-aortic nodes directly, **bypassing pelvic nodes**	—
Uterine cornu	Superficial inguinal nodes, via the **round ligament**	Deep inguinal → external iliac
Rest of the uterine body	External iliac nodes	Common iliac → para-aortic
Body adjacent to the cervix	Joins cervical lymphatics	As for cervix
Cervix	**Parametrial** (inconsistent) → **obturator**, **internal iliac**, **external iliac** (medial + anterior); posteriorly along uterosacral ligaments → **sacral**	Common iliac → para-aortic (superior lumbar)
Vagina, upper two-thirds	Same as cervix — external iliac, internal iliac, common iliac	Para-aortic
Vagina, lower one-third	Superficial inguinal (with vulva)	Occasionally external iliac directly
Vulva — labia majora, anterior half / mons	Superficial inguinal, **bilateral** (crosses midline)	—

Organ / region	Primary node(s)	Onward drainage
Vulva — labia majora, posterior half	Superficial inguinal → deep inguinal	External iliac
Labia minora & prepuce of clitoris	Superficial inguinal, bilateral	—
Glans of clitoris	**Deep inguinal and external iliac directly** (bypasses superficial inguinal)	—
Bartholin's gland	Superficial inguinal + anorectal nodes	—

Applied significance

- **Ovary/fallopian tube**: because drainage is directly to the para-aortic nodes at the level of the renal vessels, ovarian carcinoma staging and cytoreductive surgery require **para-aortic lymphadenectomy up to the renal veins**, and "skip" para-aortic metastases can occur with negative pelvic nodes.
- **Uterine fundus**: fundal endometrial carcinoma can metastasise directly to para-aortic nodes bypassing the pelvic groups, so **surgical staging samples both pelvic and para-aortic nodes**.
- **Cervix**: the parametrial → obturator/internal iliac/external iliac/sacral → common iliac → para-aortic sequence is the basis of **pelvic ± para-aortic lymphadenectomy in radical (Wertheim's) hysterectomy**, and of nodal (sentinel-node) mapping for early cervical cancer.
- **Vulva**: the **superficial inguinal nodes are the sentinel nodes**; a midline lesion (clitoris, anterior labia minora, posterior fourchette) risks **bilateral** groin spread, whereas a strictly lateral lesion with a negative ipsilateral groin rarely involves the opposite side — the basis of **uni-/bilateral inguinofemoral lymphadenectomy or sentinel-node biopsy**.
- **Vaginal venous–lymphatic overlap**: free communication of the uterine and vaginal plexuses explains vaginal wall metastases in endometrial carcinoma and choriocarcinoma.
- **Cornu-to-groin route**: the uterine cornu is the only part of the uterus that can drain (via the round ligament) to the superficial inguinal nodes — occasionally the route for isolated groin metastasis from a cornual/fundal tumour.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 5.11 — The lymphatic drainage of the female pelvis (Berek & Novak 16e, p.179)*

Label: vulva and lower vagina → superficial and deep inguinal nodes (± direct route along the dorsal vein of the clitoris to the iliac nodes, and to the opposite side); cervix and upper vagina → parametrial, obturator, external iliac nodes laterally and sacral nodes posteriorly (via the uterosacral ligaments); ovary/fundus → directly upward along the infundibulopelvic ligament to the para-aortic nodes.

High-yield exam pointers

- **Ovary/tube = only organs draining directly to para-aortic nodes** (along ovarian vessels/infundibulopelvic ligament), bypassing pelvic nodes entirely.
- **Uterine cornu, via the round ligament, is the sole route by which the uterus reaches the superficial inguinal nodes.**
- **Cervix — mnemonic "POIES"**: Parametrial, Obturator, Internal iliac, External iliac, Sacral (primary groups) → common iliac → para-aortic.
- **Vagina splits at its middle**: upper two-thirds drains as the cervix; lower one-third drains as the vulva (superficial inguinal).
- **Vulva sentinel nodes = superficial inguinal**; exception — **glans clitoris drains directly to deep inguinal/external iliac**, bypassing the superficial group.
- **Gland of Cloquet/Rosenmüller** = uppermost deep inguinal node; **absent in ~50%**, no longer treated as an obligatory relay station.
- Final common pathway for all groups: para-aortic nodes → cisterna chyli → thoracic duct → **left subclavian vein** at the left internal jugular junction.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older teaching held the gland of Cloquet/Rosenmüller to be an obligatory relay node between the superficial and deep inguinal groups; current descriptions (DC Dutta's Gynaecology 7e, Berek & Novak 16e) note it is congenitally absent in about half of individuals and that efferents may bypass it directly to the external iliac nodes.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (Chapter 2 — Blood Vessels, Lymphatic Drainage and Innervation of Pelvic Organs); Williams Obstetrics 26e (Maternal Anatomy — Pelvic Lymphatics); Berek & Novak's Gynecology 16e (Anatomy — Lymphatics, Fig. 5-11).

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Maternal immune response

Asked in: Paper I 24-Sep-2025 — RGUHS MS Obstetrics & Gynaecology

Definition — The fetus and placenta carry paternally derived antigens that are foreign to the mother, yet this "fetal allograft" is never rejected — the central paradox of reproductive immunology. The **maternal immune response** in pregnancy is the coordinated set of innate and adaptive adaptations at the maternal–fetal interface (decidua and trophoblast) that permit implantation, controlled trophoblast invasion and fetal survival to term while preserving the mother's ability to fight infection.

Basic immune system components (recap)

Feature	Innate immunity	Adaptive immunity
Response	Immediate, non-specific	Delayed, antigen-specific
Self/non-self discrimination	No	Yes
Key cells	Neutrophils, macrophages, natural killer (NK) cells, complement	T lymphocytes (helper Th, cytotoxic Tc), B lymphocytes, antigen-presenting cells
Mediators	Cytokines (TNF-α, IL-1, IL-6), chemokines (IL-8, MCP-1)	Th1 cytokines (IL-2, IFN-γ, TNF) vs Th2 cytokines (IL-4, IL-6, IL-10)
Memory	Absent	Present

Pregnancy is **not** an immunodeficient state — the mother mounts both humoral and cell-mediated responses against paternal antigens; the difference is that these responses are tightly regulated to spare the fetus (DC Dutta's Obstetrics 9e).

Mechanisms of maternal–fetal immune tolerance

- **Trophoblast HLA restriction** — Villous trophoblast (bathed by maternal blood in the intervillous space) expresses **no HLA class I or class II** molecules and is immunologically inert. Extravillous trophoblast (EVT), which invades the decidua, expresses the classical class Ia antigen **HLA-C** and the non-classical class Ib antigens **HLA-E and HLA-G**, but never the classical transplantation antigens HLA-A/-B — this avoids recognition as "non-self" while still

permitting regulated interaction with decidual NK cells (Williams Obstetrics 26e; Berek & Novak's Gynecology 16e).

- **HLA-G** — expressed only in humans and restricted to EVT; membrane-bound and soluble isoforms protect the trophoblast from NK-cell– and T-cell–mediated attack, aid trophoblast invasion, and (the soluble form) expand regulatory T cells. Failed embryo implantation in IVF is linked to absent soluble HLA-G; reduced placental HLA-G expression is linked to preeclampsia.
- **Decidual natural killer (dNK) cells** — make up about **70%** of first-trimester decidual leukocytes. Unlike peripheral NK cells, they are **poorly cytotoxic** but rich secretors of cytokines and angiogenic factors (IL-8, interferon-inducible protein-10, VEGF, placental growth factor). Their killer-immunoglobulin-like receptors (KIR) interact with trophoblast HLA-C/HLA-G to permit — and subsequently limit — trophoblast invasion and spiral-artery remodelling.
- **Decidual macrophages** — about **20%** of first-trimester decidual leukocytes; polarised to an **M2 (anti-inflammatory) phenotype**, they secrete interleukin-10, regulate dNK cytotoxicity, and produce the enzyme **indoleamine 2,3-dioxygenase (IDO)**, which depletes local tryptophan and thereby limits maternal T-cell activation against the fetus.
- **Regulatory T cells (Tregs)** — $CD4^+CD25^+FoxP3^+$ cells that expand systemically during pregnancy in an antigen-independent fashion; they suppress maternal effector responses directed against fetal alloantigens and against self.
- **T-helper 1 to T-helper 2 (Th1 → Th2) cytokine shift** — a successful pregnancy is characterised by a shift away from pro-inflammatory Th1 cytokines (interleukin-2, interferon-γ, tumour necrosis factor) toward anti-inflammatory Th2 cytokines (interleukin-4, -6, -10). This immunomodulation also explains why Th1-driven autoimmune disease (for example, rheumatoid arthritis) often improves during pregnancy.
- **Immunosuppressive humoral factors** — progesterone (the principal driver of the Th1→Th2 shift), oestrogen, human chorionic gonadotropin (hCG), alpha-fetoprotein, alpha-2-macroglobulin and placental interferon are all locally immunosuppressive; amniotic fluid is rich in immunosuppressive phospholipids. Maternal "blocking antibodies," proposed to form against the trophoblast–lymphocyte cross-reactive (TLX) antigen, are also thought to protect the fetus.
- **Complement regulation** — the placenta limits complement and cytokine activation at the maternal–fetal interface, and this local inhibition reduces immune-mediated pregnancy complications.
- **Fetomaternal microchimerism** — bidirectional trafficking of cells (fetal lymphocytes, mesenchymal and endothelial progenitor cells, cell-free fetal DNA) into the mother, and of maternal cells into the fetus, persists for decades and may itself favour long-term tolerance; it is also implicated in the female preponderance of certain autoimmune disorders.

Clinical relevance — when the maternal immune response is disturbed

Disorder	Immune mechanism
Preeclampsia	Deficient HLA-G/HLA-C–NK-cell interaction → failed extravillous trophoblast invasion and spiral-artery remodelling; reduced regulatory-T-cell number and function; insufficient Th1→Th2 shift; raised TNF-α, IL-6, IL-1β, IL-8 with low IL-10
Recurrent pregnancy loss	Persistent Th1 (cell-mediated) bias with low Th2 cytokines (IL-4, IL-10); altered decidual NK-cell populations. RCOG guidance: evidence for routine NK-cell/Treg-cytotoxicity testing or blocking-antibody testing is insufficient — not recommended
Antiphospholipid syndrome	Anticardiolipin antibody, lupus anticoagulant and anti-β2-glycoprotein-1 antibody dysregulate coagulation pathways → uteroplacental thrombosis, miscarriage, fetal growth restriction, preeclampsia
Rh(D) and ABO alloimmunisation	Maternal antibody response (anti-D, anti-A/anti-B) to fetal red-cell antigens crossing the placenta → fetal haemolysis, hydrops fetalis, kernicterus
Maternal autoimmune disease affecting the fetus	Transplacental antibody transfer: Graves disease → neonatal thyrotoxicosis; immune thrombocytopenic purpura → neonatal thrombocytopenia; myasthenia gravis → transient neonatal weakness; systemic lupus erythematosus (anti-Ro/SS-A, anti-La/SS-B) → congenital heart block

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 21.8 — Immune tolerance and activation at the maternal fetal interface (Williams Obstetrics 26e, p.419)*

- Label the antepartum (tolerance) phase: decidual NK cells matured by decidual interleukin-15 promote decidual remodelling, blastocyst implantation and extravillous-trophoblast invasion; dNK cytotoxicity is held in check by KIR–HLA-G interaction; decidual macrophages act as antigen-presenting cells and produce IDO, which limits T-cell activation.

High-yield exam pointers

- Fetus = **semi-allograft** (50% paternal antigens) not rejected — the "immunological paradox of pregnancy."
- Villous trophoblast = **no HLA class I/II** (immunologically inert); extravillous trophoblast = **HLA-C + HLA-E/HLA-G** (never HLA-A/HLA-B).

- dNK cells = ~**70%** of first-trimester decidual leukocytes, non-cytotoxic, VEGF/PlGF secretors; decidual macrophages ~**20%**, M2 phenotype, produce **IDO**.
- Tregs = $CD4^+CD25^+FoxP3^+$; expand systemically in pregnancy.
- Successful pregnancy = **Th2 dominance**; a Th1 shift is linked to miscarriage and preeclampsia. Progesterone drives the Th1→Th2 shift.
- **RCOG**: NK-cell/Treg-cytotoxicity testing is NOT recommended in the recurrent-miscarriage work-up.
- SLE anti-Ro/anti-La antibodies crossing the placenta → **congenital heart block** in the fetus (classic transplacental-antibody question).

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e (Chapter 39, "Immunology in Obstetrics"); Berek & Novak's Gynecology 16e (Recurrent Pregnancy Loss chapter).

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Mention the important sites and causes of ureteric injury. How do you prevent it?

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Ureteric injury is inadvertent trauma to the ureter — kinking, crushing, ligation, transection, devascularisation or thermal damage — occurring during pelvic surgery because of the close anatomical relationship of the ureter to the female genital organs. It carries an overall incidence of 0.5–1% of all pelvic operations, of which about 75% follow gynaecological operations (75% of these during abdominal, rather than vaginal, procedures), and is an important cause of medicolegal litigation.

Important sites of ureteric injury

Site	Why the ureter is at risk here
Infundibulopelvic (IP) ligament at the pelvic brim	Ureter runs parallel to and forms the posterior boundary of the ovarian fossa, closely applied to the ovarian vessels — at risk while clamping/ligating the IP ligament during oophorectomy/salpingo-oophorectomy
Below the ischial spine, deep in the pelvis	Ureter lies lateral to the peritoneum of the uterosacral ligament — at risk during uterosacral ligament plication/suspension and deep pelvic dissection

Site	Why the ureter is at risk here
Level of the internal cervical os, ~1.5 cm lateral to the cervix	Uterine artery crosses **over** the ureter here ("water flows under the bridge") — at risk while clamping the cardinal ligament/uterine pedicle during hysterectomy, especially on reclamping after a slipped pedicle
Anterior vaginal fornix, within the ureteric tunnel of the cardinal ligament (**tunnel of Wertheim**)	Ureter turns anteromedially to enter the bladder — at risk while securing the vaginal angle/anterior fornix, and during radical hysterectomy dissection of the tunnel
Intravesical (intramural) part, as it traverses the bladder musculature	At risk during bladder-neck/anterior colporrhaphy and colposuspension dissection
Additionally, during **pelvic peritonisation** the ureter lies in the posterior peritoneal leaf and can be caught in the closing suture	

A **duplex/congenitally aberrant ureter** is more vulnerable at any of the above levels.

Causes of ureteric injury

A. Congenital

- Aberrant ureter opening into the vault of the vagina, uterus, or urethra — an ectopic/duplex ureter is intrinsically more prone to injury at any of the sites above.

B. Acquired (the great majority) — mechanism of injury

Mechanism	How it occurs
Kinking/angulation	Ureter caught in a suture placed nearby (e.g., pelvic peritonisation, vault closure) causing obstruction without transection
Ischaemic injury	Stripping the ureter off the peritoneum during dissection devitalises its sheath and longitudinal blood supply → sloughing necrosis (classically after radical hysterectomy)
Ligature incorporation	Ureter accidentally included in a clamp/suture on the infundibulopelvic pedicle, uterine pedicle, or vault angle
Crushing injury	Clamp applied across the ureter, especially on **reclamping** a slipped pedicle (more common than on primary clamping)
Transection	Partial or complete division, accidental or (rarely) planned as part of radical excision

Mechanism	How it occurs
Segmental resection	Deliberate excision of an infiltrated ureteric segment (e.g., endometriosis, malignancy)
Thermal injury	Monopolar/bipolar diathermy or laser energy during laparoscopic surgery — a leading cause of laparoscopic ureteric injury; damage may be delayed (necrosis appearing days later)
Stapler injury	Linear cutting/stapling devices during laparoscopic pelvic surgery

C. Predisposing gynaecological conditions/operations (distorted anatomy raises risk)

- Cervical fibroid or low corporeal fibroid
- Broad ligament tumour
- Pelvic endometriosis (dense fibrosis obscures the ureter)
- Gynaecological malignancy, especially **radical hysterectomy**
- Pelvic haematoma
- Tubo-ovarian mass / dense pelvic adhesions
- Reapplication of a clamp after a slipped uterine artery pedicle
- Presacral neurectomy (endoscopic)
- Ovarian remnant excision
- Vaginal hysterectomy (uncommon, but reported)
- Colposuspension
- Laparoscopically assisted vaginal hysterectomy (LAVH)/total laparoscopic hysterectomy

Prevention of ureteric injury

1. Preoperative measures

- Thorough knowledge of pelvic anatomy and the ureter's course is the single most important safeguard.
- **Intravenous urography (IVU)/CT urogram** preoperatively in cases with distorted anatomy (large fibroids, broad-ligament tumours, suspected malignancy) to define the ureteric course and detect congenital anomalies.
- **Preoperative or intraoperative ureteral catheter/stent placement** to aid palpation and identification — though in a fibrotic pelvis (e.g., dense endometriosis) palpation of a stented ureter may still be difficult.

2. Intraoperative measures

- **Adequate exposure** — a generous incision/access; inadequate exposure predisposes to blind clamping and suturing.

- **Direct visualisation and/or palpation of the ureter** throughout its pelvic course wherever feasible; the ureter is recognised by its pale glistening appearance, longitudinal surface vessels, and visible peristalsis.
- **Open the retroperitoneal space** and identify the ureter at the pelvic brim before proceeding when anatomy is distorted (endometriosis, broad-ligament mass, malignancy) — routine practice in radical and difficult hysterectomy.
- **Meticulous sharp dissection** rather than blunt tearing, taking care not to strip the periureteric sheath (preserves its longitudinal blood supply).
- **Never clamp blindly** — the cardinal surgical axiom: any structure at risk must be carefully dissected and adequately exposed before clamping/ligating.
- Careful technique specifically at each risk site — clamp the IP pedicle away from the ureter; keep the uterine-artery clamp medial and close to the cervix; secure the vaginal angle under direct vision; avoid deep "blanket" sutures during peritonisation.
- **Judicious use of energy sources** — keep monopolar/bipolar diathermy and laser away from the ureter's course; lateral thermal spread is a recognised, often delayed, mechanism of injury.
- **Illuminated/lighted ureteric catheters (e.g., "Uriglow")** have been used for better intraoperative localisation.
- **Intraoperative cystoscopy with intravenous indigo carmine (or sodium fluorescein)** after hysterectomy, particularly laparoscopic hysterectomy, to confirm bilateral ureteric patency and efflux of dye from both ureteric orifices before closing — now a recommended routine step where the urinary tract is at increased risk.

3. Early recognition if injury occurs — a high index of suspicion (unexplained flank pain, fever, ileus, urine leakage per vagina, oliguria/anuria postoperatively) with prompt intraoperative confirmation (visual leak, dye test, on-table cystoscopy) allows immediate repair, which carries a far better outcome than delayed diagnosis.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 1.9 — Coronal section showing different parts of uterus; the relation of the ureter to the uterine artery (DC Dutta's Textbook of Gynaecology 7e, p.26)*
>
> Label on the sketch: pelvic brim crossing (IP ligament) → uterosacral ligament level (ischial spine) → uterine artery crossing the ureter at the internal os → ureteric tunnel of Wertheim at the anterior fornix → intravesical ureter — the five vulnerable points along the ureter's pelvic course.

High-yield exam pointers

- **Incidence:** 0.5–1% of pelvic operations; ~75% are gynaecological, ~75% of those abdominal (not vaginal).

- **5 vulnerable sites, top-to-bottom:** IP ligament → below ischial spine (uterosacral ligament) → uterine artery crossing at internal os (1.5 cm lateral to cervix) → tunnel of Wertheim at the anterior vaginal fornix → intravesical part.
- **"Water under the bridge"** — the uterine artery crosses **over** the ureter.
- **Reclamping > primary clamping** as a cause — remember slipped-pedicle reclamping as a classic acquired cause.
- **Diathermy/laser = commonest cause in laparoscopic surgery**, and injury may present late.
- **Prevention mnemonic — "3 D's + C":** **D**efine anatomy (IVU/CT urogram), **D**issect retroperitoneum to see the ureter, avoid blind clamping (**D**on't clamp blind), and **C**ystoscopy with indigo carmine intraoperatively.
- **Recognise ureteric tissue:** pale, glistening, longitudinal vessels, peristalsis.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Where discussed, the operative repair techniques (ureteral stenting, end-to-end ureteroureterostomy, ureteroneocystostomy with psoas hitch, Boari flap) are management of established injury and were not asked in this question, which is limited to sites, causes, and prevention.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e (dedicated chapter, "Ureteric Injury in Gynecologic Surgery," and applied anatomy chapter); Berek & Novak's Gynecology 16e (laparoscopic ureteral injury, cystoscopy/indigo-carmine recommendation); Te Linde's Operative Gynecology 13e (urinary tract injury sites during laparoscopic pelvic surgery).

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Nutrition in pregnancy

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Nutrition in pregnancy refers to the increased and qualitatively altered maternal dietary requirement needed to support fetal growth, placental development, expansion of maternal blood volume and tissues, and preparation for lactation, without compromising maternal health. Requirements are not simply the non-pregnant allowance plus a fixed increment — increased caloric

need may be partly offset by reduced physical activity, so recommendations are individualised to pre-pregnancy body mass index (BMI) and trimester.

Physiological basis of the extra nutrient cost

Component	Approximate cumulative demand
Total additional energy for pregnancy	~80,000 kcal, mostly in the last 20 weeks
Protein deposited (fetus, placenta, uterus, breast)	~1000 g in the second half; 5–6 g/day extra
Iron (fetus + placenta 300 mg; expanded maternal haemoglobin mass 500 mg)	~800–1000 mg total, mostly after mid-pregnancy
Calcium retained (mostly fetal skeleton, late pregnancy)	~30 g (only ~2.5% of total maternal calcium, mobilised from bone)

Recommended dietary allowances (RDA) in pregnancy

Nutrient	Non-pregnant	Pregnancy	Chief source
Energy	2200 kcal	+300 kcal/day (2nd half)	Cereals, fat, protein
Protein	50 g	60 g (65 g lactation)	Meat, fish, egg, milk
Iron	18 mg	40 mg (to be supplemented)	Meat, egg, green leafy vegetables
Calcium	500 mg	1000 mg (1500 mg lactation)	Milk, dairy
Folic acid	200 µg	400 µg	Green leafy vegetables, liver
Iodine	150 µg	175–220 µg	Iodised salt, seafood
Vitamin A	5000 IU	6000 IU	Vegetables, liver, fruit
Vitamin D	200 IU	400 IU (10–15 µg)	Sunlight, dairy
Vitamin B12	2 µg	2.2–2.6 µg	Animal protein only

Preferably at least half the protein is of animal (first-class) origin, supplying a complete amino-acid profile; milk (about 1 g calcium per litre) and dairy are near-ideal.

Recommended weight gain (IOM 2009, endorsed by ACOG 2020)

Pre-pregnancy BMI category	Total weight gain	Rate, 2nd–3rd trimester
Underweight (<18.5)	12.5–18 kg	~0.5 kg/week
Normal (18.5–24.9)	11.5–16 kg	~0.4 kg/week
Overweight (25–29.9)	7–11.5 kg	~0.3 kg/week

Pre-pregnancy BMI category	Total weight gain	Rate, 2nd–3rd trimester
Obese (≥30)	5–9 kg	~0.2–0.3 kg/week

Excessive gain raises the risk of gestational hypertension, pre-eclampsia, gestational diabetes, macrosomia and caesarean delivery; the risk is proportionate to the degree of excess gain.

Routine supplementation

- **Iron-folic acid (IFA):** ferrous sulfate 200 mg (providing 60 mg elemental iron) with folic acid 1 mg daily, started once nausea settles (about 16 weeks); if haemoglobin (Hb) is <10 g%, increase to 2–3 tablets/day (three tablets deliver ~45 mg absorbable iron). Continue through lactation. Williams Obstetrics/ACOG endorse a minimum of 27 mg elemental iron/day, raised to 60–100 mg/day if the woman is obese, carrying a multifetal gestation, starts supplementation late, is an irregular taker, or is already anaemic.
- **Folic acid, high-risk dosing:** 4 mg/day from one month before conception through 12 weeks' gestation in women with a previous neural-tube-defect (NTD)-affected pregnancy (cuts recurrence by >70%), multifetal gestation, anticonvulsant therapy, or haemoglobinopathy; taken as a separate tablet, not folded into a multivitamin (avoids excess fat-soluble vitamin intake).
- **Calcium and vitamin D:** dietary calcium to the RDA (about 1 litre of milk daily supplies ~1 g); supplementation helps leg cramps. Vitamin D deficiency is common with limited sun exposure, strict vegetarian diets, and darker skin.
- **Iodine:** iodised salt is advised throughout pregnancy; severe deficiency risks endemic cretinism in the offspring.
- **Vitamin A:** doses above 10,000 IU/day are teratogenic (malformations resembling those from isotretinoin); beta-carotene from fruit and vegetables carries no such risk.

