OB Obstetrics

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Acronyms

AC	abdominal circumference
ACOG	American College of Obstetricians and Gynecologists
AFI	amniotic fluid index
AFLP	acute fatty liver of pregnancy
AFV	amniotic fluid volume
AP	anteroposterior
APGAR	Appearance, pulse, grimace, activity, and respiration
aPTT	activated partial thromboplastin time
APS	antiphospholipid antibody syndrome
ARDS	acute respiratory distress syndrome
β-hCG	beta human chorionic gonadotropin
BPP	biophysical profile
C/S	Cesarean section
CHF	congestive heart failure
CMV	cytomegalovirus
CPD	cephalopelvic disproportion
CT	computed tomography scan
CTG	cardiotocography
CVS	chorionic villus sampling
CXR	chest X-ray
D&C	dilatation and curettage
DIC	disseminated intravascular coagulation
DM	diabetes mellitus
DVT	deep vein thrombosis
ECV	external cephalic version
EDD	estimated date of delivery
EFM	electronic fetal monitoring
eFTS	enhanced first trimester screen
EFW	estimated fetal weight
FDP	fibrin degradation products
FHR	fetal heart rate
FISH	fluorescence in situ hybridization
FL	femur length
FM	fetal movement
FPG	fasting plasma glucose
FTS	first trimester screen
GA	gestational age
GBS	Group B *Streptococcus*
GDM	gestational diabetes mellitus
GTN	gestational trophoblastic neoplasia
HC	head circumference
HELLP	hemolysis, elevated liver enzymes, low platelets
IMM	intramyometrial
IOL	induction of labour
IPS	integrated prenatal screen
ITP	idiopathic thrombocytopenic purpura
IUFD	intrauterine fetal death
IUGR	intrauterine growth restriction
IVH	intraventricular hemorrhage
L/S	lecithin-sphingomyelin ratio
LFT	liver function test
LLDP	left lateral decubitus position
LMP	last menstrual period
LMWH	low molecular weight heparin
MSAFP	maternal serum α-fetoprotein
MSS	maternal serum screening
MTX	methotrexate
N/V	nausea/vomiting
NIPT	non-invasive prenatal testing
NPO	nothing by mouth
NST	non-stress test
NTD	neural tube defects
NTUS	nuchal translucency ultrasound
OA	occiput anterior
OGCT	oral glucose challenge test
OGTT	oral glucose tolerance test
ONTD	open neural tube defect
OP	occiput posterior
OT	occiput transverse
PAPP-A	pregnancy-associated plasma protein A
PCR	polymerase chain reaction
PE	pulmonary embolism
PG	plasma glucose
PPD	postpartum depression
PPH	postpartum hemorrhage
PPROM	preterm premature rupture of membranes
PROM	premature rupture of membranes
PTL	preterm labour
QF-PCR	quantitative fluorescence-polymerase chain reaction
RDS	respiratory distress syndrome
RhIG	Rh immune globulin
ROM	rupture of membranes
SFH	symphysis fundal height
SOGC	Society of Obstetricians and Gynaecologists of Canada
SVD	spontaneous vaginal delivery
TENS	transcutaneous electrical nerve stimulation
TOLAC	trial of labour after Cesarean section
T1	first trimester
T2	second trimester
T3	third trimester
TB	tuberculosis
TPN	total parenteral nutrition
TTP	thrombotic thrombocytopenic purpura
U/S	ultrasound
UTI	urinary tract infection
V/Q	ventilation/perfusion lung scan
VBAC	vaginal birth after Cesarean
vWD	von Willebrand disease
VTE	venous thromboembolism