Dietary counselling & special precautions

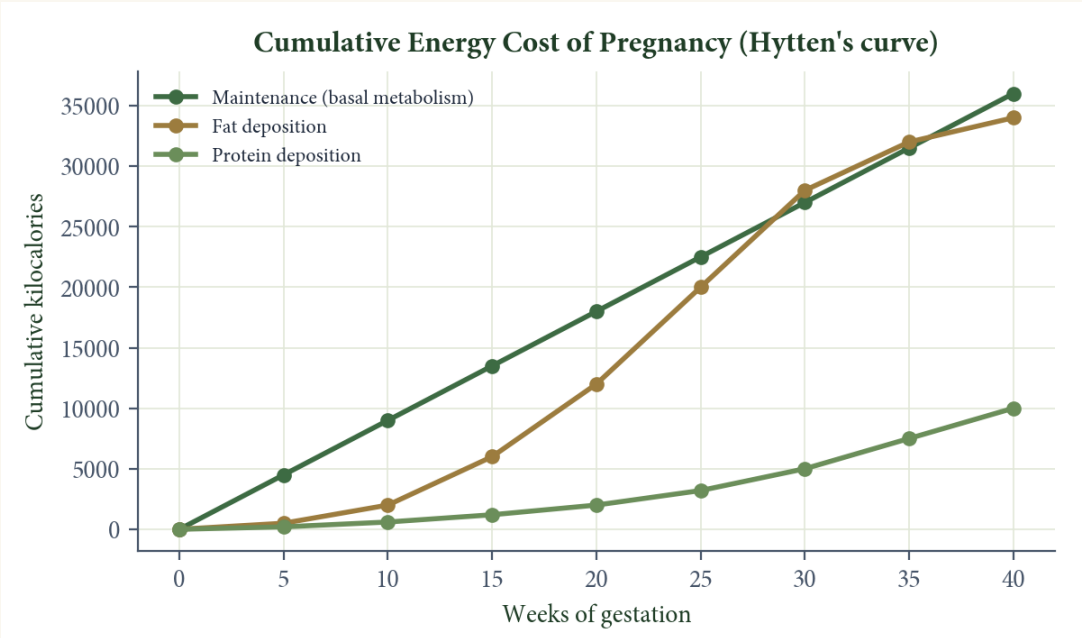
- **Vegetarian/vegan mothers:** risk of vitamin B12 deficiency in mother and breastfed infant — B12 occurs only in animal foods.
- **Seafood:** 8–12 ounces/week is safe; avoid shark, swordfish, king mackerel and tilefish (high methylmercury); limit albacore ("white") tuna to 6 ounces/week; avoid raw or undercooked fish (listeriosis risk).
- **Caffeine:** limit to <200 mg/day (about two cups of coffee); heavy intake (~5 cups/500 mg/day) modestly raises miscarriage risk.
- **Alcohol and smoking:** avoid completely — associated with fetal growth restriction, low birthweight and miscarriage.
- **Severe caloric restriction/fasting:** avoided — ketosis is potentially harmful to fetal neurodevelopment.

- **Salt:** taken to taste; routine restriction is not recommended.

Effects of malnutrition

	Undernutrition	Overnutrition / obesity
Maternal	Iron-deficiency and megaloblastic anaemia, osteomalacia, reduced work capacity, infection susceptibility	Gestational diabetes, gestational hypertension/pre-eclampsia, caesarean delivery, thromboembolism
Fetal/neonatal	Intrauterine growth restriction, low birth weight, prematurity, neural-tube defects (folate deficiency), impaired brain development, higher perinatal mortality	Macrosomia, birth trauma/shoulder dystocia, higher stillbirth risk, childhood obesity

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Maintenance rises linearly throughout; fat deposition rises steeply from mid-pregnancy then plateaus; protein deposition is gradual but steepest in the third trimester — together summing to ~80,000 kcal by term.

No anatomical figure applies to this topic; the curve above mirrors the standard obstetric teaching diagram of energy cost partitioned across gestation.

High-yield exam pointers

- Extra energy: **+300 kcal/day** in the second half; total pregnancy cost **~80,000 kcal**.
- Extra protein: **~1000 g deposited** in the second half (5–6 g/day extra); RDA **60 g/day** (India) vs **71 g/day** (US/IOM) — both cited standards, not a contradiction.

- IFA regimen: ferrous sulfate 200 mg (**60 mg elemental iron**) + folic acid **1 mg** daily from ~16 weeks; **2–3 tablets/day** if Hb <10 g%.
- Folic acid: **400 µg/day** routine prophylaxis; **4 mg/day** in high-risk women (previous NTD, multifetal gestation, anticonvulsants, haemoglobinopathy), started 1 month preconception through 12 weeks.
- IOM/ACOG weight gain by BMI: underweight 12.5–18 kg, normal 11.5–16 kg, overweight 7–11.5 kg, obese 5–9 kg.
- Vitamin A ceiling: avoid **>10,000 IU/day** (teratogenic).
- Seafood rule: 8–12 oz/week; avoid shark/swordfish/king mackerel/tilefish; albacore tuna ≤6 oz/week.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> The Indian (ICMR-based) recommended dietary allowance figures reproduced above (as in DC Dutta) run somewhat lower than the American Institute of Medicine/Dietary Reference Intake figures cited in Williams Obstetrics (for example, protein and iron); both are legitimate national standards derived from different reference populations, not a guideline conflict.

> **SOURCE & COVERAGE**
> Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; Institute of Medicine (2009) gestational weight-gain guidelines as endorsed by the American College of Obstetricians and Gynecologists (2020).

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Objective signs of diagnosis of pregnancy in first trimester

Asked in: Paper I 16-Dec-2023 — RGUHS MS Obstetrics & Gynaecology

Definition — Objective signs of pregnancy are findings elicited by an **examiner** (general/breast examination, per-abdomen and pelvic examination) or by **laboratory/imaging tests**, as opposed to subjective symptoms reported by the woman (amenorrhoea, morning sickness, breast discomfort, frequency of micturition). In the first trimester (up to 12 weeks) the uterus is still a pelvic organ, so the later "positive" signs of pregnancy — audible fetal heart sound by stethoscope, palpable fetal parts, felt active fetal movements — are **not yet available**; the objective evidence in this trimester comes from breast/pelvic examination findings, hCG-based pregnancy tests, and transvaginal sonography.

General and breast signs

- **Breast enlargement** with vascular engorgement — delicate veins visible under the skin (primigravidae only; multiparous breasts are already enlarged).

- **Pigmentation** of the nipple and primary areola, more marked in dark-skinned women.
- **Montgomery's tubercles** become prominent.
- **Colostrum** (thick, yellowish secretion) can be expressed as early as the 12th week.
- **Per-abdomen**: uterus remains pelvic till 12 weeks; only a suprapubic bulge may just be felt near term of the trimester.

Pelvic examination signs (vaginal, cervical, uterine)

Sign	Eponym	Week first seen	Finding
Dusky/bluish discoloration of vestibule and anterior vaginal wall	***Jacquemier's* (or *Chadwick's*) sign**	~8th week	Due to local vascular congestion of the vaginal walls
Increased pulsation felt through the lateral vaginal fornices	***Osiander's* sign**	~8th week	Reflects increased uterine artery pulse pressure
Copious non-irritating mucoid vaginal discharge	—	6th week	Cervical gland hyperplasia/hypersecretion
Cervical softening — feels like the lips of the mouth (non-pregnant cervix feels like the tip of the nose)	***Goodell's* sign**	~6th week (slightly earlier in multiparae)	Increased vascularity and oedema of the cervix; bluish discoloration also visible on speculum
Asymmetrical uterine enlargement, one cornu firmer than the other	***Piskacek's* sign**	Early, with lateral implantation	Symmetry restored as pregnancy advances
On bimanual palpation the abdominal and vaginal fingers seem to appose below the firm cervix because the isthmus is soft and compressible	***Hegar's* sign**	6–10 weeks (present in ~two-thirds of cases)	Upper uterine body enlarged, isthmus soft, cervix comparatively firm; examine gently — risk of abortion
Regular, rhythmic uterine contractions felt on bimanual "cupping" of the uterus for 2–3 minutes	***Palmer's* sign**	4–8 weeks	Contraction phase ~30 seconds; becomes difficult to elicit after 10 weeks as the relaxation phase lengthens

Sign	Eponym	Week first seen	Finding
Uterus enlarges hen's-egg (6 wk) → cricket-ball (8 wk) → fetal-head size (12 wk); pyriform shape becomes globular; consistency soft and elastic	—	Progressive, 6–12 weeks	Corroborates gestational age clinically

Biochemical confirmation — pregnancy (hCG) tests

Test	Sample/sensitivity	Positive from
Agglutination-inhibition / direct latex agglutination (home/office kit)	Urine, 0.2–1 IU hCG/mL	2–3 days after the missed period
Two-site sandwich immunoassay (membrane/card ELISA)	Urine 30–50 mIU/mL; serum 1.0 mIU/mL	Day of missed period
Enzyme-linked immunosorbent assay (ELISA)	Serum 1–2 mIU/mL	5 days before the missed period
Radioimmunoassay (RIA) of β-hCG	Serum 0.002 IU/mL	8–9 days after ovulation

Serum/urine hCG becomes detectable **8–11 days after conception** (3–4 days before the expected missed period); a serum/urine immunoassay is the standard confirmatory objective test in the first trimester, but is **not reliable for dating beyond 12 weeks**.

Sonographic signs — the earliest true "positive" evidence in the first trimester

Gestational age (menstrual weeks)	Finding on transvaginal ultrasonography
4½–5 weeks	Intradecidual **gestational sac** first visible
5–5½ weeks	**Yolk sac** appears within the sac
5½–6 weeks	**Fetal pole with cardiac activity** first detected
7 weeks	**Embryonic movements** visible
7–12 weeks	**Crown–rump length** (CRL) — most accurate method of dating, accurate to ±5 days
10 weeks	**Doppler ultrasound** reliably picks up the fetal heart rate

Absence of cardiac activity in an embryo with a CRL ≥7 mm on transvaginal scan is diagnostic of a non-viable pregnancy; the true gestational sac must be distinguished from a pseudo-gestational sac (central, no double decidual sign) seen with ectopic pregnancy.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 7.2 — Demonstration of Hegar's sign (DC Dutta's Obstetrics 9e, p.88)*

High-yield exam pointers

- Order of pelvic signs by week: **Goodell** (cervix soft, 6 wk) and **Palmer's** contractions (4–8 wk) earliest → **Hegar** (isthmus soft, 6–10 wk) → **Jacquemier/Chadwick** and **Osiander** (bluish discoloration/pulsation, 8 wk) → **Piskacek** (asymmetry, with implantation).
- Sonographic milestone ladder to reproduce verbatim: gestational sac 4½–5 wk → yolk sac 5–5½ wk → fetal pole + cardiac activity 5½–6 wk → embryonic movement 7 wk → CRL dating window 7–12 wk (±5 days) → Doppler FHR reliable at 10 wk.
- hCG detectable in serum **8–11 days post-conception**; urine kit turns positive around the day of the missed period.
- In the first trimester, **fetal heart sound by stethoscope, palpable fetal parts, and felt fetal movements are NOT yet elicitable** — do not list them under first-trimester signs.
- Hegar's sign carries an abortion risk if examined roughly — always mention "gentle bimanual examination."

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Minor inter-textbook variation exists in sonographic milestone weeks — DC Dutta's Obstetrics 9e lists gestational sac by 5 weeks and yolk sac by 5.5 weeks, while Williams Obstetrics 26e gives a slightly wider window (gestational sac 4½–5 weeks, yolk sac 5–6 weeks, cardiac activity 5½–6 weeks); this answer follows Williams Obstetrics 26e as the current standard.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Ovarian steroidogenesis

Asked in: Paper I Nov 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — Ovarian steroidogenesis is the synthesis and secretion of the sex steroids — estrogens, progesterone, and androgens — by the ovary from cholesterol, through cytochrome P450 and hydroxysteroid dehydrogenase enzymes that are segregated between the theca and granulosa cell

compartments of the follicle. Output is driven by the two pituitary gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), acting cooperatively in the **"two-cell" system**, whose character changes between the follicular and luteal phases.

Sites of steroid production in the ovary

Steroid	Principal cell source	Comment
Estrogens (estradiol mainly, some estrone)	Granulosa cells of the growing follicle; same cells after luteinization (corpus luteum)	Small amounts also from theca cells and ovarian stroma
Androgens (dehydroepiandrosterone [DHEA], androstenedione, testosterone)	Theca interna cells (predominant)	Also stroma and granulosa; production is LH-driven
Progesterone	Luteinized theca-granulosa cells of the corpus luteum	Trace amounts from follicular theca/granulosa and stroma before ovulation

The steroidogenic pathway — cholesterol to sex steroids

Step	Enzyme	Reaction catalysed	Location
1	**StAR** (steroidogenic acute regulatory) protein	Rate-limiting transport of cholesterol from outer to inner mitochondrial membrane	Both cell types
2	**P450scc** (cholesterol side-chain cleavage enzyme)	Cholesterol → pregnenolone	Mitochondria, both cell types
3	**P450c17** (a single enzyme with combined 17α-hydroxylase + 17,20-lyase activity)	Pregnenolone → 17-OH-pregnenolone → DHEA; progesterone → 17-OH-progesterone → androstenedione	**Theca cells only** — absent from granulosa
4	**3β-hydroxysteroid dehydrogenase (3β-HSD)**	Pregnenolone → progesterone; 17-OH-pregnenolone → 17-OH-progesterone; DHEA → androstenedione	Both compartments; rises sharply with luteinization
5	**17β-hydroxysteroid dehydrogenase (17β-HSD)**	Androstenedione ↔ testosterone; estrone ↔ estradiol	Both, mainly granulosa

Step	Enzyme	Reaction catalysed	Location
6	**P450arom / aromatase (CYP19A1)**	Androstenedione → estrone; testosterone → estradiol	**Granulosa cells only** — induced by FSH

Because P450c17 (androgen-forming) is confined to theca cells and aromatase (estrogen-forming) is confined to granulosa cells, oestrogen synthesis is obligately a two-compartment process — the biochemical basis of the two-cell theory below.

Two-cell, two-gonadotropin theory — follicular phase

- **LH receptors** are expressed only on theca interna cells; **FSH receptors** only on granulosa cells, of preantral and antral follicles.
- **LH** stimulates theca cells (StAR → P450scc → 3β-HSD → theca-exclusive P450c17) to convert cholesterol to androgens — chiefly **androstenedione** and **testosterone**.
- These androgens diffuse across the follicular basement membrane into the adjacent granulosa cells.
- **FSH** induces **aromatase (P450arom)** activity in granulosa cells, which lack P450c17/17,20-lyase and so cannot synthesise androgens de novo — they depend on theca-derived substrate.
- Aromatase converts the theca-derived androstenedione/testosterone to **estrone/estradiol**; estradiol is the dominant and most potent ovarian oestrogen secreted.
- Estrogen production therefore requires **two cell types** (theca + granulosa) acting under **two gonadotropins** (LH supplying androgen substrate, FSH driving aromatization) — the **two-cell, two-gonadotropin system**.

Luteal phase — two-cell, one-gonadotropin system

- After the mid-cycle LH surge and ovulation, granulosa cells luteinize and the follicle is vascularized, delivering low-density lipoprotein (LDL) cholesterol as substrate.
- **LH alone** (FSH support falls) now drives both **progesterone** synthesis in luteinized granulosa cells (via up-regulated StAR, P450scc and 3β-HSD) and continued aromatase activity.
- Theca-luteal cells continue supplying androstenedione, which diffuses into granulosa-luteal cells and is aromatized to estradiol — but now under LH drive alone, so the follicular "two gonadotropin" requirement collapses to a **"two-cell, one-gonadotropin (LH)" system**.
- **Progesterone** becomes the dominant secretory product of the corpus luteum, supporting the secretory endometrium and, if implantation occurs, early pregnancy until placental take-over (luteoplacental shift).

Quantitative hormonal profile across the cycle

Parameter	Follicular phase	At ovulation	Luteal phase
Estradiol — daily production (μg)	~50	150–300	~100
Estradiol — serum level (pg/mL)	~50	300–600	150–200
Progesterone — daily production (mg)	2–3	—	20–30
Progesterone — serum level (ng/mL)	<1	—	5–15 (mid-luteal)
FSH (mIU/mL)	~10	15–20	~10
LH (mIU/mL)	~5	~60	~5

Feedback control of steroidogenesis

- **Estrogen — negative feedback:** at ordinary follicular-phase levels, estradiol suppresses FSH release, both by reducing pituitary gonadotroph sensitivity to gonadotropin-releasing hormone (GnRH) and by decreasing hypothalamic GnRH pulsatility.
- **Estrogen — positive feedback:** a sustained rise of estradiol above ~200 pg/mL for 24–48 hours switches the pituitary response, triggering the **mid-cycle LH surge** that causes ovulation.
- **Progesterone:** curtails the duration of the LH surge (negative feedback) and, acting locally within the ovary, suppresses new follicular growth in the same cycle.
- **Inhibin** (from granulosa cells, FSH-dependent) exerts a preferential negative feedback on FSH secretion, complementing steroid feedback.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 7.7 — Two cell two gonadotropin theory of ovarian steroidogenesis (DC Dutta's Gynaecology 7e, p.79)*

High-yield exam pointers

- Write the exact phrase "**two-cell, two-gonadotropin theory**": LH → theca → androgens; FSH → granulosa → aromatase → estrogen.
- Enzyme localisation is the examiner's favourite trap: **P450c17** (17α-hydroxylase + 17,20-lyase) is **theca-only**; **aromatase (P450arom/CYP19A1)** is **granulosa-only**.
- **StAR protein** = rate-limiting cholesterol transport step; **P450scc** = cholesterol → pregnenolone (first enzymatic step).
- Luteal phase = "**two-cell, ONE-gonadotropin (LH)**" system — progesterone, not estrogen, is now the dominant output.

- Key numbers: peak estradiol 300–600 pg/mL at ovulation; mid-luteal progesterone 5–15 ng/mL; LH surge ~60 mIU/mL.
- Positive-feedback threshold: estradiol >200 pg/mL sustained 24–48 hours → LH surge → ovulation.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> P450c17 is a single microsomal enzyme carrying both 17α-hydroxylase and 17,20-lyase activities on the same protein (not two separate enzymes) — a frequently mis-stated detail worth stating correctly in the exam.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e.

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Pelvic diaphragm

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — The pelvic diaphragm is the musculofascial partition that spans the pelvic outlet and separates the pelvic cavity above from the anatomical perineum below. It is formed by the **levator ani** and **coccygeus** muscles of each side together with their covering superior and inferior layers of pelvic fascia, and it slings hammock-like around the urethra, vagina, and anal canal (the midline pelvic effluents).

Composition & attachments

Muscle	Origin	Insertion	Key features
Pubococcygeus (main, medial part of levator ani; = pubovisceral muscle)	Posterior surface of pubic bone and anterior part of the tendinous arch (white line over obturator internus)	Splits into: **pubovaginalis** (perineal body, alongside vagina), **puboperinealis/puboanalis** (perineal body, anal-canal wall), **puborectalis** (winds behind the anorectal junction to form a U-shaped puborectal sling)	Fibres of both sides meet behind rectum/vagina/urethra as a supporting sling; medial fibres form the **levator plate**
Iliococcygeus	Posterior part of the tendinous arch (obturator fascia) and ischial spine	Anococcygeal raphe and coccyx	Thin, aponeurotic posterolateral sheet

Muscle	Origin	Insertion	Key features
Coccygeus (ischiococcygeus)	Ischial spine and sacrospinous ligament	Lateral border of the lower sacrum and coccyx	Triangular; often described as a distinct muscle that completes the pelvic diaphragm posterolaterally along with levator ani

- **Anococcygeal raphe (levator plate):** a layered musculofibrous band (presacral fascia, tendinous plate of pubococcygeus, muscular raphe of iliococcygeus, superficial fibres of external anal sphincter) extending from the anorectal junction to the coccyx.
- **Upper (pelvic) surface:** concave, sloping down-back-and-medially, covered by the parietal layer of pelvic fascia.
- **Lower (perineal) surface:** convex, covered by anal fascia; the muscle plus its fascial coverings together constitute the **pelvic diaphragm** proper.

Gaps in the diaphragm

Gap	Bridged by	Transmits
Hiatus urogenitalis (anterior)	Muscles and fascia of the urogenital triangle (urogenital diaphragm/perineal membrane)	Urethra and vagina
Hiatus rectalis (posterior)	Anococcygeal raphe/levator plate	Anorectal canal

Relations

- **Superior (pelvic) surface** — related, anterior to posterior, to the bladder, vagina, and rectum; covered by pelvic cellular (endopelvic) tissue occupying the space between pelvic peritoneum and the levator ani; the **ureter** crosses it near the lateral vaginal fornix, with the **uterine artery above** and the **vaginal artery below**; pelvic autonomic nerves lie on this surface.
- **Inferior (perineal) surface** — faces the anatomical perineum (urogenital and anal triangles) and the ischiorectal fossa laterally.

Nerve supply

The levator ani receives a direct supply from the **3rd and 4th sacral nerve roots** on its pelvic surface (the "nerve to levator ani") and, from below, twigs of the **pudendal nerve (S2–S4)** — the **inferior rectal nerve** and its **perineal branch**. Coccygeus is supplied by S3, S4 branches directly.

Functions

- Supports the pelvic viscera — the U-shaped **pubovaginalis sling** supports the vagina, which in turn supports the bladder and uterus; tear or stretching of this sling in labour predisposes to pelvic organ prolapse.

- Counteracts the downward thrust of raised intra-abdominal pressure and guards the hiatus urogenitalis.
- Facilitates **anterior (internal) rotation** of the fetal presenting part as it presses on the puborectal sling during the second stage of labour.
- Puborectalis maintains the anorectal angle and acts as an ancillary continence mechanism alongside the external anal sphincter.
- Coccygeus helps stabilise the sacroiliac and sacrococcygeal joints.
- Steadies and supports the perineal body, which lies just below it.

Applied anatomy

- **Labour:** the levator muscles hypertrophy and become more distensible in pregnancy; in the second stage the pubovaginalis and puborectalis relax and the diaphragm is drawn up over the advancing head. Failure of timely relaxation, or excessive stretching/pudendal neuropathy during a prolonged second stage, causes **levator ani avulsion** (commonly the puborectalis) — a recognised risk factor for later pelvic organ prolapse and urinary/faecal incontinence.
- **DeLancey's three-level support theory** places the pelvic diaphragm (with levator plate and perineal body) at **Level III**, the lowest support tier; a defect here manifests as cystocele, rectocele, or urinary incontinence (Level I ligamentous defects give uterovaginal/vault prolapse; Level II fascial defects give paravaginal/pararectal defects).
- **Episiotomy** deliberately incises the perineal body and superficial perineal muscles/fascia (not the levator ani itself) to prevent an uncontrolled tear extending upward into the pelvic diaphragm.
- **Pudendal nerve block** anaesthetises the perineal branch supplying the diaphragm and perineum, useful for instrumental delivery and perineal repair.
- Chronic spasm of the muscle underlies the **levator ani syndrome** of chronic pelvic/perineal pain.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 5.7 — The pelvic diaphragm: view of the pelvic floor muscles from above/below (Berek & Novak's Gynecology 16e, p.166)*
>
> Label: pubococcygeus (with pubovaginalis, puboperinealis, puborectalis slips), iliococcygeus, coccygeus, obturator internus with tendinous arch (white line), ischial spine, sacrospinous ligament, hiatus urogenitalis, hiatus rectalis, anococcygeal raphe (levator plate).

High-yield exam pointers

- **Pelvic diaphragm = levator ani (pubococcygeus + puborectalis + iliococcygeus) + coccygeus**, with their fascial coverings.

- Pubococcygeus slips, mnemonic "**VPA**": pubo**v**aginalis → vagina/perineal body; pubo**p**erinealis(puboanalis) → perineal body/anal wall; pubo**r**ectalis → puborectal sling around anorectal junction.
- Nerve supply: direct **S3, S4** + **pudendal nerve (S2–S4)** branches (inferior rectal + perineal).
- Two hiatus: **urogenitalis** (urethra + vagina) anteriorly, **rectalis** (anorectal canal) posteriorly.
- Second-stage mechanics: puborectal sling relaxation drives **anterior (internal) rotation** of the fetal head.
- Applied: **DeLancey Level III** = pelvic diaphragm/levator plate/perineal body → cystocele/rectocele/incontinence when damaged; levator ani avulsion is an obstetric injury linked to later prolapse.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Some texts (e.g., DC Dutta) group coccygeus as the third named slip of levator ani ("ischiococcygeus") while Williams Obstetrics 26e and Berek & Novak 16e describe coccygeus as a separate muscle that, together with levator ani, constitutes the pelvic diaphragm — either description is acceptable, but state the muscle names and attachments correctly.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e (Chapter 1, Pelvic Floor/Pelvic Diaphragm); Williams Obstetrics 26e (Maternal Anatomy, Pelvic Diaphragm); Berek & Novak's Gynecology 16e (Chapter 5, Anatomy).

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Pelvic part of ureter

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — The ureter is a fibromuscular tube conveying urine from the renal pelvis to the bladder. Its **pelvic part** begins where it crosses the pelvic brim (at the bifurcation of the common iliac artery) and ends at the trigone of the bladder; it measures about **13 cm in length and 5 mm in diameter**. Because of its intimate relations to the uterine vessels, ovary and cervix, the pelvic ureter is of major surgical importance in gynaecological practice.

Course and relations

- **At the pelvic brim:** the ureter enters the pelvis in front of the bifurcation of the common iliac artery, over the sacroiliac joint — on the right side behind the root of the small-bowel mesentery, on the left behind the apex of the mesosigmoid.

- **On the side wall of the pelvis:** it descends applied to the peritoneum, lying anterior to the internal iliac artery and posterior to the ovary, forming the **posterior boundary of the ovarian fossa**; here the ovarian vessels cross it laterally within the infundibulopelvic (suspensory) ligament.
- **At the level of the ischial spine:** the ureter turns forwards and medially, running within the base of the broad ligament just lateral to the uterosacral ligament (separating it from the mesosalpinx/mesovarium).
- **In the parametrium (base of broad ligament):** it is crossed **anteriorly, from above**, by the uterine artery at right angles, about **1.5–2 cm lateral to the supravaginal cervix/internal os** — the classic "**water under the bridge**" relationship (uterine artery = bridge; ureter = water beneath). It then enters the **ureteric tunnel** (tunnel of Wertheim) within the cardinal (Mackenrodt's) ligament.
- **Over the anterior vaginal fornix:** it runs a short distance close to the lateral fornix, then turns medially.
- **Intravesical part:** it pierces the bladder wall obliquely for about 2 cm before opening at the lateral angle of the trigone.

Three points of physiological constriction: (i) where it crosses the pelvic brim, (ii) where crossed by the uterine artery, (iii) the intravesical part — clinically relevant sites for calculus impaction as well.

Structure, blood supply, lymphatics, nerve supply, development

Feature	Detail
Wall (outside in)	Fibrous sheath from visceral pelvic fascia → muscle coat (outer and inner longitudinal, middle circular) → mucosa lined by transitional epithelium
Blood supply	Segmental, from nearly all visceral branches of the anterior division of the internal iliac artery (uterine, vaginal, vesical, middle rectal, superior gluteal) running within the peri-ureteric sheath; veins correspond to these arteries
Lymphatic drainage	Lower pelvic ureter → external and internal iliac nodes; upper part → lumbar (para-aortic) nodes
Nerve supply	Sympathetic — hypogastric and pelvic plexus; parasympathetic — sacral plexus (nervi erigentes, S2–S4)
Development	Ureteric bud sprouting from the caudal end of the mesonephric (Wolffian) duct

Applied anatomy — surgical vulnerability of the pelvic ureter

Because of its close anatomical relation to the genital organs, the pelvic ureter accounts for **about 75% of all iatrogenic ureteric injuries**, virtually all following gynaecological/abdominal surgery; **about 91% of ureteric injuries occur in the pelvic segment** of the ureter (only 2% upper, 7% mid-ureteric third). Overall incidence is **0.5–1% of all pelvic operations**. Laparoscopic hysterectomy carries the highest risk and vaginal hysterectomy the lowest.

Site of vulnerability	Anatomical basis	Procedure(s) most implicated
Infundibulopelvic ligament (pelvic brim)	Ureter runs parallel/posterior to the ovarian vessels and forms the posterior boundary of the ovarian fossa	Salpingo-oophorectomy, clamping the infundibulopelvic pedicle at hysterectomy, adnexal-mass excision
Base of broad ligament, ~1.5–2 cm lateral to cervix	Uterine artery crosses ureter anteriorly ("water under the bridge"); descending cervical branch nearby	Clamping the uterine pedicle at abdominal/vaginal hysterectomy — risk is higher on **reclamping** a slipped pedicle than on primary clamping
Ureteric tunnel (tunnel of Wertheim) within the cardinal ligament	Ureter tethered within Mackenrodt's ligament tissue	Radical hysterectomy/parametrectomy
Vaginal angle / anterior vaginal fornix	Ureter lies close to the lateral fornix before turning to enter the bladder	Vaginal hysterectomy, colposuspension, sacrospinous fixation
Posterior peritoneal leaf	Ureter lies within/adjacent to the posterior peritoneal fold at closure	Pelvic peritonisation after hysterectomy
Intravesical (intramural) part	Oblique course through the bladder wall	Bladder-neck/trigonal surgery, mid-urethral sling procedures

Intraoperative identification of the ureter — recognised by (i) pale, glistening appearance, (ii) visible **peristalsis** on gentle mechanical stimulation, (iii) a **plexus of longitudinal blood vessels** on its surface.

Factors raising risk: endometriosis, broad-ligament fibroid, pelvic inflammatory adhesions, gynaecological malignancy and duplex ureter distort normal landmarks at every site above.

Nature of injury: kinking/angulation, ischaemic devascularisation (from stripping the peri-ureteric sheath), inadvertent ligature incorporation, crush injury from clamps, partial/complete transection, and thermal injury from monopolar/bipolar energy or laser during minimally invasive surgery.

Single best safeguard: careful identification and, wherever possible, direct visualisation of the ureter throughout its pelvic course — using a retroperitoneal approach if needed — **before** securing the infundibulopelvic ligament or the uterine artery.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 2.20 — The broad ligament from the side showing the relation of the ureter to the uterine artery (Jeffcoate's Principles of Gynaecology 9e, p.23)*

High-yield exam pointers

- Pelvic ureter: **~13 cm long, 5 mm diameter**; three constrictions — pelvic brim, uterine artery crossing, intravesical part.
- **"Water under the bridge"**: uterine artery crosses **anterior to and above** the ureter, ~1.5–2 cm lateral to the supravaginal cervix/internal os.
- Ureter forms the **posterior boundary of the ovarian fossa** — key relation at the infundibulopelvic ligament.
- Recognise the ureter by: pale glistening look, peristalsis, longitudinal vessel plexus.
- Numbers to reproduce: **91%** of ureteric injuries are in the pelvic ureter; **~75%** of all iatrogenic ureteric injuries follow gynaecological surgery; overall incidence **0.5–1%** of pelvic operations.
- Highest-risk procedure: laparoscopic hysterectomy; lowest-risk: vaginal hysterectomy.
- Five named danger sites in sequence: infundibulopelvic ligament → base of broad ligament (uterine artery crossing) → ureteric (Wertheim) tunnel → vaginal angle → posterior peritoneal leaf/intravesical part.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e.

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Perineal body

Asked in: Paper I 29-Jul-2021 · Paper I Nov 2018 · Paper I May 2007 (3×) — RGUHS MS Obstetrics & Gynaecology

Definition — The perineal body (synonyms: **obstetrical perineum**, **central point of the perineum**, **central tendon of the perineum**) is a pyramidal fibromuscular mass in the midline between the vagina and the anal canal, at the junction of the urogenital and anal triangles of the perineum. It measures about **4 cm × 4 cm**, its base is covered by perineal skin and its apex is continuous above with the

rectovaginal septum, and it forms the "hub of the wheel" into which **nine muscles and two fascial sheets** converge to support the pelvic floor.

Situation, extent and boundaries

Feature	Description
Location	Midline, between the lower one-third of the vagina anteriorly and the anal canal posteriorly
Shape	Pyramidal, base below and apex above
Base	Covered by perineal skin, between the fourchette and the anus
Apex	Pointed; continuous superiorly with the **rectovaginal septum** (fascia of Denonvilliers)
Dimensions	About 4 cm × 4 cm (~1.5 inch)
Superior limit	The floor of the pouch of Douglas, about 6–7 cm above the anal orifice
Lateral relation	Ischiorectal fossae on each side

Composition — fascial and muscular architecture

Layer	Structures
Superficial fascia	Superficial fatty layer + deeper membranous **Colles' fascia**
Deep fascia	Inferior and superior fascial layers of the urogenital diaphragm (perineal membrane), together forming the **triangular ligament**
Muscles converging (9 in all)	**Superficial transverse perinei** (paired); **deep transverse perinei** (paired); **bulbospongiosus** (paired); **pubococcygeus** part of levator ani (paired), at the junction of the upper two-thirds and lower one-third of the vagina; **external anal sphincter** (subcutaneous/superficial fibers)

Relations

Direction	Relation
Anterior	Lower one-third of the vagina and urethra
Posterior	Anal canal and anococcygeal body
Superior	Rectovaginal septum, floor of the pouch of Douglas

Direction	Relation
Lateral	Ischiorectal fossae; bulbospongiosus and superficial transverse perineal muscles attach it to the ischiopubic rami/ischial tuberosities

Functions of the perineal body

- Acts as the **central point of attachment** for the perineal muscles, fasciae and the pelvic diaphragm — "hub of the wheel."
- **Supports the levator ani** placed above it and helps maintain the horizontal levator plate.
- By supporting the posterior vaginal wall, it **indirectly supports the anterior vaginal wall, bladder base and uterus**, and maintains the normal **vaginal axis**.
- Forms the fibromuscular partition separating the urogenital compartment from the anal (anorectal) compartment.
- Provides the anchoring point where the perineal (Level III) supports of DeLancey integrate with the pelvic (Level I/II) supports.

Applied anatomy — obstetric and surgical significance

- **Vulnerable to childbirth injury** — it is stretched and thinned as the fetal head crowns; overstretching or tearing disrupts the vaginal axis and predisposes to later **rectocele** and **relaxed perineum**.
- **Episiotomy** is the deliberate surgical incision of the perineal body (and its converging muscles) to enlarge the introitus and prevent uncontrolled tearing; the same muscles (bulbospongiosus, superficial transverse perineal, pubococcygeus fibers, external anal sphincter fibers) are reapproximated in a layered episiotomy/perineal tear repair.
- **Perineal tears are graded by the depth of structures disrupted** — first degree (skin only) to fourth degree (posterior vaginal wall + perineal body + full anal sphincter complex + anorectal mucosa); full staged management is a separate long-answer topic (see *Complete perineal tear*).
- **POP-Q system** (International Continence Society, Bump et al.) formally measures the perineal body (point "**pb**") — from the posterior margin of the genital hiatus to the mid-anal opening — as one of the standard site-specific measurements alongside genital hiatus (gh) and total vaginal length (tvl).
- **Perineorrhaphy/perineoplasty** (posterior colpoperineorrhaphy) surgically restores a torn or lax perineal body during pelvic floor/prolapse repair; restoration of the perineal body is considered essential to re-establish the normal vaginal axis.
- Clinically assessed per vaginum by flexing the examining finger posteriorly and palpating the perineal body against the thumb placed externally, to judge its integrity and tone before repair or prolapse surgery.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 1.20 — Anatomy of the pelvic floor, perineal view. (Te Linde 13e, p.91)*

Label: perineal skin (base), the nine converging muscles (bulbospongiosus, superficial and deep transverse perinei, pubococcygeal fibers of levator ani, external anal sphincter), the rectovaginal septum at the apex, and the ischiorectal fossae laterally.

High-yield exam pointers

- Synonyms to write first: **obstetrical perineum = central point of perineum = central tendon of perineum**.
- Dimensions: **4 cm × 4 cm**, pyramidal, base = skin, apex = rectovaginal septum.
- Mnemonic for the **9 converging muscles**: 2 bulbospongiosus + 2 superficial transverse perinei + 2 deep transverse perinei + 2 pubococcygeal (levator ani) + 1 external anal sphincter = 9, the "hub of the wheel."
- Two fascial sheets: superficial perineal fascia (fatty layer + Colles' fascia) and urogenital diaphragm (= triangular ligament).
- Damage to the perineal body → loss of normal vaginal axis → rectocele/relaxed perineum; restoring it is the key surgical principle in posterior repair.
- POP-Q: perineal body point (pb) = genital hiatus posterior margin → mid-anal opening.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta gives the perineal body's classic teaching dimensions and the "9-muscle hub" description used across Indian exams; Williams Obstetrics and Te Linde corroborate the same fascial/muscular convergence and additionally ground its role in the ICS POP-Q system and modern pelvic-floor-repair anatomy.

SOURCE & COVERAGE

DC Dutta's Textbook of Obstetrics 9e; DC Dutta's Textbook of Gynaecology 7e; Williams Obstetrics 26e; Te Linde's Operative Gynecology 13e.

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Pharmacology of magnesium sulfate

Asked in: Paper I Jun 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — Magnesium sulfate (MgSO4) is an inorganic salt that acts as a physiological calcium antagonist at the neuromuscular junction and central synapses. In obstetrics it is the drug of choice for

the prevention and treatment of eclamptic seizures, for fetal neuroprotection before very preterm birth, and was historically used as a tocolytic.

Mechanism of action

Site	Effect
Neuromuscular junction	Competes with calcium presynaptically, reduces acetylcholine release → stabilises the muscle membrane, reduces neuromuscular irritability (curariform action); this underlies loss of deep tendon reflexes with rising levels
CNS (anticonvulsant/neuroprotective)	Blocks the calcium channel of the glutamatergic **N-methyl-D-aspartate (NMDA) receptor**; reduces presynaptic release of glutamate; potentiates adenosine action; improves mitochondrial calcium buffering; blocks calcium entry via voltage-gated channels — raises the seizure threshold
Vascular smooth muscle	Calcium-channel blockade → vasodilation; a 4-g IV dose produces a small fall in mean arterial pressure with a transient (~13%) rise in cardiac index lasting about 15 minutes
Myometrium	Dose-dependent relaxation, but serum levels of 8–10 mEq/L are needed to inhibit contractions — the (now abandoned) rationale for tocolytic use

Pharmacokinetics

Parameter	Detail
Route	Parenteral only (IV or deep IM) — not given orally for systemic effect
Distribution	Crosses the placenta freely; equilibrates in fetal serum, less so in amniotic fluid
Metabolism	Not metabolised
Excretion	Renal, almost entirely unchanged; clearance ≈ one-third of the glomerular filtration rate (estimated from serum creatinine)
Therapeutic (anticonvulsant) range	**4–7 mEq/L (4.8–8.4 mg/dL, 2.0–3.5 mmol/L)**

Obstetric indications & dose regimens

Indication	Regimen
Eclampsia (treatment) and **severe pre-eclampsia (seizure prophylaxis)** — drug of choice	See dosage table below

Indication	Regimen
Recurrent seizure despite therapy	Additional bolus of 2 g IV over 3–5 minutes (up to 4 g if the woman is large)
Fetal neuroprotection before anticipated birth <32 weeks	6-g IV bolus over 20–30 minutes, then 2 g/hour maintenance (continued up to 12 hours if delivery not imminent; per ACOG/SMFM Committee Opinion No. 455, reaffirmed 2020)
Historic use as **tocolytic**	No longer recommended — not proven effective; the FDA (2013) warned against use beyond 5–7 days because of fetal bone thinning/fractures from fetal hypocalcemia

Standard seizure-prophylaxis/treatment dosage schedule:

Regimen	Loading dose	Maintenance dose
Intramuscular (Pritchard)	4 g (20% solution) IV over 3–5 min, followed by 10 g of 50% solution deep IM (5 g in each buttock)	5 g (50%) deep IM every 4 hours in alternate buttocks
Intravenous (Zuspan/Sibai)	4–6 g IV diluted, over 15–20 min	1–2 g/hour continuous IV infusion

Magnesium sulfate is continued for **24 hours after delivery** (or 24 hours after the last convulsion in postpartum eclampsia). Only the maintenance infusion rate — never the loading dose — is reduced in renal impairment (serum creatinine ≥1.0 mg/dL), since the loading dose achieves the target level regardless of renal function.

Evidence base: The MAGPIE trial (2002; >10,000 women with severe pre-eclampsia) showed a 58% lower risk of eclampsia with magnesium sulfate versus placebo, with no increase in maternal or perinatal harm. The BEAM trial (Rouse, 2008) established the neuroprotection regimen above, showing reduced moderate-to-severe cerebral palsy in survivors born before 32 weeks.

Monitoring & toxicity

Monitor	Acceptable/target
Deep tendon (patellar) reflex	Must be present before each dose
Respiratory rate	≥12–14/minute
Urine output	>25–30 mL/hour (>100 mL over the preceding 4 hours)
Serum magnesium	Checked if serum creatinine ≥1.0 mg/dL or oliguria; keep within 4–7 mEq/L

Serum level	Effect
4–7 mEq/L	Therapeutic (anticonvulsant)
~10 mEq/L	Loss of patellar reflex (early warning sign)
>10 mEq/L	Weakened respiration
≥12 mEq/L	Respiratory paralysis/arrest
Higher levels	Cardiac conduction defects, arrest

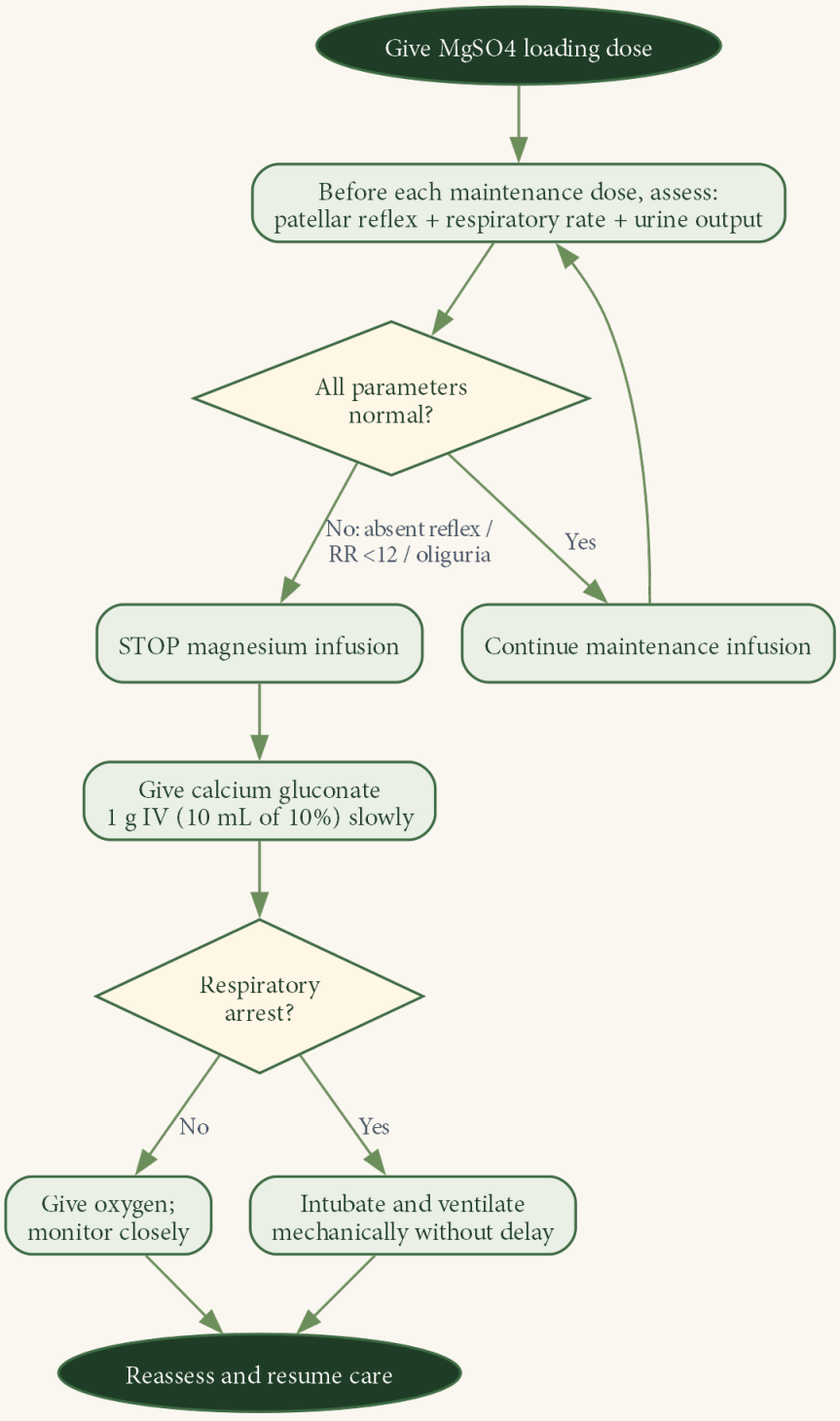
Management of toxicity:

- Stop the magnesium infusion immediately.
- Give **calcium gluconate 1 g IV (10 mL of 10% solution) slowly** — the physiological antagonist; reverses mild-to-moderate respiratory depression but its effect may be short-lived if a steady-state toxic level has been reached.
- Give oxygen; if respiratory arrest occurs, intubate and ventilate mechanically without delay.
- Fluid loading and forced diuresis (or dialysis in established renal failure) to hasten clearance.

Contraindications & interactions

- **Absolute:** myasthenia gravis, heart block/cardiac conduction defects.
- **Caution:** significant renal impairment (reduce maintenance rate, monitor levels); concurrent **nifedipine** — the combination can cause profound hypotension and neuromuscular blockade from a synergistic effect; potentiates non-depolarising neuromuscular blocking agents and other CNS depressants.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Toxicity-monitoring algorithm for magnesium sulfate.

High-yield exam pointers

- Pritchard regimen (IM): 4 g IV + 10 g IM (5 g each buttock) load, then 5 g IM 4-hourly.
- Zuspan/Sibai regimen (IV): 4–6 g load over 15–20 min, then 1–2 g/hour infusion.

- Therapeutic range 4–7 mEq/L; reflex loss ~10 mEq/L; respiratory arrest ≥12 mEq/L.
- Antidote: calcium gluconate 1 g (10 mL 10%) IV slow.
- MAGPIE trial — 58% reduction in eclampsia; BEAM trial — fetal neuroprotection regimen (6 g/20–30 min load + 2 g/hr) before 32 weeks.
- Contraindicated in myasthenia gravis and heart block; caution with nifedipine (synergistic toxicity).

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Some contemporary protocols use a slightly modified continuous-IV-only regimen and no longer measure routine serum magnesium levels in normal-risk women (ACOG/RCOG); the Pritchard/Zuspan schedules above remain the standard reproducible answer.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Obstetrics 9e; ACOG/SMFM Committee Opinion No. 455 (reaffirmed 2020); MAGPIE Trial Collaborative Group (2002); Rouse et al., BEAM trial (2008); FDA Drug Safety Communication (2013).

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Respiratory changes during pregnancy

Asked in: Paper I 19-Nov-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Pregnancy produces mechanical (structural), physiological (volume/capacity) and biochemical (gas-exchange/acid-base) changes in the respiratory system, driven chiefly by **progesterone** acting on the central respiratory centre and by the mechanical effect of the enlarging uterus. The net result is a state of chronic, compensated **hyperventilation with mild respiratory alkalosis** that favours transplacental gas exchange.