Basic Anatomy Review

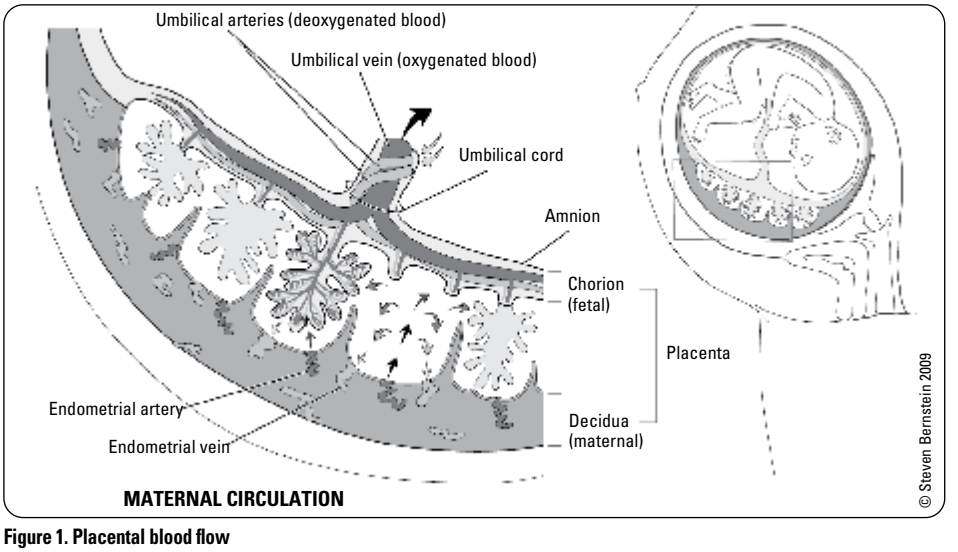

Figure 1. Placental blood flow

Placenta

- site of fetal nutritive, respiratory, and excretory function
- discoid mass composed of fetal (chorion frondosum) and maternal (decidua basalis) tissues divided by fissures into cotyledons (lobules) on the uterine side
- produces hormones such as progesterone, placental lactogen, estrogen, relaxin, β-hCG, and infant growth factors
- poor implantation can lead to spontaneous abortion
- abnormal location, implantation, or detachment can lead to antepartum hemorrhage (see *Obstetrical Hemorrhage*, OB13)

Pregnancy

Diagnosis of Pregnancy

History

- symptoms: amenorrhea, nausea and/or vomiting, breast tenderness, urinary frequency, and fatigue
- obstetrical and gynecological history: year, location, mode of delivery, duration of labour, sex, gestational age, birth weight, and complications of every pregnancy; organize into GTPAL format
  - Gravidity (G)
    - **G**: total number of pregnancies of any gestation (multiple gestation=one pregnancy)
    - includes current pregnancy, abortions, ectopic pregnancies, and hydatidiform moles

- Parity (TPAL)
  - **T**: number of term deliveries (>37 wk)
  - **P**: number of premature deliveries (20-36+6 wk)
  - **A**: number of abortions (ending <20 wk)
    - induced (therapeutic) and spontaneous (miscarriage)
  - **L**: number of living children

Physical Signs
- uterine enlargement
- breast engorgement, areola darkening, and prominent vascular patterns
- Goodell's sign: softening of the cervix (4-6 wk)
- Chadwick's sign: bluish discolouration of the cervix and vagina due to pelvic vasculature engorgement (6 wk)
- Hegar's sign: softening of the cervical isthmus (6-8 wk)

Investigations
- β-hCG: peptide hormone composed of α and β subunits produced by placental trophoblastic cells – maintains the corpus luteum during pregnancy
  - positive in serum 9 d post-conception, positive in urine 28 d after 1st day of LMP
  - plasma levels usually double every 1.4-2.0 d, peak at 8-12 wk, then fall, but continue to be measurable until delivery
- levels less than expected suggest ectopic pregnancy, abortion, inaccurate dates, or some normal pregnancies
- levels greater than expected suggest: multiple gestation, molar pregnancy, Trisomy 21, or inaccurate dates
- U/S:
  - transvaginal
    - 5 wk GA: gestational sac visible
    - 6 wk GA: fetal pole visible
    - 7-8 wk GA: fetal heart activity visible
  - transabdominal
    - 6-8 wk GA: intrauterine pregnancy visible

β-hCG Rule of 10s
10 IU at time of missed menses
100,000 IU at 10 wk (peak)
10,000 IU at term

Trimesters
- T1 (first trimester): 1-14 wk
- T2 (second trimester): 14-28 wk
- T3 (third trimester): 28-42 wk
- Normal pregnancy term: 37-42 wk