Mechanical (anatomical) changes

Structure	Change in pregnancy
Diaphragm	Elevated by **4 cm**; excursion nevertheless **increases by 1–2 cm** — breathing becomes more diaphragmatic
Subcostal angle	Widens from **68° to 103°**
Transverse diameter of chest	Increases by **2 cm**
Chest circumference	Increases by **5–7 cm**

Structure	Change in pregnancy
Rib cage	Flares outward, compensating for diaphragmatic elevation so that total lung capacity falls only marginally
Nasopharyngeal mucosa	Becomes hyperaemic and oedematous (oestrogen effect) — causes nasal stuffiness, occasional epistaxis

Lung volumes and capacities (term vs non-pregnant)

Parameter	Non-pregnant	Term pregnancy	Change
Respiratory rate	15/min	15/min	Unchanged
Vital capacity	3200 mL	3300 mL	Almost unaltered
Tidal volume	500 mL	700 mL	**+ 30–40%**
Inspiratory capacity	2500 mL	2650 mL	+ 5–10%
Minute ventilation	7.5 L/min	10.5 L/min	**+ 30–40%**
Residual volume	965 mL	765 mL	– 20 to 25%
Functional residual capacity (ERV + RV)	—	1350 mL	**– 20%**
Total lung capacity	4200 mL	4000 mL	– 5%

- Lung **compliance is unaffected**; airway conductance increases and total pulmonary resistance falls, probably a progesterone effect.
- Peak expiratory flow rate rises progressively as gestation advances.
- The hyperventilation is achieved almost entirely by an **increase in tidal volume, not respiratory rate** — rate and vital capacity stay essentially unchanged.

Ventilation, gas exchange and acid–base changes

Parameter	Non-pregnant	Pregnancy (term)	Comment
$PaCO_2$	~ 38–40 mm Hg	**~ 28–32 mm Hg**	Falls due to maternal hyperventilation
PaO_2	~ 95 mm Hg	~ 105 mm Hg	Rises slightly
Arterial pH	7.40	~ 7.42–7.44	Mild rise (≈ 0.02 unit)
Plasma bicarbonate	26 mEq/L	~ 22 mEq/L	Renal compensation (partial) via increased bicarbonate excretion
Base excess	—	≈ – 2 mEq/L	Confirms compensated respiratory alkalosis

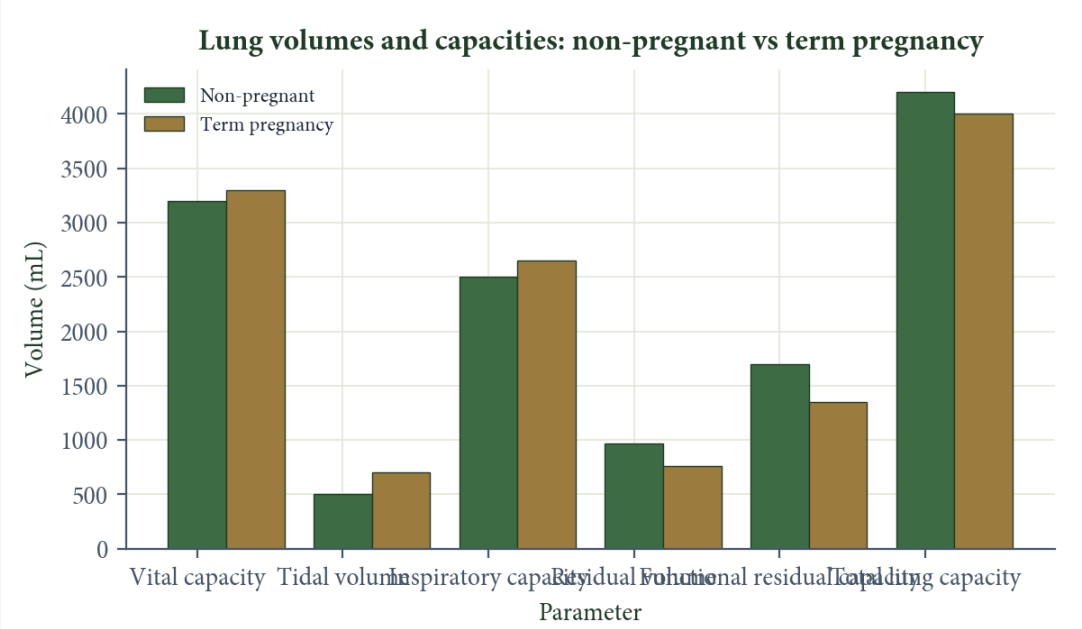
Parameter	Non-pregnant	Pregnancy (term)	Comment
Maternal O_2 consumption	Baseline	**+ 20–40%** (up to 40–60% in labour)	Meets fetal, placental and maternal metabolic demand

- **Mechanism:** progesterone acts centrally on the respiratory centre — it lowers the apnoeic threshold and raises chemoreceptor sensitivity to CO_2 (oestrogen contributes to a lesser extent). The resulting fall in $PaCO_2$ widens the CO_2 gradient from fetus to mother, aiding fetal CO_2 clearance.
- The small pH rise shifts the maternal oxygen-haemoglobin dissociation curve **left** (Bohr effect, ↑ affinity), but a compensatory rise in **2,3-diphosphoglycerate** shifts it back right — preserving oxygen release to the fetus.
- Because of this reset baseline, a $PaCO_2$ of 40 mm Hg in a pregnant woman already represents relative CO_2 retention, not a "normal" value.

Clinical significance

- **Physiological dyspnoea of pregnancy** — a subjective "air hunger" from the greater tidal volume and lowered $PaCO_2$; common (worse in the third trimester), does not restrict ordinary activity, and must be distinguished from pathological (cardiac/pulmonary) dyspnoea.
- **Reduced oxygen reserve** — a lower functional residual capacity combined with higher oxygen consumption means a pregnant woman desaturates much faster during apnoea; this mandates thorough **pre-oxygenation before induction of general anaesthesia/intubation**.
- **Airway oedema** — the hyperaemic, friable nasopharyngeal and laryngeal mucosa predisposes to traumatic, bleeding intubation; a **smaller-calibre endotracheal tube** is preferred.
- **Altered reference ranges** — "normal" arterial blood gas values are reset; failure to recognise a rising $PaCO_2$ towards the non-pregnant normal range (e.g., in asthma or pulmonary embolism) can mask impending respiratory failure.
- Reduced ventilatory reserve means pre-existing respiratory disease (asthma, pneumonia) tends to **decompensate faster** in pregnancy.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Tidal volume and inspiratory capacity rise modestly, residual volume and functional residual capacity fall (~20-25%), while vital capacity and total lung capacity remain almost unaltered.

High-yield exam pointers

- Tidal volume and minute ventilation both **rise 30–40%**; respiratory rate and vital capacity are **unchanged** — hyperventilation is rate-independent.
- Functional residual capacity falls **~20%**, but total lung capacity falls only **~5%** because the rib cage flares to offset diaphragmatic elevation of 4 cm.
- Gas values to reproduce verbatim: **$PaCO_2$ falls to ~30 mm Hg, PaO_2 rises to ~105 mm Hg, HCO_3^- falls to ~22 mEq/L** — a state of compensated respiratory alkalosis.
- Driver = **progesterone** (central respiratory centre stimulant, ↑CO_2 sensitivity); oestrogen contributes via mucosal hyperaemia.
- Maternal O_2 consumption rises **20–40%** at rest and **40–60%** in labour.
- Clinical hook: reduced FRC + increased O_2 consumption = rapid desaturation on apnoea → always pre-oxygenate before obstetric general anaesthesia.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Textbook figures vary slightly on the exact $PaCO_2$ (~30 mm Hg in Williams vs ~32 mm Hg in DC Dutta) because of different measurement cohorts; either figure is acceptable in the exam as both reflect the same compensated-respiratory-alkalosis pattern.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e.

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Role of Antiphospholipid Antibodies (APLA) on Pregnancy

Asked in: Paper I 26-May-2025 — RGUHS MS Obstetrics & Gynaecology

Definition — Antiphospholipid syndrome (APS) is an acquired autoimmune thrombophilia defined by persistently positive antiphospholipid antibodies (APLA) — **lupus anticoagulant (LAC)**, **anticardiolipin antibody (aCL)**, and **anti-β2-glycoprotein-I (anti-β2GP1)** — occurring together with vascular thrombosis or specific pregnancy morbidity, per the revised Sapporo (Sydney) classification criteria (*Miyakis* et al., 2006). It is **primary** (isolated) or **secondary** (with systemic lupus erythematosus [SLE] or another connective tissue disease); both forms impair placentation and are a treatable cause of recurrent pregnancy loss.

Diagnostic criteria (revised Sapporo/Sydney criteria, Miyakis 2006)

Category	Criteria
Clinical (≥1 required)	• ≥3 unexplained consecutive spontaneous miscarriages <10 weeks' gestation, or • ≥1 unexplained fetal death ≥10 weeks (morphologically normal fetus), or • ≥1 preterm birth ≤34 weeks due to severe pre-eclampsia/eclampsia or placental insufficiency, or • ≥1 episode of arterial, venous, or small-vessel thrombosis
Laboratory (≥1 required; positive on **two occasions ≥12 weeks apart**)	• Lupus anticoagulant (International Society on Thrombosis and Haemostasis method) • Medium/high-titre IgG or IgM anticardiolipin antibody • Anti-β2-glycoprotein-I IgG or IgM antibody >99th percentile

Diagnosis = **at least one clinical + one laboratory criterion**. Primary APS accounts for 3–5% of recurrent pregnancy loss (Speroff 9e). Testing for non-criteria antibodies (anti-annexin V, antiphosphatidylserine, etc.) is **not recommended** — it adds no diagnostic value (ACOG Practice Bulletin No. 132).

How APLA affect pregnancy — mechanisms

- **Direct antibody binding** to β2GP1, which is expressed in high concentration on the syncytiotrophoblast surface → inhibits trophoblast proliferation, invasion, syncytialisation, and hCG secretion.

- **Defective endovascular trophoblast invasion** of spiral arteries → failure of physiological (low-resistance) transformation → decidual vasculopathy with fibrinoid necrosis.
- **Thromboxane A2/prostacyclin imbalance** — APLA raise thromboxane A2 (vasoconstrictor, platelet-aggregant) and lower prostacyclin (vasodilator) from placental and vascular endothelium.
- **Reduced annexin V** — this natural anticoagulant "shield" is normally expressed on trophoblast and endothelium; its depletion removes protection against local thrombosis.
- **Complement activation** (C3, C5) at the maternal–fetal interface causes inflammatory tissue injury independent of thrombosis.
- **Net effect** — intervillous space and uteroplacental vessel thrombosis with placental infarction → chronic uteroplacental insufficiency → fetal hypoxia (DC Dutta's Obstetrics 9e).

Effects on pregnancy — obstetric complications

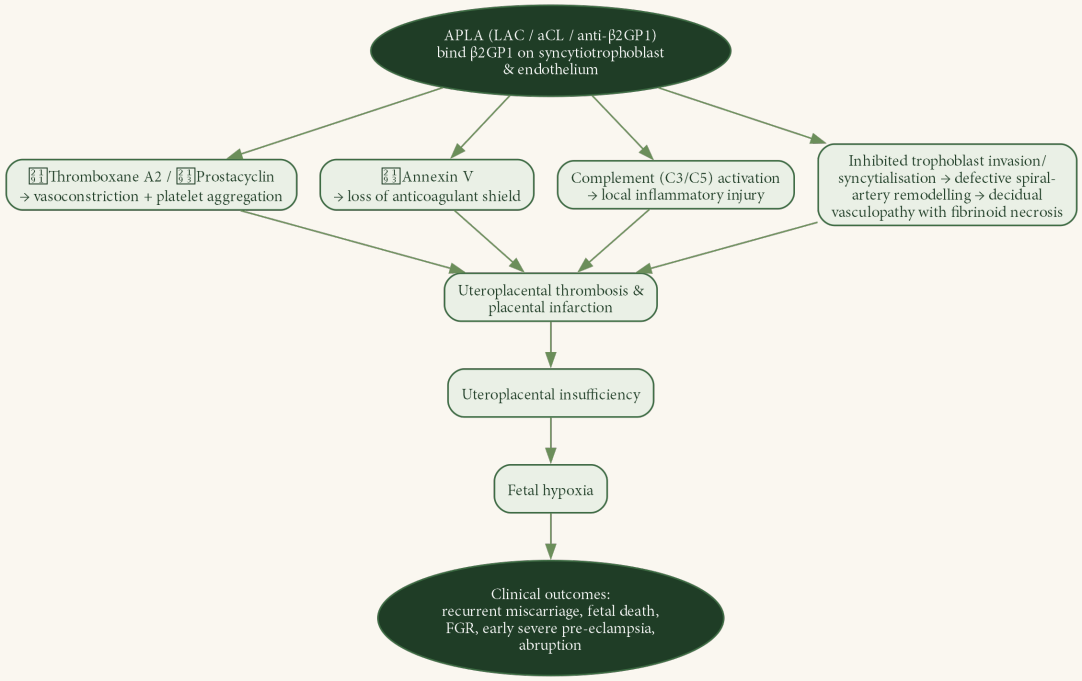
Complication	Basis
Recurrent pregnancy loss (<10 weeks)	Failed trophoblast invasion/implantation
Fetal death (≥10 weeks)	More characteristic of APS than of most other recurrent-loss causes
Early-onset severe pre-eclampsia/eclampsia, HELLP syndrome	Placental vascular insufficiency
Fetal growth restriction (FGR), oligohydramnios	Chronic uteroplacental insufficiency
Preterm birth	Usually iatrogenic, for placental insufficiency/severe pre-eclampsia
Placental abruption	Decidual vasculopathy with fibrinoid necrosis
Maternal arterial/venous thrombosis, thrombocytopenia, livedo reticularis	Systemic (non-obstetric) APS features
Catastrophic APS (CAPS/Asherson syndrome)	Simultaneous thrombosis of ≥3 organs within days; high mortality (cytokine storm)

Management in pregnancy

- **Pre-conception:** start low-dose aspirin (75–100 mg/day orally); continue throughout pregnancy.
- **Once pregnancy confirmed:** add heparin — unfractionated heparin (UFH) 5,000–10,000 units subcutaneously every 12 hours, or low-molecular-weight heparin (LMWH, e.g., enoxaparin 40 mg SC once daily) — continued through gestation; aspirin plus heparin is the most effective regimen and raises live-birth rates to >70%.
- **Prior thromboembolic event:** therapeutic-dose anticoagulation throughout pregnancy and continued for **6 weeks postpartum**.

- **Obstetric APS only (no prior thrombosis):** prophylactic/intermediate-dose heparin plus aspirin; postpartum anticoagulation is still advised.
- **Refractory disease / catastrophic APS:** full-dose anticoagulation, high-dose corticosteroids, plasma exchange and/or intravenous immunoglobulin (IVIG 0.4 g/kg/day for 5 days, or 1 g/kg monthly).
- **Secondary APS with active SLE:** corticosteroids treat the SLE flare, not the APS itself; corticosteroids are **not** used in primary APS.
- **Contraception:** avoid estrogen-containing contraceptives (thrombosis risk).
- **Surveillance:** serial fetal growth ultrasound with umbilical artery Doppler, and third-trimester antenatal testing (non-stress test/biophysical profile); watch closely for pre-eclampsia.
- **LMWH preference:** many centres prefer LMWH over UFH — fewer bleeding complications, lower risk of heparin-induced thrombocytopenia and osteopenia, longer half-life allowing once-daily dosing (Speroff 9e).
- **Adjuncts (refractory disease):** hydroxychloroquine may be added to low-dose aspirin — currently regarded as investigational (Williams 26e).

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Mechanism pathway: APLA binding drives four converging injury pathways to uteroplacental thrombosis, chronic insufficiency, fetal hypoxia, and the clinical outcomes of APS in pregnancy.

High-yield exam pointers

- Criteria = **revised Sapporo/Sydney criteria** (*Miyakis*, 2006; updated *Branch*, 2010) — 1 clinical + 1 laboratory criterion, laboratory test positive **twice, ≥12 weeks apart**.
- Three antibodies to name: **LAC, aCL, anti-β2GP1**.
- Standard regimen: **low-dose aspirin (75–100 mg/day) + heparin (UFH 5,000–10,000 IU SC every 12 h, or LMWH)** — write this exact combination.
- **Fetal death ≥10 weeks** is the pregnancy-loss pattern most typical of APS (unlike early loss in most other RPL causes).
- **CAPS/Asherson syndrome** = ≥3 organs thrombosed within days, high mortality — treat with full anticoagulation + high-dose steroids + plasma exchange/IVIG.
- Avoid estrogen-containing contraceptives; continue anticoagulation **6 weeks postpartum** if prior thrombosis.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Obstetrics 9e states an older aspirin dose of 50 mg/day; current standard practice (Williams 26e, Berek & Novak 16e, Speroff 9e, ACOG) uses 75–100 mg/day — follow the current higher dose.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; Berek & Novak's Gynecology 16e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; ACOG Practice Bulletin No. 132, "Antiphospholipid Syndrome" (December 2012, reaffirmed 2019).

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Role of hysteroscopy in gynaecology

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Hysteroscopy is direct endoscopic visualisation of the endocervical canal and endometrial cavity through a rigid or flexible telescope passed transcervically, with a distension medium separating the uterine walls to give a panoramic view. It serves a **diagnostic** role (identifying the cause of abnormal uterine bleeding, AUB, infertility or a Müllerian anomaly) and, via an operating sheath or resectoscope, a **therapeutic (operative)** role — correcting the same intracavitary pathology in the same sitting, often sparing the patient a laparotomy or hysterectomy.

Instrumentation and distension media

Medium	Type	Typical use	Key limit/complication
Carbon dioxide (CO2)	Gas	Diagnostic (office) hysteroscopy	Delivered by a purpose-built hysteroflator, flow ≤100 mL/min and pressure ≤100 mmHg — a standard laparoscopic insufflator's higher flow risks gas embolism

Medium	Type	Typical use	Key limit/complication
Normal saline	Isotonic liquid	Operative hysteroscopy with bipolar energy or mechanical (morcellator) resection	Not usable with monopolar current (conducts electricity); a larger volume can be absorbed safely — the current American Association of Gynecologic Laparoscopists (AAGL) practice guideline sets a safe ceiling of about 2.5 L in a healthy woman
Glycine 1.5% / sorbitol 3% / mannitol 5%	Hypo- or iso-osmolar, electrolyte-free liquid	Operative hysteroscopy with a monopolar resectoscope	Electrolyte-free — excess systemic absorption causes dilutional hyponatraemia and cerebral/pulmonary oedema; per the AAGL guideline, a fluid deficit **>1000 mL** mandates immediate serum electrolytes ± intravenous furosemide, and the procedure is **terminated at a deficit of 1500 mL**
Dextran 70	Hyperosmolar liquid	Rarely used now	Anaphylaxis, coagulopathy; volume must stay below 300 mL

An intrauterine pressure of 70–80 mmHg, kept below the mean arterial pressure, distends the cavity adequately while limiting extravasation; a sudden jump in the fluid deficit is often the first sign of uterine perforation.

Diagnostic role

- **Abnormal uterine bleeding** — menorrhagia, intermenstrual bleeding, postmenopausal bleeding: direct visualisation with a targeted biopsy is more accurate than a blind dilatation and curettage.
- **Infertility and recurrent pregnancy loss** — work-up of an abnormal hysterosalpingogram (filling defect, synechiae), submucous fibroid, endometrial polyp or Asherman syndrome.
- **Congenital Müllerian anomalies** — arcuate, septate and bicornuate uterus, uterus didelphys; combined with laparoscopy to distinguish a septate from a bicornuate uterus by the external fundal contour.

- **Misplaced intrauterine contraceptive device (IUCD)** with lost threads — localisation and removal.
- **Chronic pelvic pain** from an obstructive uterine anomaly or submucous fibroid, laparoscopy being added to exclude other pelvic pathology.
- **Suspected endometrial pathology on imaging** (thickened/irregular endometrium) — targeted biopsy for hyperplasia or carcinoma; diagnosis of endometrial haemangioma or arteriovenous malformation.
- **Second-look hysteroscopy** — confirms cavity restoration after synechiolysis for Asherman syndrome.

Therapeutic (operative) role

Procedure	Indication	Notes
Polypectomy / hysteroscopic myomectomy	Endometrial polyp; submucous leiomyoma	Resectoscope with a cutting loop; the European Society of Hysteroscopy grades a submucous myoma by its intramural extension — **G0** pedunculated, entirely intracavitary; **G1** endocavitary component >50%; **G2** endocavitary component <50% (deeper grades are technically harder and carry a higher perforation risk)
Synechiolysis	Asherman syndrome	Adhesions divided under direct vision; an intrauterine barrier/balloon and cyclical oestrogen therapy usually follow
Metroplasty	Septate uterus	Septum incised/resected under simultaneous laparoscopic or ultrasound guidance to avoid perforation
Transcervical resection of the endometrium (TCRE) or **laser/roller-ball ablation of the endometrium (LAE)**	Heavy menstrual bleeding refractory to medical therapy	Alternative to hysterectomy; endometrium (including the basal layer and spiral arterioles) is destroyed to a depth of 3–5 mm from cornu to cornu; endometrium is thinned pre-operatively with a gonadotropin-releasing hormone (GnRH) agonist or danazol for 4–6 weeks; 80–85% report a good symptomatic response

Procedure	Indication	Notes
Removal of a foreign body/retained IUCD	Lost threads	—
Tubal cannulation	Proximal tubal block (mucus plug/spasm) on hysterosalpingogram	A fine catheter is passed through the tubal ostium to the interstitial segment to relieve the obstruction
Hysteroscopic sterilisation	Permanent contraception	Interstitial tubal coagulation or a hysteroscopically placed micro-insert; now largely superseded by laparoscopic methods

Contraindications

Contraindication	Reason
Pelvic infection	The distension medium reflexes through the tubes and can disseminate infection into the peritoneal cavity
Pregnancy	Exception — IUCD removal when the threads are missing
Invasive cervical carcinoma	A friable cervix traumatises and bleeds easily; risk of tumour dissemination
Profuse active uterine bleeding	Obscures the view
Significant cardiopulmonary disease	Poor tolerance of anaesthesia and of the gas embolism/fluid-overload risk intrinsic to hysteroscopy

Cervical stenosis is only a relative contraindication — pre-operative prostaglandin E2 gel softens the cervix and eases dilatation.

Complications

Timing/type	Complication
Distension-medium-related	Fluid overload, pulmonary/cerebral oedema, dilutional hyponatraemia (electrolyte-free media), CO2 gas embolism
Mechanical	Cervical laceration; uterine perforation, occasionally with injury to bowel, bladder or major vessels
Energy-related	Thermal injury to adjacent viscera from monopolar/bipolar current or laser

Timing/type	Complication
Haemorrhage	Intra- or post-operative, especially after myomectomy or septal resection
Infection	Endometritis, rarely pelvic sepsis
Anaesthesia-related	As for any general/regional anaesthetic used for operative procedures
Late	Recurrence of bleeding after incomplete TCRE/LAE; haematometra or pyometra from cervical stenosis after ablation near the internal os; rare pregnancy following TCRE

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 54.29A — Diagrammatic view of a hysteroscope inside the uterine cavity (Jeffcoate's Principles of Gynaecology 9e, p.927)*

High-yield exam pointers

- Diagnostic medium = **CO2** (flow ≤100 mL/min, pressure ≤100 mmHg); operative monopolar = **glycine/sorbitol/mannitol** (electrolyte-free); operative bipolar/mechanical = **normal saline**.
- AAGL fluid-deficit thresholds: electrolyte-free medium — check electrolytes/consider furosemide at **>1000 mL**, terminate at **1500 mL**; normal saline — safe ceiling ~**2500 mL** in a healthy woman.
- **TCRE/LAE**: endometrium destroyed to **3–5 mm** depth, pre-treated with a GnRH agonist/danazol for **4–6 weeks**; 80–85% good response.
- European Society of Hysteroscopy grades submucous myoma **G0/G1/G2** by intracavitary/intramural proportion — guides resectability and perforation risk.
- Absolute contraindications to remember: **pelvic infection, pregnancy (except lost-thread IUCD removal), invasive cervical cancer**.
- A sudden rise in fluid deficit intra-operatively = first clue to **uterine perforation**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Older editions of DC Dutta's Gynaecology quote a lower glycine-specific deficit-alarm figure (500 mL); the thresholds used above follow the current AAGL (American Association of Gynecologic Laparoscopists) practice guideline on hysteroscopic distending media, which is the standard in active clinical use.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (Ch. 36 — Endoscopic Surgery in Gynecology); Berek & Novak's Gynecology 16e (Ch. 26 — Hysteroscopy, distending media and complications); Jeffcoate's Principles of Gynaecology 9e; AAGL practice guideline for the management of hysteroscopic distending media (Munro MG et al.).

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Supports of the uterus

Asked in: Paper I 15-Nov-2022 · Paper I 19-Nov-2020 (2×) — RGUHS MS Obstetrics & Gynaecology

Definition — The uterus normally lies anteverted and anteflexed between the bladder and rectum, with the external os at the level of the **ischial spines**. It is held in this position by ligamentous, fascial and muscular structures classically grouped into an **upper, middle and inferior tier** (DC Dutta); the same anatomy is described by *DeLancey (1992)* as **three levels of vaginal support**, which is now the standard framework.

Three-tier classification of uterine supports

Tier	DeLancey level	Structures	Action
Upper tier	— (positional)	Endopelvic fascia over the uterus; **round ligaments**; **broad ligaments** with intervening cellular tissue	Maintain **anteversion** only — act as a "guy rope"; **do not** prevent descent
Middle tier	**Level I**	Pericervical ring + **cardinal (Mackenrodt's/transverse cervical) ligament**, **uterosacral ligament**, **pubocervical ligament/fascia**	**Strongest support** — suspends the cervix and upper vagina at the interspinous level; prevents descent
Inferior tier	**Level II & III**	**Levator ani** (pubovaginalis, puborectalis), endopelvic fascia, **levator plate**, **perineal body**, urogenital diaphragm	**Indirect support** — guards the hiatus urogenitalis, resists rise in intra-abdominal pressure

Upper-tier structures (detail)

Structure	Course	Function
Round ligament	Arises from the uterine cornu (in front of the fallopian tube) → runs forward in the broad ligament → traverses the deep inguinal ring, inguinal canal, superficial inguinal ring → ends in the labium majus	Pulls the fundus forward, maintaining **anteversion**; hypertrophies in pregnancy (round-ligament pain)
Broad ligament	Double fold of peritoneum from the lateral uterine border to the lateral pelvic wall; encloses the fallopian tube, round ligament, ovarian ligament, uterine vessels and the ureter at its base (parametrium)	Steadying "guy rope" effect only; not truly a ligament and contributes **no** resistance to descent

Middle-tier ligaments — the strongest support (detail)

Ligament	Origin	Insertion	Contents	Function
Cardinal (Mackenrodt's/transverse cervical) ligament	Parietal fascia over **obturator internus** (lateral pelvic wall)	Fans out into the lateral supravaginal cervix and upper vagina; continuous with the pericervical ring	Uterine artery and vein, uterovaginal (uterosacral) nerve plexus, smooth muscle; **ureter passes beneath the uterine artery** within its upper part	Lateral stabilisation of the cervix at the level of the ischial spines; primary vascular conduit to uterus/vagina
Uterosacral ligament	Periosteum over **sacral vertebrae S2–S4**	Posterolateral cervix at the level of the internal os; blends with the pericervical ring	Autonomic (uterosacral) nerve plexus, smooth muscle, minimal vessels	Primary proximal suspensory ligament — holds the cervix posteriorly at the ischial spines, keeps the uterus anteflexed, suspends the vagina over the levator plate

Ligament	Origin	Insertion	Contents	Function
Pubocervical ligament/fascia (bladder pillar)	Back of the pubic bone and arcus tendineus fasciae pelvis	Anterolateral supravaginal cervix; blends with the pericervical ring and cardinal ligament	Vessels of the bladder pillar	Supports the bladder base and anterior vaginal wall
Pericervical ring	—	Collar of fibroelastic tissue encircling the cervicovaginal junction; anchors all three ligaments above (anteriorly to pubocervical, laterally to cardinal, posteriorly to uterosacral/rectovaginal septum)	—	Stabilises the cervix at the interspinous diameter

DeLancey's levels of vaginal support and correlation with prolapse

Level	Vaginal site	Structures	Defect if lost
I (upper)	Vaginal apex	Cardinal–uterosacral ligament complex	Uterovaginal prolapse, enterocele, vault prolapse
II (middle)	Mid-vagina	Pubocervical and rectovaginal fascia attached laterally to the **arcus tendineus fasciae pelvis**	Paravaginal/pararectal defects → cystocele, rectocele
III (lower)	Distal vagina	Urogenital diaphragm, perineal muscles, perineal body, levator plate	Urinary incontinence, perineal deficiency

The round and broad ligaments (upper tier) merely steady the fundus; clinically significant weakness for **pelvic organ prolapse** occurs when the middle-tier ligaments (Level I) and/or the levator ani–perineal body complex (Levels II–III) are damaged, most often by vaginal childbirth, chronic straining, or menopausal atrophy.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 16.6 — Ligamentous supports of uterus: pericervical ring with cardinal (transverse cervical), uterosacral and pubocervical ligaments (DC Dutta's Gynaecology 7e, p.187)*

Also sketch a mid-sagittal section of the pelvis showing the three tiers stacked vertically — uterus/round-broad ligaments above, the cardinal–uterosacral hammock at the cervix, and the levator ani/perineal body forming the pelvic floor below — to show how each tier acts at a different level.

High-yield exam pointers

- **3 tiers (Dutta) = 3 levels (DeLancey, 1992)**: Upper/positional → Middle (Level I, strongest) → Inferior (Levels II–III).
- Mnemonic for the middle-tier trio meeting at the **pericervical ring**: Mackenrodt's (cardinal), Uterosacral, Pubocervical — "**MUP**".
- Round + broad ligaments = "**guy ropes**" — maintain anteversion only, **no role in preventing prolapse**.
- Uterosacral ligament origin = **sacral vertebrae S2–S4**; cardinal ligament origin = fascia over **obturator internus**.
- Surgical pearl: the **ureter runs beneath the uterine artery inside the cardinal ligament** ("water under the bridge") — the classic site of ureteric injury during hysterectomy clamping.
- External os at the level of the **ischial spines** = the anatomical reference point for assessing uterine descent.
- Loss of middle + inferior tier support → **uterovaginal (pelvic organ) prolapse**.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DeLancey's three-level classification of vaginal support (1992) is superimposed on the older Dutta three-tier description of the same structures; RGUHS examiners accept either framework, and both should be quoted together for full marks.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (pp.17–18, 165–167); Berek & Novak's Gynecology 16e (DeLancey levels of support, pp.211–212); Williams Obstetrics 26e (cardinal/uterosacral ligament anatomy, cross-checked).

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Surfactants

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Pulmonary surfactant is a surface-active lipoprotein complex synthesised and secreted by type II alveolar pneumocytes that lowers surface tension at the alveolar air-liquid interface, preventing end-expiratory alveolar collapse and permitting lung expansion after birth. Its appearance in amniotic fluid in adequate amount is the biochemical marker of fetal lung maturity.

Site of Synthesis & Composition

Component	Approximate share	Remarks
Type II pneumocytes	—	Site of synthesis; characterised by lamellar bodies (multivesicular storage/assembly organelles) that release surfactant into alveolar fluid during fetal breathing movements
Phospholipids	~80–90% of dry weight	Principal surface-tension-lowering fraction
— Phosphatidylcholine (lecithin)	~70–80% of phospholipid	Principal active component is **dipalmitoyl phosphatidylcholine (DPPC)**
— Phosphatidylglycerol (PG)	~8–15%	Appears late (marker of full biochemical maturity); role less critical — infants without PG can still do well
— Phosphatidylinositol (PI)	minor	Predominant early in gestation, falls as PG rises
Surfactant proteins	~8–10%	**SP-A** (glycoprotein, 28,000–35,000 Da; gene on chromosome 10 as SP-A1/SP-A2) and **SP-D** are hydrophilic collectins with host-defence/immune roles; **SP-B** and **SP-C** are small hydrophobic proteins essential for surface-film spreading and re-forming
Neutral lipids	~8%	Structural, minor surface activity

Development of the Surfactant System

- **Pseudoglandular stage (5–17 weeks):** intrasegmental bronchial tree forms; no gas exchange units.
- **Canalicular stage (16–25 weeks):** respiratory bronchioles and terminal sacs appear; capillary network develops.

- **Terminal saccular stage (25 weeks–term):** type II pneumocytes differentiate and begin surfactant production.
- **Alveolar stage (36 weeks onward, continues to ~8 years postnatally):** true alveoli form; surfactant output rises sharply from ~34–35 weeks (biochemical maturity), well after anatomical maturity.

Tests of Fetal Lung Maturity

Test	Principle	Maturity cut-off
Lecithin/sphingomyelin (L/S) ratio (Gluck)	Lecithin rises while sphingomyelin stays constant with gestation	L/S = 1 at 31–32 weeks; **L/S ≥ 2 indicates pulmonary maturity**
Shake/bubble test (Clements)	Surfactant forms a stable foam with ethanol on shaking	Stable bubbles at the meniscus for ≥15 minutes = mature
Foam stability index (FSI)	Quantifies shake-test foam using serial dilutions	**FSI > 47 virtually excludes risk of RDS**
Fluorescence polarisation	Automated ratio of surfactant to albumin in amniotic fluid	≥55 mg surfactant/g albumin = mature
Lamellar body count	Lamellar bodies (surfactant storage form) counted on a haematology analyser (particle size ≈ platelets)	Count > 30,000/μL = mature
Presence of phosphatidylglycerol	PG is the last phospholipid to appear	Presence confirms full maturity even if L/S is borderline

Factors Modulating Surfactant Production

Stimulate (accelerate maturation)	Inhibit/delay maturation
Glucocorticoids (endogenous cortisol surge and exogenous antenatal steroids)	Maternal diabetes mellitus/fetal hyperinsulinaemia — relative deficiency of PG and surfactant even at term
Thyroid hormone and thyrotropin-releasing hormone (TRH)	Rh isoimmunisation with fetal hydrops
Prolactin	Elective caesarean delivery without labour (no catecholamine/cortisol surge) — risk of transient tachypnoea of the newborn
Cyclic adenosine monophosphate (cAMP) and epidermal growth factor	Second (male) twin, male sex in general
Stress states — preterm labour, prolonged rupture of membranes	—

Physiological & Clinical Significance

- **Function:** reduces alveolar surface tension (Laplace's law), preventing alveolar collapse at end-expiration, maintaining functional residual capacity, reducing the work of breathing, and stabilising alveoli of differing radii against each other.
- **Deficiency state:** inadequate surfactant is the primary cause of **neonatal respiratory distress syndrome (RDS)/hyaline membrane disease**, whose incidence falls steeply with advancing gestation (from ~75% at 28 weeks to ~52% at 30 weeks).
- **Antenatal corticosteroids** — accelerate fetal surfactant synthesis when given to the mother before anticipated preterm birth:

Drug	Regimen
Betamethasone	12 mg intramuscularly, 2 doses, 24 hours apart
Dexamethasone	6 mg intramuscularly, 4 doses, 12 hours apart

  - Recommended for a single course between **$23^{0}/_{7}$ and 34 weeks** of gestation with threatened preterm birth (American College of Obstetricians and Gynecologists, 2020); a single course is also advised for **$34^{0}/_{7}$–$36^{6}/_{7}$ weeks** (late-preterm) if not already given.
  - Effect begins ~24 hours after the first dose and lasts about 7 days; reduces RDS, and also lowers periventricular/intraventricular haemorrhage and necrotising enterocolitis.
  - A first dose is given regardless of the likelihood of completing the full course, since even a partial course improves outcome.
- **Exogenous surfactant replacement therapy** (neonatal, not maternal): natural preparations — beractant (bovine, Survanta) or poractant alfa (porcine) — are preferred over synthetic agents; given prophylactically within 15 minutes of birth in very preterm infants or as rescue therapy within 2 hours of onset of RDS, instilled intratracheally. Typical beractant dose: **100 mg phospholipid/kg (4 mL/kg) body weight**, using the "Intubate-Surfactant-Extubate to CPAP" technique where feasible. Reduces neonatal mortality and pulmonary morbidity; pulmonary haemorrhage is a recognised complication.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 33.1 — Composition of pulmonary surfactant (DC Dutta's Obstetrics 9e, p.466)*

High-yield exam pointers

- DPPC (dipalmitoyl phosphatidylcholine) = principal surface-tension-lowering component of surfactant.
- L/S ratio ≥2 = pulmonary maturity; L/S = 1 at 31–32 weeks.
- FSI > 47 virtually excludes RDS; lamellar body count > 30,000/μL = mature.

- Betamethasone 12 mg IM × 2 doses (24 h apart); Dexamethasone 6 mg IM × 4 doses (12 h apart) — window $23^0/^7$–34 weeks (ACOG 2020).
- Type II pneumocytes → lamellar bodies → surfactant; SP-A gene on chromosome 10.
- Maternal diabetes and elective caesarean without labour delay/impair surfactant-mediated lung adaptation.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Textbooks round surfactant's lipid:protein split slightly differently (DC Dutta: ~84% phospholipid + 8% neutral lipid + 8% protein; Williams: ~90% lipid + 10% protein) — the underlying composition (phospholipid-dominant, DPPC as principal agent) is identical across sources.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; American College of Obstetricians and Gynecologists (ACOG) Committee Opinion on antenatal corticosteroid therapy (2020a).

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Tocolytic agents

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — Tocolytics are drugs that suppress uterine contractions in threatened or established **preterm labour** to delay delivery, classically for **48 hours**. This window is used to complete a course of antenatal corticosteroids for fetal lung maturation and to arrange in-utero transfer to a centre with a **neonatal intensive care unit (NICU)**. No tocolytic cures the underlying cause of preterm labour, and none has been shown to directly improve perinatal outcome — the benefit is entirely from the time bought for corticosteroids and transfer.

Indications and contraindications

- **Indications:** regular, painful uterine contractions (≥4 in 20 minutes) with objective cervical change, between the limit of viability (~24 weeks) and 34 weeks of gestation, with intact membranes and a reassuring fetal status, to allow completion of corticosteroids ± in-utero transfer.

Contraindication group	Specific conditions
Maternal	Uncontrolled diabetes, thyrotoxicosis, severe hypertension/pre-eclampsia with severe features, cardiac disease, antepartum haemorrhage (placenta praevia/abruption)
Fetal	Non-reassuring fetal status/fetal distress, intrauterine fetal death, lethal congenital malformation, gestation beyond 34 weeks
Others	Ruptured membranes, chorioamnionitis/intrauterine infection, cervical dilatation >4 cm

Classification and mechanism of action

Class	Agents	Mechanism
Calcium-channel blockers	Nifedipine, nicardipine	Block voltage-gated calcium channels, ↓ calcium influx into myometrial cells, ↓ myosin light-chain kinase (MLCK) activation
Magnesium sulfate (MgSO4)	—	Competes with calcium at the motor end-plate; ↓ acetylcholine release and calcium influx; direct myometrial depressant
Prostaglandin synthetase (cyclo-oxygenase) inhibitors	Indomethacin, sulindac	↓ prostaglandin synthesis → ↓ intracellular free calcium and MLCK activation
β2-adrenergic agonists (betamimetics)	Ritodrine, terbutaline, isoxsuprine	Stimulate β2-receptors → ↑ adenylate cyclase/cAMP/protein kinase A → ↓ intracellular free calcium, inhibits MLCK → smooth-muscle relaxation
Oxytocin receptor antagonists	Atosiban	Competitively blocks myometrial oxytocin receptors, ↓ intracellular calcium release and prostaglandin release
Nitric oxide donors	Glyceryl trinitrate (GTN)	Smooth-muscle relaxation via nitric oxide/cGMP pathway

Individual agents — dose, efficacy and side effects

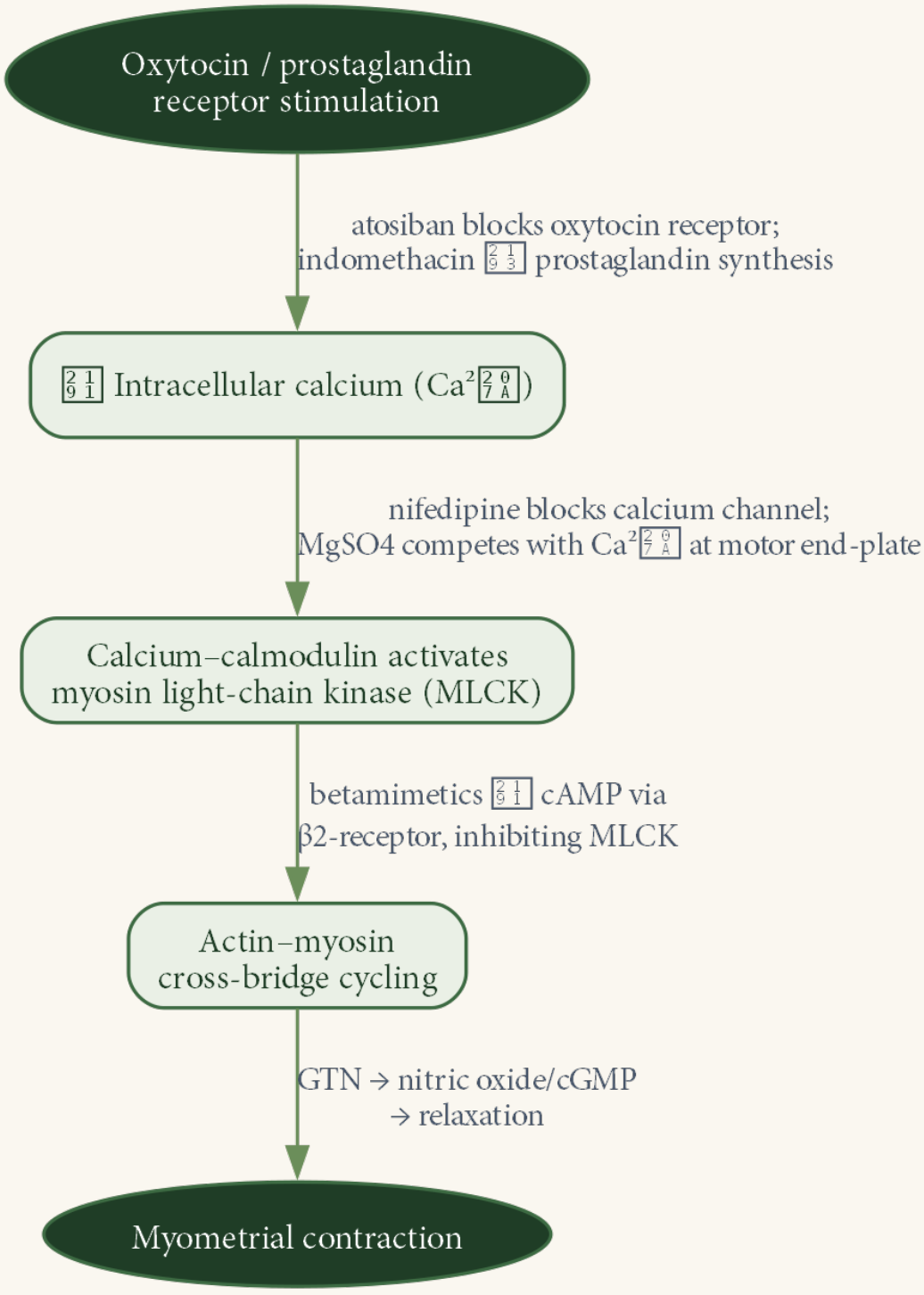
Agent	Dose/regimen	Key side effects and precautions
Nifedipine	Oral (never sublingual): loading 20 mg, may repeat 20 mg after 30 minutes if contractions persist; maintenance 10–20 mg every 4–6 hours, usually limited to 48 hours	Maternal hypotension, headache, flushing, tachycardia; **combination with MgSO4 or betamimetics should be avoided** (risk of synergistic neuromuscular blockade — reversible with IV calcium gluconate)
Magnesium sulfate	Loading 4–6 g IV (10–20% solution) over 20–30 minutes, then infusion 1–2 g/hour, continued until 12 hours after contractions stop	Flushing, sweating, headache, muscle weakness; rarely respiratory depression/cardiac arrest in neonate. Contraindicated in myasthenia gravis, impaired renal function. **Tocolytic efficacy is poor**; current evidence (ACOG, Cochrane) finds it ineffective for arresting labour — its proven obstetric role is **fetal neuroprotection <32 weeks**, not tocolysis
Indomethacin	Loading 50 mg orally/per rectum, then 25 mg every 6 hours, limited to 48 hours	Maternal GI bleeding, platelet dysfunction; fetal ductal constriction, oligohydramnios, neonatal pulmonary hypertension, necrotising enterocolitis — avoid beyond 32 weeks or with oligohydramnios
Terbutaline	0.25 mg subcutaneously every 3–4 hours (acute use); the same 0.25-mg SC dose is used for acute tachysystole	Maternal tachycardia, palpitation, pulmonary oedema, hyperglycaemia; fetal tachycardia. US FDA (2011) boxed warning against prolonged/outpatient use
Ritodrine	IV infusion 50 µg/min, increased by 50 µg every 10 minutes until contractions cease, continued ~12 hours after cessation	Same class effects as terbutaline; voluntarily withdrawn from the US market (2003)
Atosiban	IV bolus, then loading infusion (~300 µg/min) for 3 hours, followed by a lower-dose infusion, to a maximum of 48 hours (per RCOG Green-top Guideline No. 1b)	Well tolerated (nausea, rarely chest pain); **not FDA-approved** in the USA but used in Europe/RCOG practice

Agent	Dose/regimen	Key side effects and precautions
GTN (nitric oxide donor)	Transdermal patch or IV infusion	Headache, maternal hypotension; may also ripen the cervix

Choice of agent and monitoring

- **First-line agents** (ACOG Practice Bulletin No. 234, 2021): calcium-channel blockers (nifedipine) or prostaglandin inhibitors (indomethacin, <32 weeks) — better maternal safety profile than betamimetics.
- **Betamimetics and magnesium sulfate** are alternatives but carry more maternal side effects; maintenance tocolytic therapy beyond the initial 48 hours is **not effective** and is not recommended.
- **Monitoring during therapy:** maternal pulse, blood pressure and fluid balance (pulmonary oedema risk with betamimetics/MgSO4); deep tendon reflexes, respiratory rate and urine output with MgSO4; continuous fetal heart rate monitoring; serial amniotic fluid volume with indomethacin.
- **Never combine nifedipine with magnesium sulfate** — synergistic calcium-channel blockade can cause severe neuromuscular weakness and cardiorespiratory depression.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Common final pathway of myometrial contraction, showing where each tocolytic class intervenes.

High-yield exam pointers

- **48 hours** is the number to write everywhere — the sole proven benefit of tocolysis is buying time for corticosteroids ± transfer, not improving neonatal outcome directly.
- **Never combine nifedipine + MgSO4** — synergistic neuromuscular blockade; antidote is IV calcium gluconate.
- **Indomethacin** — avoid beyond 32 weeks (oligohydramnios, ductal constriction); limit to 48 hours.
- **Terbutaline** carries a US FDA boxed warning against prolonged or outpatient use.
- **Atosiban** — not FDA-approved in the USA; used per RCOG in Europe.
- **Ritodrine** is the only agent historically FDA-approved for tocolysis, but voluntarily withdrawn from the US market in 2003.
- **Maintenance tocolysis beyond 48 hours has no proven benefit** — do not prolong therapy.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Magnesium sulfate is listed among tocolytics for completeness, but current evidence (ACOG, Cochrane) shows poor efficacy for arresting preterm labour — its established obstetric role today is fetal neuroprotection below 32 weeks, using the same loading/maintenance regimen as for pre-eclampsia seizure prophylaxis.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Obstetrics 9e; Williams Obstetrics 26e; ACOG Practice Bulletin No. 234 (2021), "Prediction and Prevention of Spontaneous Preterm Birth"; RCOG Green-top Guideline No. 1b (Tocolysis for Women in Preterm Labour).

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Toxoplasmosis

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Toxoplasmosis is a zoonotic infection caused by *Toxoplasma gondii*, an obligate intracellular protozoan parasite with the cat as its definitive host. It is one of the classic **TORCH group** of infections because primary (acute) maternal infection during pregnancy can cross the placenta and cause **congenital toxoplasmosis**, a fetopathy of ocular and intracranial lesions with growth delay.

Aetiology, life cycle & transmission

Route	Mechanism
Foodborne	Eating raw or undercooked meat containing tissue cysts (bradyzoites)

Route	Mechanism
Environmental (oocyst)	Ingesting soil, water, or unwashed fruits/vegetables contaminated with sporulated oocysts shed in cat faeces
Transplacental (vertical)	Rapidly dividing **tachyzoites** cross the placenta during maternal parasitaemia of *acute* infection
Rare	Blood transfusion, organ transplantation, laboratory accident

- **Definitive host** — the cat; the feline (sexual) stage of the parasite occurs in the cat gut, and unsporulated oocysts are excreted in faeces.
- **Intermediate host** — humans and other mammals; ingested tissue cysts/oocysts release bradyzoites, which invade small-intestinal epithelium and transform into tachyzoites (the invasive, acute stage that crosses the placenta).
- Humoral and cell-mediated immunity clears most tachyzoites, but **tissue cysts persist lifelong** — the chronic/latent form of infection.
- The fetus is at risk **only** when a seronegative mother acquires *primary* infection during pregnancy; prepregnancy infection confers immunity and (in immunocompetent women) eliminates vertical-transmission risk. In immunocompromised women, reactivation can occur and may be severe (encephalitis, chorioretinitis).

Maternal and fetal infection

- **Maternal infection** is usually **subclinical**, detected only on serological screening; a minority have a flu-like illness with cervical lymphadenopathy and low-grade fever.
- **Vertical-transmission risk rises, but severity of fetal damage falls, with advancing gestational age at maternal infection** — the classic inverse relationship tested in exams:

Gestational age at maternal infection	Risk of vertical transmission (SYROCO Study Group, 2007)	Risk/severity of fetal damage if infected
~13 weeks (1st trimester)	~15%	Highest — severe, often clinically obvious disease
~26 weeks (2nd trimester)	~44%	Intermediate
~36 weeks (3rd trimester)	~71%	Lowest — near 0% at term, usually subclinical at birth

- **Congenital toxoplasmosis — classic triad:** chorioretinitis + intracranial (cerebral) calcification + hydrocephalus, often with convulsions.
- Other features: microcephaly, hepatosplenomegaly, jaundice, anaemia, low birth weight, fetal growth restriction (FGR), ascites, seizures, and later learning disability/mental retardation.

- Most congenitally infected neonates are born **without obvious stigmata** but remain at risk of late sequelae (chorioretinitis, learning disability) if untreated.

Screening & diagnosis

Test	Finding/purpose
IgG/IgM serology (ELISA)	Screening; IgM appears by ~10 days, peaks at 1–2 months, but may persist for years — **IgM alone is not used to diagnose acute infection**
IgG avidity test	High-avidity IgG excludes infection acquired in the preceding 3–5 months; used to time infection when IgM is positive
Toxoplasma Serologic Profile (reference laboratory)	Resolves equivocal acute-vs-chronic serology
Ultrasonography (serial, 20–22 weeks)	Ventriculomegaly, intracranial/hepatic calcification, microcephaly, hepatosplenomegaly, ascites, placental thickening, hyperechoic bowel, FGR — findings overlap with congenital cytomegalovirus
Amniocentesis with PCR for *T. gondii* DNA	Confirms **fetal** infection when maternal acute infection is confirmed or sonography is suggestive; sensitivity is lowest before 18 weeks' gestation, so testing is deferred to/after 18 weeks
Cordocentesis (fetal IgM)	Historic adjunct test, largely superseded by amniotic-fluid PCR

- The American College of Obstetricians and Gynecologists (ACOG, 2020) does **not** recommend routine universal prenatal screening for toxoplasmosis in low-prevalence settings; screening is targeted to immunocompromised women or when ultrasound findings are suggestive.

Management

Regimen	Dose	Indication/timing
Spiramycin	3 g/day orally (in divided doses)	Acute maternal infection **before 18 weeks**/before fetal infection is confirmed — reduces the risk of vertical transmission. Spiramycin **does not cross the placenta**, so it cannot treat an already-infected fetus

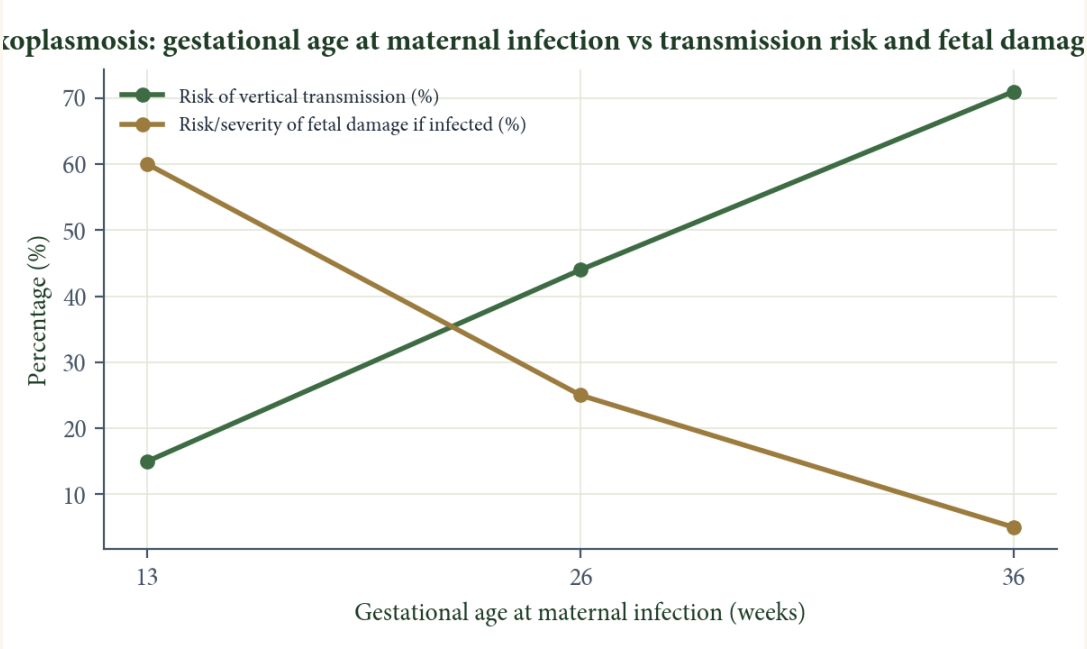
Regimen	Dose	Indication/timing
Pyrimethamine + Sulfadiazine + Folinic acid (leucovorin)	Pyrimethamine 25 mg orally daily + Sulfadiazine 1 g orally four times a day, with folinic acid added to offset bone-marrow toxicity; a 4–6-week course is usual	Maternal infection confirmed **after 18 weeks**' gestation, or **confirmed/suspected fetal infection**. **Pyrimethamine is avoided in the first trimester** — it is a folate antagonist and teratogenic

- The two regimens may be used sequentially (spiramycin until fetal infection is excluded/confirmed, then switching if infection is confirmed).
- Treatment reduces the risk of serious neurological sequelae and neonatal demise, though evidence that early treatment reduces the transmission rate itself is weaker (SYROCO Study Group, 2007).
- Extended courses are needed in immunocompromised patients.
- If the fetus is infected and hydrocephalus is already present, counselling regarding termination of pregnancy is offered.

Prevention

- Cook meat to safe internal temperatures; avoid raw or undercooked meat.
- Wash or peel fruits and vegetables thoroughly.
- Clean all food-preparation surfaces and utensils that contact raw meat.
- Wear gloves when gardening or handling soil.
- Avoid changing cat litter during pregnancy; if unavoidable, wear gloves, change the litter box daily, and wash hands afterward.
- Keep cats indoors and avoid feeding them raw/undercooked meat.
- **No vaccine is currently available.**

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



SYROCO Study Group (2007, as cited in Williams Obstetrics 26e): transmission risk rises with gestational age (15% at 13 weeks, 44% at 26 weeks, 71% at 36 weeks) while severity of fetal damage falls (~60% in the first trimester to near 0% at term) — the classic inverse relationship.

Classic inverse relationship: transmission risk rises with gestational age while damage severity falls.

High-yield exam pointers

- TORCH organism: *Toxoplasma gondii* (obligate intracellular protozoan); cat = definitive host.
- Risk paradox: transmission risk **rises** with gestational age (15% → 44% → 71% at 13/26/36 weeks) but severity of damage **falls** with gestational age (~60% → ~0%).
- Classic congenital triad: **chorioretinitis + intracranial calcification + hydrocephalus** (± convulsions).
- Drug rule: **Spiramycin 3 g/day** (does NOT cross placenta) before 18 weeks to cut transmission; **pyrimethamine 25 mg/day + sulfadiazine 1 g QID + folinic acid**, 4–6 weeks, after 18 weeks or if fetal infection confirmed; pyrimethamine contraindicated in the first trimester (antifolate/teratogenic).
- IgM alone is unreliable (persists for years) — use IgG avidity testing; amniotic-fluid PCR confirms fetal infection (best after 18 weeks).
- ACOG (2020): no routine universal antenatal screening in low-prevalence areas.
- Prevention: cook meat, wash produce, avoid cat litter/wear gloves; no vaccine exists.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's traditional trimester-wise figures (15%/30%/60%) are a rounded teaching approximation of the same relationship; the gestational-age-specific data above (SYROCO Study Group, 2007, cited in Williams Obstetrics 26e) are the currently cited, more precise figures.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin — Cytomegalovirus, Parvovirus B19, and Toxoplasmosis in Pregnancy (2020); SYROCO Study Group, *Lancet* 2007 (as cited in Williams Obstetrics 26e).

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Transformation zone

Asked in: Paper I May 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — The transformation zone (TZ) of the cervix is the dynamic area between the **original squamocolumnar junction (SCJ)** (present since fetal life) and the **new, physiologically active SCJ** (the current meeting point of columnar and squamous epithelium), within which endocervical columnar epithelium has undergone **squamous metaplasia**. It is the site where almost all cervical intraepithelial neoplasia (CIN) and squamous cell carcinoma originate.

Formation and boundaries

Boundary/landmark	Description
Original SCJ	The squamocolumnar junction present at birth, where native (original) squamous epithelium of the ectocervix meets columnar epithelium; marks the **outer/distal limit** of the transformation zone
New (active) SCJ	The current, physiologically active squamocolumnar junction after metaplasia has advanced inward; marks the **inner/proximal limit** of the transformation zone, closer to the external os
Markers of the original SCJ	**Nabothian cysts** (mucus-retention cysts formed when metaplastic squamous epithelium seals a gland crypt) and **gland/crypt openings** — the only way to identify where the original SCJ once lay

Boundary/landmark	Description
Columnar epithelium	Single layer of mucus-secreting columnar cells with clefts/villi, lining the endocervical canal proximal to the new SCJ

- The **squamocolumnar junction is not fixed** — it moves with life stage and hormonal status (puberty, reproductive years, pregnancy, menopause), so the size and position of the transformation zone changes throughout a woman's life.
- In the **neonate and prepubertal girl**, the SCJ lies on the exocervix (maternal estrogen effect in utero causes eversion). It moves outward (**ectopy/eversion**) again at **puberty and during pregnancy** under high estrogen, and recedes **into the endocervical canal after menopause** as estrogen falls, making the TZ progressively harder to visualise with age.

Mechanism — how the transformation zone develops

- **Trigger:** Estrogen (at menarche, and again in pregnancy) causes glycogen deposition in vaginal/ectocervical squamous epithelium.
- **Lactobacilli** act on glycogen to produce **lactic acid**, lowering vaginal pH.
- The **acid pH stimulates subcolumnar reserve cells** beneath the exposed columnar epithelium (at the tips of columnar villi, which meet the acid environment first) to proliferate and differentiate.
- Two mechanisms replace columnar epithelium with squamous epithelium:
  - **Squamous metaplasia** — subcolumnar reserve cells proliferate and differentiate directly into squamous cells.
  - **Squamous epidermidisation** — squamous epithelium from the adjacent ectocervix grows inward under the columnar epithelium.
- Metaplastic cells are initially **immature** (large nuclei, scant cytoplasm, no glycogen); with maturation they acquire glycogen and become indistinguishable from native squamous epithelium colposcopically and histologically — the **"healed" (mature) transformation zone**, which is relatively resistant to oncogenic stimuli.
- This process is **most active at menarche and during/after a first pregnancy** (high-estrogen, low vaginal-pH phases) — the periods of maximum vulnerability to malignant transformation if an oncogenic trigger (high-risk HPV) is present.

Histology

Layer (mature original/metaplastic squamous epithelium)	Feature
Basal layer	Single row of small immature cells with large nuclei
Parabasal layer	2–4 rows of immature cells, normal mitoses, replace overlying cells

Layer (mature original/metaplastic squamous epithelium)	Feature
Intermediate layer	4–6 rows, larger cytoplasm, intercellular bridges, glycogen begins
Superficial layer	5–8 rows of flattened, glycogen-filled cells; nuclei pyknotic; exfoliate — basis of Pap cytology

- **Immature metaplastic epithelium** lacks glycogen and the full four-layer architecture; it is the epithelium most vulnerable to persistent high-risk HPV infection and subsequent neoplastic transformation.

Clinical significance

Significance	Explanation
Site of origin of CIN/cervical cancer	CIN typically arises at the **advancing (new) SCJ** within the TZ; the **anterior lip** is affected roughly twice as often as the posterior lip, and lateral angles are rarely involved. Untreated CIN spreads horizontally within the TZ but rarely replaces native squamous epithelium beyond it
Colposcopic assessment	A **satisfactory colposcopy** requires the **entire transformation zone and the SCJ to be visible**; if not, it is graded **unsatisfactory**, mandating endocervical curettage/sampling
IFCPC (2011) TZ typing	Colposcopic assessment records **transformation zone type 1, 2 or 3** — Type 1: entirely ectocervical and fully visible; Type 2: has an endocervical component but is fully visible; Type 3: has an endocervical component that is not fully visible. This determines whether an **excisional** (LEEP/LLETZ, cone) or **ablative** (cryotherapy, laser vaporisation) treatment is appropriate
Cervical screening	Cervical cytology (Pap smear/liquid-based cytology) must sample **both the ectocervical TZ and the endocervical canal** (spatula + endocervical brush) for an adequate smear, since dysplastic cells arise here
Treatment of CIN 2/3	Requires **destruction or excision of the entire transformation zone** (not just the visible lesion) because proximal extension into cervical crypts/glands harbours the most severe disease; **LEEP/LLETZ is the preferred outpatient technique**

Significance	Explanation
Age-related visualisation	TZ is **everted and easily visualised** at puberty and in pregnancy (physiological ectopy); after menopause it **recedes into the endocervical canal**, often producing an unsatisfactory colposcopy in older women
HPV vulnerability	Immature metaplastic cells of the TZ (particularly adjacent to the active SCJ) are the principal site of **high-risk HPV entry via microtrauma (coitus)** — the basis for cervical carcinogenesis

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 16.2 — The cervix and the transformation zone. (Berek & Novak 16e, p.916)*

Label: original SCJ, new (active) SCJ, transformation zone in between, nabothian cysts/gland openings marking the original SCJ, and the columnar epithelium proximal to the new SCJ.

High-yield exam pointers

- TZ = area between the **original SCJ** (outer limit) and the **new/active SCJ** (inner limit).
- Mechanism: estrogen → glycogen → lactobacilli → lactic acid (low pH) → subcolumnar reserve cell metaplasia ± squamous epidermidisation.
- **Nabothian cysts / gland openings** mark the original SCJ.
- **CIN arises at the active SCJ** within the TZ; anterior lip affected more than posterior.
- **IFCPC 2011 TZ types 1/2/3** — determines excisional vs ablative treatment choice and colposcopy adequacy.
- **LEEP/LLETZ** = must remove the *entire* transformation zone, not just the visible lesion.
- TZ is everted (visible) at puberty/pregnancy; recedes into canal after menopause.

SOURCE & COVERAGE

Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e (2019); DC Dutta's Textbook of Gynaecology 7e; IFCPC 2011 colposcopy terminology classification (as cited in Jeffcoate 9e).

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Transformation zone of the cervix

Asked in: Paper I Jun 2016 — RGUHS MS Obstetrics & Gynaecology

Definition — The transformation zone (TZ) is the dynamic ring of the cervix that lies between the **original squamocolumnar junction (SCJ)** — where columnar and squamous epithelium met at birth — and the **new (physiologically active) SCJ**, the current boundary after ongoing squamous metaplasia. Within this zone, endocervical columnar epithelium is progressively replaced by metaplastic squamous epithelium under the influence of vaginal acidity and oestrogen. Because this metaplastic epithelium is immature and mitotically active, the transformation zone is the site of origin of over 90% of cervical intraepithelial neoplasia (CIN) and squamous cell carcinoma of the cervix.

Location of the SCJ and TZ through life

The position of the SCJ is not fixed at the external os — it shifts outward (ectocervix) or inward (endocervical canal) with the oestrogen state of the woman, so the transformation zone migrates across the life cycle.

Life stage / oestrogen state	Position of SCJ / transformation zone
Fetal life & neonate	High maternal oestrogen pushes columnar epithelium onto the ectocervix — **congenital ectopy**
Childhood (low oestrogen)	SCJ recedes towards or into the external os as maternal oestrogen withdraws
Puberty & reproductive years	Rising oestrogen causes eversion of columnar epithelium onto the ectocervix — physiological **ectopy/eversion**; the active TZ lies on the visible portio vaginalis
Pregnancy & combined oral contraceptive use	High oestrogen exaggerates eversion; TZ is maximally exposed and colposcopically well seen
Perimenopause & postmenopause	Falling oestrogen causes the new SCJ and TZ to recede into the endocervical canal, often no longer visible on speculum — colposcopy becomes "unsatisfactory"

Histology of the transformation zone

Epithelial component	Key histological features
Original (native) squamous epithelium	Non-keratinised stratified squamous epithelium of the ectocervix/vagina in 4 layers: (1) basal — single row, high nuclear-cytoplasmic ratio; (2) parabasal — 2–4 rows, mitotically active, replenish surface; (3) intermediate — 4–6 rows, glycogenated, intercellular bridges; (4) superficial — 5–8 rows, flattened, glycogen-filled, pyknotic nuclei, exfoliate to form the basis of the Papanicolaou (Pap) smear
Columnar (endocervical) epithelium	Single layer of mucus-secreting columnar cells over ridges, clefts and infoldings ("glands"); subcolumnar **reserve cells** lie beneath it
Metaplastic squamous epithelium	Immature squamous cells derived from reserve-cell proliferation, replacing columnar epithelium from the tips of the columnar villi inward; matures to resemble native squamous epithelium once fully glycogenated

Mechanism of squamous metaplasia (formation of the TZ)

- Oestrogen-driven glycogenation of vaginal/ectocervical epithelium lowers vaginal pH (lactobacilli acting on glycogen).
- The acidic environment irritates the everted columnar epithelium and stimulates **subcolumnar reserve cells** to proliferate.
- Reserve cells undergo **squamous metaplasia**, lifting and replacing the columnar epithelium, beginning at the tips of the columnar villi (most exposed to acid) and progressing into the cervical clefts.
- As metaplastic cells mature, the central capillary of each villus regresses, the epithelium flattens, and glycogen production begins — producing the typical 4-layered squamous architecture (**mature/healed TZ**).
- Some deep clefts are not fully replaced, trapping mucus-secreting columnar epithelium beneath squamous cover — these retention cysts are **Nabothian follicles**; gland/crypt openings and Nabothian cysts mark the outer border of the original TZ.
- The zone between the original SCJ and the new SCJ, containing epithelium at all stages of this metaplastic process, constitutes the transformation zone.

Clinical significance

Feature	Relevance
Site of neoplasia	>90% of CIN and squamous cervical cancer arise at the advancing new SCJ within the TZ (anterior lip affected roughly twice as often as posterior; lateral angles rarely involved) — immature metaplastic cells are most vulnerable to persistent high-risk human papillomavirus (HPV) infection
Cervical crypt (gland) involvement	CIN can extend proximally into the cervical crypts beneath the surface TZ; ablative or excisional treatment must destroy the *entire* TZ (surface + crypt depth), not just the visible lesion
Nabothian cysts	Retention cysts of trapped columnar epithelium; benign, mark extent of a healed TZ, need no treatment unless symptomatic
Colposcopic assessment (International Federation for Cervical Pathology and Colposcopy [IFCPC] 2011, Rio de Janeiro terminology)	TZ is typed by visibility of the new SCJ: **Type 1** — entirely ectocervical, fully visible; **Type 2** — has an endocervical component, but fully visible (with or without eversion aids); **Type 3** — has an endocervical component that is *not* fully visible. A "satisfactory/adequate" colposcopy requires complete visualisation of the SCJ and TZ (Type 1 or 2); Type 3 mandates endocervical sampling
Screening & sampling	Papanicolaou (Pap) smear and liquid-based cytology sample exfoliated superficial cells from across the TZ; an adequate smear must contain both squamous and endocervical/metaplastic cells confirming TZ sampling
Treatment planning	Ablation (cryotherapy, laser vaporisation) is suitable only when the entire TZ is visible (Type 1/2) and invasive disease is excluded; excisional methods (loop electrosurgical excision procedure/large loop excision of the transformation zone [LEEP/LLETZ], cone biopsy) are required when the TZ is Type 3, or when a histological (not merely cytological) diagnosis is needed
Ageing effect	Postmenopausal recession of the TZ into the canal explains the higher rate of unsatisfactory colposcopy and the need for endocervical curettage in older women

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

☐ *Fig 16.2 — The cervix and the transformation zone. (Berek & Novak 16e, p.916)*

Label: original SCJ, new (physiologically active) SCJ, native squamous epithelium, columnar epithelium, transformation zone in between, gland (crypt) openings and Nabothian cysts marking the original TZ border.

High-yield exam pointers

- TZ = area **between original SCJ and new SCJ**; formed by squamous metaplasia of columnar epithelium.
- **>90%** of CIN/cervical cancer arises in the TZ, at the advancing new SCJ; anterior lip > posterior lip.
- Ectopy/eversion = high-oestrogen state (puberty, pregnancy, combined oral contraceptive pills); TZ recedes into canal after menopause.
- Nabothian cysts + gland openings = landmarks of the **original** TZ border.
- IFCPC 2011 (Rio de Janeiro) colposcopic **TZ types 1/2/3** — visibility of the SCJ determines "satisfactory" vs "unsatisfactory" colposcopy and ablation-vs-excision choice.
- Entire TZ (including crypt depth) must be destroyed/excised in CIN treatment — not just the visible lesion.
- Pap smear adequacy requires sampling of the TZ (squamous + endocervical/metaplastic component).

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

The IFCPC 2011 Rio de Janeiro terminology (TZ types 1/2/3) is the current international colposcopic classification and has superseded the earlier 1975/1990/2002 systems that older textbook editions may still describe.

SOURCE & COVERAGE

Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e; DC Dutta's Textbook of Gynaecology 7e; Williams Obstetrics 26e; International Federation for Cervical Pathology and Colposcopy (IFCPC) 2011 Rio de Janeiro colposcopic terminology.

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Ultrasound guided interventions in pregnancy

Asked in: Paper I 21-Jun-2024 — RGUHS MS Obstetrics & Gynaecology

Definition — Ultrasound-guided interventions are invasive diagnostic or therapeutic procedures on the amniotic sac, placenta, umbilical cord, or fetus, performed with continuous real-time sonographic visualisation of the needle or instrument. Real-time guidance lets the operator target the pocket of fluid/vessel precisely while avoiding fetal parts, cord, and placenta, and has markedly reduced complication rates compared with the earlier "blind" technique.

Classification

Category	Procedures
Diagnostic (prenatal diagnosis)	Amniocentesis (genetic); chorionic villus sampling (CVS); cordocentesis/percutaneous umbilical blood sampling (PUBS)
Therapeutic (fetal therapy)	Amnioreduction; amnioinfusion; intrauterine fetal transfusion (IUFT); fetoscopic laser photocoagulation for twin-twin transfusion syndrome (TTTS); vesicoamniotic and thoracoamniotic shunting; selective fetal reduction/feticide; fetoscopic tracheal occlusion (FETO) for congenital diaphragmatic hernia (CDH)
Adjunct, non-needle	Real-time ultrasound monitoring during external cephalic version (ECV)

Diagnostic procedures

Procedure	Timing	Technique	Key indications
Amniocentesis (genetic)	15–20 weeks	20- or 22-gauge spinal needle inserted transabdominally under real-time ultrasound into a fluid pocket away from fetal parts; first 1–2 mL discarded (maternal-cell contamination), then 20–30 mL withdrawn	Karyotype/chromosomal microarray, neural-tube defect (amniotic-fluid alpha-fetoprotein), infection PCR (toxoplasma, CMV, parvovirus), fetal genotype in Rh disease
Chorionic villus sampling (CVS)	10–13 weeks (avoid before 10 weeks)	Transabdominal — 18- or 20-gauge needle into chorion frondosum; or transcervical — flexible catheter with malleable stylet; villi aspirated into culture medium	Earlier karyotype/CMA than amniocentesis, e.g. after a high-risk first-trimester/NT screen

Procedure	Timing	Technique	Key indications
Cordocentesis (PUBS)	Usually after 18 weeks	22- or 23-gauge spinal needle into the umbilical vein (near cord insertion, or a free loop) under direct ultrasound; blood aspirated into a heparinised syringe	Confirm/treat fetal anaemia, platelet alloimmunisation, rapid karyotype for mosaicism found on amniocentesis/CVS

Therapeutic procedures (fetal therapy)

Procedure	Indication	Technique
Amnioreduction	Symptomatic polyhydramnios/TTTS causing maternal respiratory compromise or preterm labour	Large-volume amniocentesis with an 18- or 20-gauge needle; fluid drained into a vacuum bottle/syringe till the deepest vertical pocket falls below 5 cm
Amnioinfusion	Antenatal oligohydramnios (to prevent pulmonary hypoplasia/cord compression); dilution of meconium-stained liquor	Warmed normal saline instilled trans-abdominally (or transcervically) under ultrasound
Intrauterine fetal transfusion (IUFT)	Fetal anaemia (Rh-isoimmunisation, parvovirus B19) with middle-cerebral-artery peak systolic velocity >1.5 MoM, or haematocrit <30% (hydrops if <15%)	Intravascular, into the umbilical vein (intraperitoneal if the vein cannot be safely accessed); type-O, D-negative, CMV-negative, irradiated, leucocyte-poor packed cells to a target haematocrit of 40–50%; volume (mL) ≈ estimated fetal weight (g) × 0.02 per each 10% rise in haematocrit desired; repeated every 2–4 weeks; done before 34–35 weeks
Fetoscopic laser photocoagulation	TTTS, Quintero stage II–IV, monochorionic-diamnionic twins, 16–26 weeks	Fetoscope into the recipient sac; arteriovenous anastomoses along the vascular equator individually photocoagulated (or entire equator ablated — Solomon technique); amnioreduction at the end

Procedure	Indication	Technique
Vesicoamniotic shunt	Lower urinary tract obstruction (e.g., posterior urethral valves) with preserved renal function	Amnioinfusion for visualisation, then trocar/cannula into the fetal bladder; double-pigtail catheter deployed, distal coil in bladder, proximal end draining into the amniotic cavity
Thoracoamniotic shunt	Fetal pleural effusion/large cystic lung mass with hydrops risk	Effusion first drained with a 22-gauge needle; if it recurs, a double-pigtail catheter placed through the chest wall via trocar
Selective fetal reduction/feticide	Discordant fetal anomaly, twin-reversed-arterial-perfusion (TRAP) sequence, severe TTTS not amenable to laser	Radiofrequency ablation, bipolar cord coagulation, or laser to occlude the umbilical vessels of the affected twin
Fetoscopic tracheal occlusion (FETO)	Severe CDH with lung-to-head ratio <1.4	Detachable balloon placed in fetal trachea at 26–30 weeks; removed fetoscopically or by ultrasound-guided puncture at ~34 weeks

Prerequisites and general principles

- Detailed counselling and written informed consent, explaining procedure-specific loss/complication rates.
- Pre-procedure ultrasound to confirm gestational age, viability, fetal number, and placental/cord position.
- Aseptic skin preparation (povidone-iodine); local anaesthesia is optional and not proven to reduce discomfort.
- Continuous, real-time ultrasound visualisation of the needle/instrument tip throughout — the needle is inserted perpendicular to the skin, puncturing (not tenting) the membranes, avoiding fetal parts, cord, and placenta where possible.
- **Anti-D immunoglobulin** to every Rh D-negative, unsensitised woman after the procedure — DC Dutta's Obstetrics gives 50 microgram IM after CVS and 100 microgram IM after mid-trimester amniocentesis; current Western obstetric practice (ACOG/RCOG) uses a full 300 microgram (or equivalent) dose for any second-trimester invasive procedure.
- Post-procedure: document fetal cardiac activity, observe the puncture site for bleeding, and advise the woman to report cramping, bleeding, or fluid leakage.

Complications

Procedure	Complication rate
Amniocentesis	Procedure-related fetal loss 0.1–0.3%; fluid leak/spotting 1–2%
CVS	Loss rate comparable to amniocentesis (~0.1–0.3%); limb-reduction defects if done before 10 weeks
Cordocentesis	Fetal loss ~1–2%; cord haematoma, fetal bradycardia from arterial puncture
Intrauterine transfusion	Fetal death ~2%; emergency caesarean ~1%; infection/PPROM ~0.3% each
Laser for TTTS	Perinatal mortality falls from 70–100% (untreated severe TTTS) to 30–50% after laser; PPROM ~25%, twin anaemia-polycythaemia sequence ~16%

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 41.12 — Amniocentesis—direct ultrasound control (DC Dutta's Obstetrics 9e, p.635)*

High-yield exam pointers

- Amniocentesis: 20–22 G needle, **15–20 weeks**, loss rate **0.1–0.3%**.
- CVS: **10–13 weeks**, never before 10 weeks (limb-reduction defects); transabdominal 18–20 G needle or transcervical catheter.
- Cordocentesis (PUBS): **22–23 G** needle into umbilical vein; loss rate **1–2%**.
- IUT dose rule: EFW(g) × 0.02 per 10% haematocrit rise wanted; target haematocrit 40–50%; transfuse if fetal Hct <30% (hydrops if <15%).
- TTTS: Quintero staging; fetoscopic laser is treatment of choice for stage II–IV, done at **16–26 weeks**.
- Anti-D immunoglobulin to every Rh D-negative unsensitised woman after any invasive procedure.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

DC Dutta's Obstetrics (9e) gives 50 microgram anti-D after CVS and 100 microgram after amniocentesis; current ACOG/RCOG practice instead gives one standard full-dose anti-D immunoglobulin injection after any second-trimester invasive procedure in an unsensitised Rh D-negative woman.

SOURCE & COVERAGE

Williams Obstetrics 26e; DC Dutta's Textbook of Obstetrics 9e; Arias' High-Risk Pregnancy & Delivery 5e (CVS figure/technique).

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Use of Laser in Gynaecology

Asked in: Paper I Nov 2017 — RGUHS MS Obstetrics & Gynaecology

Definition — LASER is an acronym for Light Amplification by Stimulated Emission of Radiation — a beam of monochromatic, coherent, collimated light that is focused to a small spot size and delivers energy that cuts, coagulates, or vaporises tissue. It has been used in gynaecological surgery for over five decades, chiefly for genital-tract lesions and endoscopic procedures, because it allows precise, layer-by-layer tissue destruction with minimal lateral thermal damage.

Physical Principles and Laser Systems Used in Gynaecology

The physical properties that make laser useful surgically are **monochromacity** (light of one wavelength), **coherence** (light waves perfectly aligned and unidirectional), and **collimation** (parallel, non-divergent beams). A convex lens focuses the beam to a **spot size**; **power density** (watts/cm^2) — the key determinant of tissue effect — rises as spot size falls. The commonly used gynaecological laser systems are:

Laser type	Wavelength	Tissue penetration	Principal gynaecological use
Carbon dioxide (CO2)	10.6 μm	0.1 mm	Most versatile — cervix, vulva, vagina, laparoscopy
Neodymium:Yttrium-Aluminium-Garnet (Nd:YAG)	1.06 μm	0.6–4.2 mm	Deepest penetration — hysteroscopic endometrial ablation
Potassium titanyl-phosphate (KTP 532)	0.532 μm	0.4–0.8 mm	Fibreoptic laser laparoscopy — precise targeting, good haemostasis
Argon	0.5 μm	0.2 mm	Fibreoptic laser laparoscopy

Laser type	Wavelength	Tissue penetration	Principal gynaecological use
Erbium:YAG (Er:YAG)	2.94 μm	Superficial (epidermis/mucosa)	Fractional laser vaginal therapy (e.g., *FemTouch*, *IntimaLase* devices) for genitourinary syndrome of menopause

Fibreoptic laser laparoscopy (KTP/Argon) offers accurate targeting, higher precision, minimal effect on surrounding tissue, better haemostasis, and less laser plume.

Mechanism of Laser–Tissue Interaction

- Laser energy is absorbed by intracellular water (about 80% of cell volume), which boils instantly at 100°C; the cell explodes and vaporises, and cell protein/minerals are incinerated, leaving a **charred crater**.
- Depth of tissue destruction depends on **power (watts), spot size, power density, and tissue contact time**; a smaller, faster-moving beam gives a precise cut with a very thin (as little as 0.1 mm) zone of residual thermal necrosis.
- **Suprathreshold** energy density causes cellular vaporisation; **sub-ablative** fluence causes reversible coagulation and protein denaturation without vaporisation — the basis of newer non-ablative/fractional techniques.
- **Fractional lasers** deliver an array of microbeams that create microscopic ablation columns surrounded by untouched tissue; the resulting heat-shock-protein–mediated release of transforming growth factor-beta (TGF-β) drives neocollagenesis — the principle behind fractional CO2/Er:YAG "vaginal laser" treatment of vulvovaginal atrophy.

Uses of Laser in Gynaecology

- **Cervix** — treatment of cervical intraepithelial neoplasia (CIN):
  - *Vaporisation conisation*: CO2 laser via colposcope, day-care, usually without general anaesthesia; margins outlined, cervix divided into four quadrants and vaporised to a depth of 7 mm. Requires the lesion and transformation zone to be fully visualised and endocervical adenocarcinoma excluded.
  - *Excisional laser conisation*: used when the lesion extends into the canal, the transformation zone cannot be fully seen, endocervical curettage is positive, or invasive cancer cannot be excluded — yields a specimen for histology.
- **Vulva** — vaporisation of condyloma acuminata; ablation of vulvar intraepithelial neoplasia (VIN) under colposcopic guidance (spot size 2–3 mm, power 15–50 W).

- **Vagina** — ablation of vaginal intraepithelial neoplasia (VAIN) (spot size 2 mm, power 15–30 W); fractional CO2/Er:YAG vaginal laser therapy for genitourinary syndrome of menopause (vulvovaginal atrophy).
- **Laparoscopy** — adhesiolysis; vaporisation/excision of endometriotic implants and endometriomas, laparoscopic uterosacral nerve ablation (LUNA) and presacral neurectomy for dysmenorrhoea; laser myomectomy (pedunculated/subserous fibroids); laparoscopic ovarian drilling in clomiphene-resistant polycystic ovarian syndrome; tubal surgery — *Bruhat's* salpingostomy for ectopic pregnancy and tubal disease; assisted division of pedicles in laparoscopic-assisted vaginal hysterectomy.
- **Hysteroscopy** — Nd:YAG laser endometrial ablation (depth 4–5 mm, producing a therapeutic *Asherman's* syndrome/amenorrhoea) as an alternative to hysterectomy; resection of uterine septum (metroplasty), submucous fibroids, and intrauterine synechiae.

Advantages of Laser Surgery

Advantage	Detail
Precision	Very precise depth of destruction, minimal lateral thermal spread
Haemostasis	Good haemostatic effect, especially with KTP/Argon fibreoptic systems
Field of access	Reaches areas difficult for knife/electrosurgery
Outpatient care	Vaporisation procedures done under local anaesthesia, day-care
Laser vs cold-knife conisation	Less tissue damage and blood loss; less postoperative pain/discharge; earlier re-epithelialisation (3–4 weeks); all grades of CIN treatable; fertility and pregnancy outcome unaffected

Limitations and Hazards

Category	Points
Limitations	Expensive equipment; technically complex, needs trained personnel
Hazards to eye/skin	Visual loss from corneal or retinal damage; skin damage; injury from laser smoke
General hazards	Burn injury (avoid spirit and paper drapes); care with inflammable anaesthetic gases; dangerous beam reflection (avoid shiny instruments); fire risk — extinguisher must be available; smoke plume must be extracted

Category	Points
Precautions	Laser used only by a trained person; laser-controlled area (LCA) with warning signage; protective spectacles for operator, assistant, and theatre staff

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 64.4A — Different gynaecological LASER machines: (A) CO2 laser—FemiLift; (B) CO2 laser—FemTouch; (C) Er:YAG laser—IntimaLase (Jeffcoate's Principles of Gynaecology 9e, p.1157)*

High-yield exam pointers

- LASER = Light Amplification by Stimulated Emission of Radiation.
- CO2 laser (10.6 μm) is the most versatile gynaecological laser but has the shallowest tissue penetration (0.1 mm); Nd:YAG penetrates deepest (0.6–4.2 mm), hence used for hysteroscopic endometrial ablation.
- Power density (W/cm^2) is the key determinant of laser effect — smaller spot size, higher power density.
- Vaporisation conisation of the cervix is done to a depth of 7 mm, quadrant by quadrant.
- Advantages of laser over cold-knife conisation: outpatient/local anaesthesia, less blood loss, faster re-epithelialisation (3–4 weeks), fertility preserved.
- Hazard groups to recall: eye/skin/smoke damage to personnel; burn/inflammable-gas/reflection/fire/plume risks in theatre — hence mandatory protective eyewear and a laser-controlled area.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

Fractional CO2/Er:YAG vaginal laser therapy for genitourinary syndrome of menopause is a newer, non-ablative application; it is gaining use but is not yet established as first-line over topical vaginal oestrogen.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e (Ch. 10 — Laser in Gynecology; Table 35.1 — advantages of laser over cold-knife conisation); Jeffcoate's Principles of Gynaecology 9e (Ch. 64 — Applications of Laser in Gynaecology); Berek & Novak's Gynecology 16e (laser ablation for VIN/VAIN, endometriosis, endometrial ablation).

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Use of progestogens in gynecology

Asked in: Paper I May 2018 — RGUHS MS Obstetrics & Gynaecology

Definition — Progesterone is a natural C-21 steroid secreted mainly by the corpus luteum (placenta after the first trimester of pregnancy) that converts a proliferative, oestrogen-primed endometrium into a secretory endometrium. Because natural progesterone is rapidly inactivated when swallowed, synthetic compounds with progesterone-like activity — **progestational agents, gestagens, progestogens or progestins** — have been developed for oral, parenteral, and local (intrauterine/vaginal) use across gynaecological practice.

Classification of progestogens

Structural class	Representative agents	Distinguishing property
I. Progesterone	Natural/micronized progesterone	No androgenic or anti-androgenic effect; does not alter carbohydrate metabolism
II. Pregnanes (17-OH-progesterone derivatives)	17α-hydroxyprogesterone caproate, medroxyprogesterone acetate (MPA), chlormadinone acetate, cyproterone acetate	Do not alter carbohydrate metabolism; cyproterone acetate is strongly anti-androgenic
III. Norpregnanes	Nomegestrol acetate, gestonorone caproate	Anti-androgenic, minimal metabolic effect
IV. Retroprogesterone	Dydrogesterone	Does **not** inhibit ovulation
V. 19-norprogesterones	Demegestone, promegestone, nestorone, trimegestone	High progestational potency, minimal androgenicity
VI-A. 19-nortestosterone — estranes	Norethisterone (NET), NET acetate, norethynodrel, ethynodiol diacetate, lynestrenol	Mildly androgenic; slightly alter carbohydrate/lipid metabolism
VI-B. 19-nortestosterone — gonanes	Levonorgestrel (LNG), desogestrel, gestodene, norgestimate	Excellent contraceptive efficacy and cycle control; more potent, fewer side effects than estranes
VII. Spironolactone derivative	Drospirenone	Anti-mineralocorticoid + anti-androgenic
VIII. Unsaturated 19-nor steroid	Gestrinone	Androgen/progesterone agonist-antagonist; used in endometriosis

Progestational potency is graded 1 (progesterone) to 10 (most potent, e.g., trimegestone); each agent is also graded for androgenic, anti-androgenic activity and effect on sex hormone–binding globulin (SHBG).

Mechanism of action

- Converts the oestrogen-primed proliferative endometrium into a secretory endometrium (differentiation, not further growth).
- Downregulates endometrial oestrogen receptors and induces 17β-hydroxysteroid dehydrogenase, which converts oestradiol to the weaker oestrone — an overall **anti-oestrogenic** action on the endometrium.
- Inhibits mitotic activity of endometrial glands; high-dose continuous use causes glandular atrophy and stromal decidualisation.
- Thickens cervical mucus, making it hostile to sperm penetration.
- At ovulatory-suppressive doses, exerts negative feedback on the hypothalamo-pituitary axis, blunting the mid-cycle LH surge.
- Reduces myometrial excitability and prostaglandin-driven contractions.

Clinical uses in gynaecology

Indication	Progestogen & dose	Notes
Diagnostic — progesterone challenge test	MPA 10 mg/day orally for 5 days	Withdrawal bleeding confirms an intact hypothalamo-pituitary-ovarian axis, adequate endogenous oestrogen (>40 pg/mL), a responsive endometrium and a patent genital tract — used in the work-up of amenorrhoea
Abnormal uterine bleeding (AUB), anovulatory type (older term: dysfunctional uterine bleeding, DUB)	Acute bleeding: norethisterone or MPA 5–10 mg 3 times/day till bleeding stops (controls bleeding in 3–7 days), tapered over 21 days. Cycle regulation: norethisterone 5 mg or MPA 10 mg from day 5–25 (or 15–25) for 3 cycles	Progestogens are most effective in **anovulatory** AUB (secretory transformation); the 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS) is now first-line medical therapy for heavy menstrual bleeding where fertility is not desired (FIGO/ACOG/NICE)
Endometriosis / adenomyosis	Norethisterone 5 mg or MPA 10 mg 2–3 times/day for 6–9 months (induces amenorrhoea); depot MPA 150 mg IM 3-monthly; dienogest 2 mg/day (current preferred oral progestin); LNG-IUS for pelvic pain	Mechanism: decidualisation, glandular atrophy, and fibrosis of ectopic endometriotic implants; reduces nerve-fibre density in lesions
Dysmenorrhoea	Dydrogesterone 5–10 mg/day, day 5–24	Reduces uterine contractions without suppressing ovulation

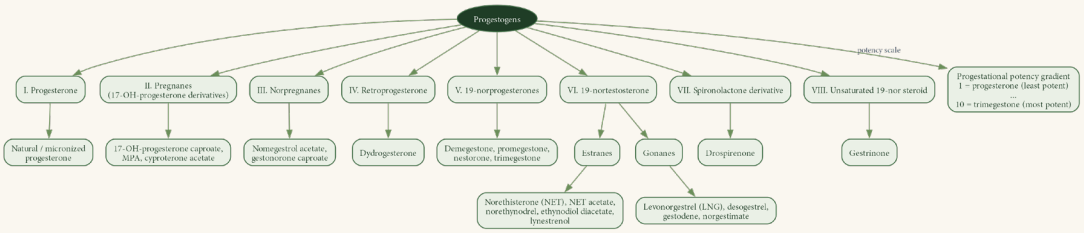
Indication	Progestogen & dose	Notes
Luteal phase defect / ART luteal support	Micronized progesterone 100 mg 3 times/day (oral or vaginal), or vaginal suppository 200 mg twice daily starting 2–3 days after ovulation, continued till menses or, if conception occurs, to 10–12 weeks; progesterone-in-oil 12.5–50 mg IM daily	Vaginal/IM routes preferred — oral natural progesterone is rapidly hepatically metabolised
Endometrial hyperplasia without atypia	LNG-IUS 52 mg (first-line); continuous oral MPA 10–20 mg/day or norethisterone if IUS declined	Current guideline (RCOG/BGCS, ACOG) prefers LNG-IUS over cyclical oral progestogen for higher regression rates
Atypical hyperplasia / grade-1 endometrial cancer (fertility-sparing)	Megestrol acetate 40–160 mg/day or continuous MPA, ± LNG-IUS, for at least 3–6 months with repeat endometrial biopsy to confirm regression	Response depends on oestrogen/progesterone receptor density; ~25% never respond — hysterectomy remains standard once fertility is no longer desired
Advanced/recurrent endometrial carcinoma	Megestrol acetate 80 mg twice daily, or MPA 50–100 mg 3 times/day	Response rate 15–25%, better with well-differentiated, receptor-positive, disease-free-interval-favourable tumours
Premenstrual syndrome	Dydrogesterone 5–10 mg/day, day 5–24, for 3–6 cycles	Evidence for progesterone-deficiency hypothesis is weak; benefit is inconsistent
Postponement of menstruation	Norethisterone 5 mg 3 times/day starting 3 days before expected period, continued till desired	No contraceptive protection during use; period resumes 2–3 days after stopping
Threatened miscarriage with prior miscarriage	Vaginal micronized progesterone 400 mg twice daily from presentation until 16 weeks	Supported by recent trial evidence in women with both current bleeding and a history of prior miscarriage — not indicated for threatened abortion in general
Contraception	Progestogen-only pill (e.g., desogestrel 75 µg daily); depot MPA (DMPA) 150 mg IM 3-monthly; norethisterone enanthate (NET-EN) 200 mg IM 2-monthly; LNG emergency contraception 1.5 mg single dose; LNG-IUS; subdermal implants	Mechanisms: anovulation, thick hostile cervical mucus, endometrial atrophy

Indication	Progestogen & dose	Notes
Hormone replacement therapy (HRT)	Progestin added to oestrogen — cyclical for the last 12–14 days of the cycle, or continuous combined	Mandatory in women with an intact uterus to prevent unopposed-oestrogen endometrial hyperplasia/carcinoma; not needed post-hysterectomy

Side effects of progestogens

- Nausea — usually subsides with continued use
- Weight gain (salt and water retention), leg cramps, mastalgia
- Acne, oily skin, hirsutism/virilism — with androgenic progestins (e.g., norethisterone-derived estranes)
- Breakthrough bleeding or scanty periods/amenorrhoea
- Headache; migraine must be excluded before continuing
- Depression and mood change — attributed to altered tryptophan metabolism/relative pyridoxine deficiency
- Adverse lipid profile (raised LDL, lowered HDL) with older androgenic progestins; newer agents (dydrogesterone, dienogest, drospirenone) are largely lipid-neutral
- Increased venous thromboembolism risk when combined with oestrogen in certain formulations

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS



Figure

Classification tree of progestogens into the eight structural classes with representative agents, plus the progestational-potency gradient.

High-yield exam pointers

- Progesterone challenge test dose: **MPA 10 mg/day × 5 days orally**.
- Acute AUB control: **norethisterone/MPA 5–10 mg tds**, bleeding stops in 3–7 days; taper over 21 days.
- LNG-IUS (52 mg) is now first-line for heavy menstrual bleeding AND endometrial hyperplasia without atypia — remember this over older "cyclical oral progestin" answers.

- Atypical hyperplasia fertility-sparing dose: **megestrol acetate 40–160 mg/day**, minimum 3–6 months, repeat biopsy.
- Luteal support: **micronized progesterone 100 mg tds** oral/vaginal, or **200 mg vaginal suppository bd**.
- Dydrogesterone is the progestogen that does **not** inhibit ovulation — used in dysmenorrhoea, PMS, luteal phase disorders.
- Side-effect mnemonic: weight gain, acne/virilism, mood change, adverse lipids, breakthrough bleeding.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
> Older texts label anovulatory AUB as "dysfunctional uterine bleeding (DUB)"; current terminology follows the FIGO PALM-COEIN classification (FIGO/ACOG 2011), and current guidelines (RCOG/BGCS, ACOG, NICE) favour the LNG-IUS over cyclical oral progestogens as first-line therapy for both heavy menstrual bleeding and endometrial hyperplasia without atypia.

> **SOURCE & COVERAGE**
> DC Dutta's Textbook of Gynaecology 7e; Berek & Novak's Gynecology 16e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; FIGO PALM-COEIN classification (FIGO/ACOG 2011).

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Uterine anomalies

Asked in: Paper I May 2019 — RGUHS MS Obstetrics & Gynaecology

Definition — Uterine anomalies are congenital malformations of the uterus arising from defective development of the paired **paramesonephric (Müllerian) ducts** — failure of duct formation, failure of fusion of the two ducts, or failure of resorption of the intervening septum — which normally form the fallopian tubes, uterus, cervix, and upper two-thirds of the vagina by the 20th week of gestation. They occur in **3–4% of women overall**, rising to 5–10% in women with early pregnancy loss and up to 25% in those with second- or third-trimester loss.

Embryological basis and classification

Three basic embryological defects produce the anomalies: (1) **agenesis/hypoplasia** of one or both ducts, (2) **failure of fusion (lateral)** of the two ducts, and (3) **failure of resorption** of the septum between fused ducts. Because the urinary system develops in close proximity to the paramesonephric ducts, **renal anomalies coexist in about 40%** of cases (most often an absent unilateral kidney), and **skeletal**

anomalies in about 12%; urinary tract imaging (ultrasonography, MRI, or intravenous pyelography) is mandatory whenever a Müllerian anomaly is diagnosed.

The **American Fertility Society (AFS)/American Society for Reproductive Medicine (ASRM) classification (1988)** remains the standard framework used in Indian and RGUHS teaching:

Class	Anomaly	Embryological defect	Approx. frequency among anomalies
I	Segmental Müllerian agenesis/hypoplasia (vaginal, cervical, fundal, tubal, or combined)	Agenesis of duct segment(s)	Includes Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome
II	Unicornuate uterus (± rudimentary horn — communicating, non-communicating, or with no cavity/no horn)	Failure of development of one duct	10%
III	Uterus didelphys	Complete failure of fusion — double uterus, double cervix, often double/septate vagina	8%
IV	Bicornuate uterus (complete to internal os / partial)	Partial failure of fusion	26%
V	Septate uterus (complete/partial, i.e. subseptate)	Failure of septal resorption	35% (commonest)
VI	Arcuate uterus	Minor residual fundal septal indentation	18%
VII	Diethylstilboestrol (DES)-related anomalies (T-shaped cavity, cervical collar/cockscomb cervix)	In-utero DES exposure	Now rare

Clinical features

Gynaecological

- Often **asymptomatic** and discovered incidentally during infertility work-up, dilatation and curettage, manual removal of placenta, or caesarean section.
- **Primary amenorrhoea** — if agenesis of uterus/vagina (Class I, e.g. MRKH syndrome).

- **Cryptomenorrhoea, cyclical pain, haematometra/haematocolpos** — if there is a non-communicating rudimentary horn or an obstructed hemivagina (e.g. OHVIRA/Herlyn-Werner-Wunderlich syndrome: obstructed hemivagina and ipsilateral renal agenesis with uterus didelphys).
- **Dysmenorrhoea** — in bicornuate uterus or from pent-up menstrual blood in an obstructed horn.
- **Menorrhagia** — from the increased endometrial surface area in a bicornuate uterus.
- **Dyspareunia** — with an associated vaginal septum.
- **Infertility** — more closely linked to pregnancy wastage than to infertility per se, since anomaly prevalence is similar in fertile and infertile women (exception: Müllerian agenesis, which precludes pregnancy without a gestational carrier).

Obstetric

- **Recurrent first- and second-trimester miscarriage** — the commonest presentation, most marked with septate uterus.
- **Cornual (rudimentary horn) ectopic pregnancy** — from transperitoneal sperm/ovum migration; typically ruptures around 16–20 weeks with life-threatening haemorrhage.
- **Cervical insufficiency** — uterine anomalies are a recognised risk factor.
- **Malpresentation** — transverse lie (arcuate/subseptate), breech (bicornuate, unicornuate, complete septate).
- **Preterm labour, fetal growth restriction, intrauterine death** — from reduced cavity size/muscle mass and abnormal uterine blood flow.
- **Prolonged/obstructed labour** — incoordinate uterine action; obstruction by a non-gravid horn.
- **Retained placenta and postpartum haemorrhage** — especially when the placenta implants over a uterine septum (poor vascularity).

Diagnosis

Modality	Utility
Hysterosalpingography (HSG)	Delineates internal cavity contour; cannot assess external fundal contour, so cannot reliably distinguish septate from bicornuate uterus; contraindicated in pregnancy
Transvaginal ultrasonography (2-D)	First-line; ~90–92% accuracy for cavity assessment
3-D transvaginal ultrasonography	~97% accuracy; images both internal cavity and external fundal contour in the coronal plane — the key to differentiating septate (flat/convex fundus, narrow inter-cavity angle) from bicornuate (concave fundal cleft) uterus

Modality	Utility
Magnetic resonance imaging (MRI)	Gold standard, up to ~100% accuracy; best for complex anatomy and pre-surgical planning; safe in pregnancy without contrast
Saline infusion sonography (SIS)	Distends cavity to define internal contour; contraindicated in pregnancy, requires a patent cavity
Hysteroscopy + laparoscopy	Combined "gold standard" for direct visualisation — hysteroscopy defines the internal cavity/septum, laparoscopy defines the external fundal contour; also allows simultaneous treatment
Renal tract imaging (ultrasonography/MRI/IVP)	Mandatory in every confirmed Müllerian anomaly to detect the ~40% coexistent renal anomaly

Passage of a uterine sound revealing two separate cavities, or finding a septate vagina with two cervices on speculum/bimanual examination, are simple clinical clues; a significant proportion, however, are diagnosed only intraoperatively (during curettage, manual removal of placenta, or caesarean section).

Management

General principle: Mere presence of a uterine anomaly is *not per se* an indication for surgery — treatment is reserved for symptomatic cases (recurrent pregnancy loss, obstruction, or cornual ectopic risk) after other causes of infertility/pregnancy loss are excluded.

- **Rudimentary non-communicating horn** — surgical excision (with the ipsilateral fallopian tube) is recommended, both to relieve obstructive symptoms and to eliminate the risk of rudimentary-horn (cornual) ectopic pregnancy.
- **Septate uterus — hysteroscopic metroplasty** (septal resection with a resectoscope or laser) is the treatment of choice for recurrent pregnancy loss: high success rate (80–89% live-birth improvement), short hospital stay, low morbidity, and it permits subsequent vaginal delivery.
- **Bicornuate uterus / uterus didelphys — abdominal metroplasty (unification operation)** is reserved for highly selected, otherwise-unexplained recurrent late miscarriage: septum excision (Strassman, Jones and Jones techniques) or septum incision (Tompkins technique). Live-birth success rates are variable (5–75%); caesarean delivery is mandatory in future pregnancies after abdominal metroplasty because of the risk of uterine rupture.
- **Arcuate uterus** — no treatment required; obstetric outcome is comparable to a normal uterus.
- **Cervical cerclage** — considered in women with a uterine anomaly and repetitive second-trimester loss, or with associated cervical hypoplasia/partial atresia, using the same candidacy criteria (history- or ultrasound-indicated) as for women without a uterine defect.
- **Antenatal surveillance** in a known uterine anomaly — serial growth scans (risk of fetal growth restriction), watch for malpresentation and preterm labour, and individualise mode of delivery

(caesarean is favoured for a rudimentary/main unicornuate horn pregnancy, obstructing horn, or after prior metroplasty).

- **Reproductive outcome without treatment** (guides counselling): best in uterus didelphys (~64% successful pregnancy) and septate uterus (~86%), intermediate in bicornuate uterus (~50%), and poorest in unicornuate uterus (~40%), for which no surgical correction is generally effective.

DIAGRAMS TO DRAW — IMAGE SUGGESTIONS

- ☐ *Fig 12.8 — American Fertility Society classification of various uterine malformations (Jeffcoate's Principles of Gynaecology 9e, p.227)*

High-yield exam pointers

- **AFS/ASRM 1988 seven-class system** — memorise the Roman numerals: I agenesis/hypoplasia, II unicornuate, III didelphys, IV bicornuate, V septate, VI arcuate, VII DES-related.
- Approximate frequencies: **septate 35% > bicornuate 26% > arcuate 18% > unicornuate 10% > didelphys 8%** — septate is commonest and also the anomaly most linked to reproductive loss.
- **Renal anomaly ~40%, skeletal anomaly ~12%** coexist — always image the urinary tract.
- Differentiating septate vs bicornuate needs the **external fundal contour**, seen only on **3-D ultrasonography, MRI, or laparoscopy** — HSG/2-D ultrasound/hysteroscopy alone cannot do this.
- **Treatment of choice:** hysteroscopic septal resection for septate uterus; excision for a non-communicating rudimentary horn (prevents cornual ectopic); abdominal metroplasty (Strassman/Jones/Tompkins) only for selected bicornuate/didelphys cases with recurrent loss.
- **OHVIRA/Herlyn-Werner-Wunderlich** = uterus didelphys + obstructed hemivagina + ipsilateral renal agenesis.
- **MRKH syndrome** = Müllerian (uterovaginal) agenesis with normal ovaries/karyotype/secondary sexual characteristics — cause of primary amenorrhoea with normal breast development.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

The AFS/ASRM 1988 classification is what Indian textbooks and RGUHS answers are built around; the newer ESHRE/ESGE (2013) morphology-based classification is used internationally and may be mentioned as a recent-advance addendum but is not required for full marks.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Williams Obstetrics 26e; Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e.

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What are the implications of uterine anomalies in Obstetrics & Gynaecology?

Asked in: Paper I 29-Jul-2021 — RGUHS MS Obstetrics & Gynaecology

Definition — Uterine (Müllerian) anomalies result from failure of normal development, midline fusion, or septal resorption of the paired paramesonephric (Müllerian) ducts during embryogenesis, which normally complete by 20 weeks of gestation. They range from mild (arcuate uterus) to complete duplication (didelphys) or absence (agenesis), and are best classified by the American Fertility Society/American Society for Reproductive Medicine (AFS/ASRM, 1988) seven-class system on 3-D ultrasound or MRI. Overall prevalence is 3-4% in the general population, rising to 5-10% after early pregnancy loss and up to 25% after recurrent second- or third-trimester loss.

Classification (AFS/ASRM, 1988)

Class	Anomaly	Embryologic defect
I	Segmental hypoplasia/agenesis (vaginal, cervical, fundal, tubal, or combined)	Müllerian hypoplasia/agenesis; vaginal + uterine agenesis = *Mayer-Rokitansky-Küster-Hauser (MRKH)* syndrome
II	Unicornuate uterus (± communicating/non-communicating rudimentary horn, ± no cavity, ± no horn)	One duct fails to develop fully
III	Uterine didelphys	Complete failure of fusion — two separate hemiuteri and cervices, ± longitudinal vaginal septum
IV	Bicornuate uterus (complete to internal os / partial)	Partial failure of fusion
V	Septate uterus (complete / partial)	Failure of septal resorption after fusion
VI	Arcuate uterus	Minor residual resorption defect — mildest form
VII	Diethylstilbestrol (DES)-related (T-shaped cavity)	In-utero DES exposure

Obstetric implications

Complication	Mechanism / most-linked anomaly
Recurrent first- and second-trimester miscarriage	Reduced cavity volume, poor placentation and vascularity over a septum — most marked with **septate uterus**

Complication	Mechanism / most-linked anomaly
Cornual (rudimentary horn) rupture	Pregnancy in a **non-communicating rudimentary horn** (unicornuate, class II); literature review found ~50% rupture, 80% of these before the third trimester, with only ~6% neonatal survival — a surgical emergency
Malpresentation (breech, transverse lie)	Reduced/distorted cavity space; a common cause of *habitual/recurrent* malpresentation
Preterm labour and birth	Diminished cavity capacity, coexisting cervical insufficiency
Fetal growth restriction	Abnormal uterine blood flow and reduced muscle mass (especially unicornuate main horn)
Cervical insufficiency	Congenitally associated cervical weakness; may warrant cerclage
Abnormal uterine action (inertia, incoordinate/asymmetric contractions)	Disordered myometrial architecture and action-potential propagation
Obstructed labour	Impaction of the fetal head/presenting part against the **non-pregnant horn of a bicornuate uterus**
Malplacentation (praevia, morbidly adherent placenta)	Implantation over a septum or near a cornu
Postpartum haemorrhage and retained placenta	Poor myometrial contractility, aberrant placentation
Increased operative delivery	Malpresentation, smaller/asymmetric cavity, uncertain safety of trial of labour after caesarean
Uterine rupture	Prior septal resection/metroplasty scar, or an unscarred gravid cornu in labour
Uterine torsion	Associated with bicornuate uterus (often with a coexisting fibroid)

Gynaecological implications

- **Infertility** — severe anomalies (Müllerian agenesis) preclude natural conception; for milder/moderate anomalies the prevalence is similar in fertile and infertile women, so the *obstetric* impact (pregnancy wastage) outweighs the fertility impact — the exception is agenesis, where only in-vitro fertilisation (IVF) with a gestational carrier permits a genetically related child.
- **Outflow obstruction** (non-communicating rudimentary horn, obstructed hemivagina, transverse vaginal septum) causes cryptomenorrhoea, haematometra/haematometrocolpos, and cyclical pelvic pain; the **OHVIRA/Herlyn-Werner-Wunderlich syndrome** (obstructed hemivagina + ipsilateral renal agenesis) is a classic triad with uterine didelphys.

- **Endometriosis** is more frequent when obstruction causes retrograde menstruation, adding dysmenorrhoea and dyspareunia.
- **Comorbid renal tract anomalies** are frequent because the paramesonephric and mesonephric systems develop in proximity — up to 40% with unicornuate uterus; renal imaging is mandatory whenever any Müllerian anomaly is diagnosed.
- **Cornual (rudimentary horn) ectopic pregnancy** risk, requiring prophylactic excision of an asymptomatic non-communicating horn even outside pregnancy.
- **Psychosexual impact** of vaginal agenesis/MRKH — need for vaginal dilators or surgical neovagina, and counselling regarding fertility options.

Diagnosis

Modality	Role / limitation
2-D transvaginal ultrasound	First-line screen; ~90-92% accuracy but cannot reliably define external fundal contour
3-D transvaginal ultrasound	Distinguishes septate from bicornuate uterus by fundal contour/interostial angle; ~97% accuracy; safe in pregnancy
MRI	Gold standard (up to 100% accuracy); best for rudimentary horns, associated renal anomalies; safe without contrast in pregnancy
Hysterosalpingography (HSG)	Defines cavity/tubal patency only, not external contour; contraindicated in pregnancy; may miss non-cavitary rudimentary horns
Sonohysterography (saline infusion sonography)	Improves internal cavity delineation; contraindicated in pregnancy
Hysteroscopy + laparoscopy	Combined reference standard in the non-pregnant fertility work-up; hysteroscopy is contraindicated in pregnancy

Management principles

- Image the renal tract whenever a Müllerian anomaly is found.
- Excise an asymptomatic **non-communicating rudimentary horn** (with the ipsilateral fallopian tube) prophylactically to prevent rupture or cornual ectopic pregnancy.
- **Hysteroscopic septal resection** in a septate uterus with recurrent pregnancy loss improves subsequent live-birth rates, though it does not improve infertility per se.
- **Metroplasty** (Strassman-type unification) for bicornuate uterus/didelphys is reserved for highly selected women with otherwise-unexplained recurrent second-trimester loss; scheduled delivery before labour onset is advised afterwards to avoid uterine rupture.

- **Cervical cerclage** is offered on the same criteria used for a normally shaped uterus, per current American College of Obstetricians and Gynecologists (ACOG)/Society for Maternal-Fetal Medicine guidance.
- Antenatally: serial growth scans and vigilance for malpresentation; a lower threshold for external cephalic version attempt where cavity permits.
- In labour: vaginal delivery is preferred where feasible; caesarean delivery for malpresentation, an obstructing non-pregnant horn, or failure to progress; the cavity is explored manually at caesarean if an anomaly is first suspected intraoperatively.
- Anticipate and actively manage postpartum haemorrhage and retained placenta given the higher baseline risk.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 5.4 — Types of congenital abnormalities. A: Double uterus (uterus didelphys) and double vagina. B: Double uterus with single vagina. C: Bicornuate uterus. D: Bicornuate uterus with a rudimentary left horn. E: Septate uterus. F: Unicornuate uterus. (Berek & Novak 16e, p.156)*

High-yield exam pointers

- Classify by **AFS/ASRM 1988, Class I-VII**: agenesis - unicornuate - didelphys - bicornuate - septate - arcuate - DES-related.
- Rudimentary horn pregnancy: ~50% rupture, 80% before the third trimester, ~6% neonatal survival — excise prophylactically if non-communicating.
- Obstetric mnemonic: **miscarriage, malpresentation, preterm birth, FGR, PPH/retained placenta, obstructed labour, increased caesarean rate.**
- Renal anomaly screening is mandatory with any Müllerian anomaly (up to 40% with unicornuate uterus).
- **OHVIRA/Herlyn-Werner-Wunderlich** = uterine didelphys + obstructed hemivagina + ipsilateral renal agenesis.
- 3-D ultrasound/MRI (not HSG) needed to tell septate from bicornuate uterus — this distinction decides whether hysteroscopic resection is possible.
- Hysteroscopic septal resection improves **pregnancy outcome**, not the underlying infertility rate.

> **NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM**
>
> Congenital uterine malformations are also being reclassified by the European Society of Human Reproduction and Embryology/European Society for Gynaecological Endoscopy (ESHRE/ESGE) system; the AFS/ASRM 1988 seven-class scheme above remains the one in current use across the cited textbooks and is sufficient for exam purposes.

SOURCE & COVERAGE

Williams Obstetrics 26e; Berek & Novak's Gynecology 16e; DC Dutta's Textbook of Obstetrics 9e.

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Congenital Abnormalities of the Uterus and their Significance

Asked in: Paper I 14-Jul-2020 — RGUHS MS Obstetrics & Gynaecology

Definition — Congenital uterine anomalies (Müllerian duct anomalies) result from a defect in the development, fusion, or resorption of the paired paramesonephric (Müllerian) ducts between the 7th and 20th weeks of intrauterine life, producing structural variation of the uterine corpus, cervix and/or vagina while ovarian function — of separate coelomic-epithelial origin — remains normal. Overall incidence is 3–4% of women, rising to 5–20% among women with recurrent miscarriage or preterm birth.

Embryological basis

- **Failure of duct development (agenesis)** — unilateral failure gives a unicornuate uterus; bilateral failure gives Müllerian agenesis, the Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome.
- **Failure of fusion of the two ducts (lateral fusion defect)** — complete failure gives uterus didelphys; partial failure gives a bicornuate uterus.
- **Failure of resorption of the midline septum** after the ducts have fused — gives a septate uterus (complete or partial/subseptate) or, when minimal, an arcuate uterus.
- **Failure of vertical fusion/canalisation** with the urogenital sinus — gives a transverse vaginal septum or cervical agenesis.
- Aetiology is incompletely understood — polygenic/multifactorial inheritance, HOX-gene (HOXA13) and WNT4 mutations, and teratogens (in-utero diethylstilbestrol, DES) are all implicated.

Classification

American Fertility Society (AFS, now ASRM) classification (1988), based on Buttram & Gibbons (1979):

Class	Anomaly	Description	Approx. relative frequency
I	Müllerian agenesis/hypoplasia	Segmental — vaginal, cervical, fundal, tubal or combined (MRKH syndrome)	Uncommon

Class	Anomaly	Description	Approx. relative frequency
II	Unicornuate uterus	Single-horned uterus ± a rudimentary horn (with or without a communicating/functioning cavity)	~10%
III	Uterus didelphys	Complete non-fusion — double uterus, double cervix, often double vagina	~8%
IV	Bicornuate uterus	Partial non-fusion — bicornis bicollis (two cervices) or unicollis (one cervix)	~26%
V	Septate uterus	Fused externally, but a fibromuscular septum divides the cavity — complete or partial	~35% (commonest)
VI	Arcuate uterus	Minimal fundal septal remnant — broad, shallow indentation	~18%; now regarded as a normal variant
VII	Diethylstilbestrol (DES)-related anomaly	T-shaped/hypoplastic cavity, cervical "cockscomb"/collar, from in-utero DES exposure	Rare now (DES withdrawn 1971)

Clinical & reproductive significance

Anomaly	Gynaecological significance	Obstetric significance	Favourable pregnancy outcome
Unicornuate	Endometriosis from retrograde flow via a non-communicating rudimentary horn; cryptomenorrhoea/dysmenorrhoea	Highest rate of miscarriage, preterm labour and malpresentation of all classes; a **rudimentary-horn (cornual) pregnancy** is a surgical emergency, typically rupturing around the 16th week	~40% (poorest)

Anomaly	Gynaecological significance	Obstetric significance	Favourable pregnancy outcome
Didelphys	Obstructed hemivagina with ipsilateral renal agenesis (OHVIRA syndrome) in 15–20%, right-sided in 65%	Each hemi-uterus can carry an independent pregnancy; preterm labour and malpresentation	~64% (best)
Bicornuate	Dysmenorrhoea; menorrhagia (increased endometrial surface area)	Cervical insufficiency, malpresentation, obstructed labour by the non-gravid horn, retained placenta/postpartum haemorrhage if the placenta implants over the septum	~50%
Septate	Commonest anomaly; least gynaecological morbidity, does not itself cause infertility	Highest risk of recurrent (especially 2nd-trimester) miscarriage, preterm labour, IUGR, malpresentation; miscarriage rate falls from 21–44% (untreated) to ~10% after hysteroscopic septal resection	~86% after treatment
Arcuate	None — normal anatomical variant	No adverse effect on reproductive outcome; no treatment needed	Normal

Associated anomalies — significance for work-up

- **Renal tract anomalies coexist in ~40%** of Müllerian anomalies (unilateral renal agenesis, ectopic/pelvic/horseshoe kidney) — particularly the ipsilateral kidney in a unicornuate uterus and in OHVIRA (didelphys). Renal ultrasonography (± intravenous pyelogram/MRI) is mandatory whenever a uterine anomaly is diagnosed.
- **Skeletal anomalies coexist in ~12%.**
- **MRKH syndrome** = vaginal agenesis + uterine agenesis/hypoplasia with normal ovaries, normal 46,XX karyotype and normal secondary sexual characters — an important cause of primary amenorrhoea; associated renal (40%) and skeletal (12%) anomalies must be actively sought.

Diagnosis & management principles

- **Transvaginal ultrasonography** (2-D/3-D) is first-line and distinguishes septate from bicornuate uteri by the fundal contour — a single, broad, sometimes slightly concave fundus in the septate uterus versus two entirely separate fundi divided by a distinct midline cleft in the bicornuate uterus.
- **Hysterosalpingography** outlines the endometrial cavity but cannot assess the outer fundal contour, so it cannot reliably separate a septate from a bicornuate uterus.
- **MRI** is most accurate for complex/combined anomalies; combined **hysteroscopy + laparoscopy** (simultaneous internal and external assessment) remains definitive when imaging is equivocal and is used to plan surgery.
- **Mere presence of an anomaly is, by itself, not an indication for surgery.**
- **Septate uterus** with recurrent miscarriage/infertility → **hysteroscopic septal resection** (resectoscope or laser): success 80–89%, shorter hospital stay, and permits vaginal delivery thereafter, unlike abdominal metroplasty.
- **Bicornuate/didelphys** with otherwise-unexplained recurrent poor outcome → **abdominal metroplasty** — excision (Strassman; Jones and Jones) or incision (Tompkins) of the septum; rarely performed now, and mandates caesarean delivery in future pregnancies.
- **Rudimentary horn** (communicating, or non-communicating with functioning endometrium) → laparoscopic excision to prevent cornual ectopic pregnancy/haematometra.
- **Cervical cerclage** where cervical insufficiency coexists (bicornuate/didelphys uterus).
- **MRKH** → graduated vaginal dilators (Frank method) first-line; McIndoe-Reed vaginoplasty if needed; biological pregnancy is possible only via IVF with a gestational carrier, since ovarian function is normal.

> **DIAGRAMS TO DRAW — IMAGE SUGGESTIONS**
>
> ☐ *Fig 51.5 — Diagrammatic demonstration of congenital uterine abnormalities according to the ESHRE/ESGE classification (Jeffcoate's Principles of Gynaecology 9e, p.880)*

High-yield exam pointers

- **AFS/Buttram-Gibbons classification, Classes I–VII** — I agenesis, II unicornuate, III didelphys, IV bicornuate, V septate, VI arcuate, VII DES-related.
- **Septate = commonest** (~35%) but best post-surgical outcome (86%); **unicornuate = worst outcome** (~40%).
- **Renal anomaly in ~40%**, skeletal anomaly in ~12% — always image the renal tract.
- **OHVIRA** = Obstructed Hemi-Vagina + Ipsilateral Renal Agenesis, a didelphys variant, usually right-sided (65%).

- Rudimentary-horn pregnancy ruptures around **16 weeks** — excise a functioning, non-communicating rudimentary horn prophylactically.
- Hysteroscopic metroplasty success **80–89%** vs abdominal metroplasty **5–75%** (the latter mandates future caesarean delivery).
- Arcuate uterus = **normal variant**, no treatment required.

NOTE — FOR REFERENCE, NOT TO BE WRITTEN IN THE EXAM

A newer ESHRE/European Society for Gynaecological Endoscopy (ESGE) consensus classification (2013) is used in some centres alongside the classic AFS/Buttram-Gibbons system reproduced above; the RGUHS-standard texts (DC Dutta's Gynaecology, Berek & Novak) still teach the AFS (1988) scheme, which remains the expected exam answer.

SOURCE & COVERAGE

DC Dutta's Textbook of Gynaecology 7e; Speroff's Clinical Gynecologic Endocrinology & Infertility 9e; Berek & Novak's Gynecology 16e; Jeffcoate's Principles of Gynaecology 9e.

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