Maternal Physiologic Adaptations to Pregnancy

Table 1. Physiologic Changes During Pregnancy

Skin	Increased pigmentation of perineum and areola, chloasma (pigmentation changes under eyes and on bridge of nose), linea nigra (midline abdominal pigmentation), spider angiomas, palmar erythema due to increased estrogen, and striae gravidarum due to connective tissue changes
Cardiovascular	Hyper-dynamic circulation Increased cardiac output, heart rate, and blood volume Decreased blood pressure: decreased PVR and decreased venous return from enlarging uterus compressing IVC and pelvic veins Increased venous pressure leads to risk of varicose veins, hemorrhoids, and leg edema
Hematologic	Hemodilution causes physiologic anemia and apparent decrease in hemoglobin and hematocrit Increased leukocyte count but impaired function leads to improvement in some autoimmune diseases Gestational thrombocytopenia: mild (platelets >70,000/μL) and asymptomatic, normalizes within 2-12 wk following delivery Hypercoagulable state: increased risk of DVT and PE but also decreased bleeding at delivery
Respiratory	Increased incidence of nasal congestion Increased O_2 consumption to meet increased metabolic requirements Elevated diaphragm (i.e. appears more "barrel-chested") Increased minute ventilation leads to decreased CO_2 resulting in mild respiratory alkalosis that helps CO^2 diffuse across the placenta from fetal to maternal circulation Decreased total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV) No change in vital capacity (VC) and FEV_1
Gastrointestinal	GERD due to increased intra-abdominal pressure and progesterone (causing decreased sphincter tone and delayed gastric emptying) Increased incidence of gallstones due to progesterone causing increased gallbladder stasis Constipation due to progesterone causing decreased GI motility and hemorrhoids as a result of constipation and increased intra-abdominal pressure
Genitourinary	Increased urinary frequency due to increased total urinary output Increased incidence of UTI and pyelonephritis due to urinary stasis (see *Urinary Tract Infection*, OB29) Glycosuria that can be physiologic especially in the T3; consider testing for GDM if noted in first 2 trimesters Ureters and renal pelvis dilation (R>L) due to progesterone-induced smooth muscle relaxation and uterine enlargement Increased CO and thus increased GFR leads to decreased creatinine (normal in pregnancy 35-44 mmol/L), uric acid, and BUN
Neurologic	Increased incidence of carpal tunnel syndrome and Bell's palsy
Endocrine	Thyroid: moderate enlargement (not clinically detectable) and increased basal metabolic rate Increased total thyroxine and thyroxine binding globulin (TBG) Normal free thyroxine index and FSH levels Adrenal: increased maternal cortisol throughout pregnancy (total and free) Calcium: decreased total maternal Ca^{2+} due to decreased albumin Free ionized Ca^{2+} (i.e. active) proportion remains the same due to parathyroid hormone (PTH), resulting in increased bone resorption and gut absorption, and increased bone turnover (but no loss of bone density due to estrogen inhibition) (see *Diabetes Mellitus*, OB26)

PVR – pulmonary vascular resistance; FEV_1 – forced expiratory volume in 1 second; CO – cardiac output; GFR – glomerular filtration rate; BUN – blood urea nitrogen

Antepartum Care

- can be provided by an obstetrician, family physician, midwife, or multidisciplinary team (based on patient preference and risk factors)

Preconception Counselling

- 3-8 wk GA is a critical period of organogenesis, so early preparation is vital
- **past medical history**: optimize medical conditions and review medications prior to pregnancy (see *Medical Complications of Pregnancy*, OB26, and *Medications*, OB49)
- supplementation
  - folic acid: encourage diet rich in folic acid and consider supplementation from 8-12 wk pre-conception until end of T1 to prevent NTD
    - 0.4-1 mg daily in all women; 5 mg if previous NTD, antiepileptic medications, DM, or BMI >35 kg/m^2
  - iron supplementation (in cases of iron deficiency anemia), prenatal vitamins
- **risk modification**
  - lifestyle/social: smoking, alcohol, drug use, domestic violence, occupational risks, poor social support, balanced nutrition, and physical fitness (see Family Medicine)
  - medications: discuss teratogenicity of medications so they may be adjusted, replaced, or stopped if necessary
  - infection screening: rubella, HBsAg, VDRL, Pap smear, gonorrhea/chlamydia, HIV, TB testing based on travel and working in health care, history of varicella or vaccination, parvovirus immunity if exposed to small children, cytomegalovirus immunity if health care worker, and toxoplasmosis serology in case of proximity to cats or gardening
  - genetic testing as appropriate for high risk groups (see *Prenatal Screening*, Table 2); consider genetics referral in known carriers, recurrent pregnancy loss/stillbirth, family members with developmental delay, birth anomalies, genetic diseases, and consanguinity

Family doctors and midwives to consider OB consultation if:
- Insulin-dependent GDM
- VBAC
- HTN
- Multiple gestation
- Malpresentation
- Active antepartum hemorrhage
- PTL/PPROM
- Failure to progress/descend
- Induction/augmentation if high risk
- Tears: 3rd or 4th degree
- Retained placenta

Note: Guidelines vary by institution and by provincial midwifery colleges

Advise all women capable of becoming pregnant to supplement their diet with 0.4 mg/d of folic acid (CTFPHC Grade II-2-A Evidence)

Prenatal and genetic screening are voluntary and require proper counselling and informed consent before proceeding HIV is done automatically in some provinces as opt-out testing; need to inform patient of this

Initial Prenatal Visit

- usually within 8-12 wk of the 1st day of LMP or earlier if <20 or >35 yr old, bleeding, very nauseous, or other risk factors present

History

- gestational age by dates from the 1st day of the LMP
  - Naegele's rule: 1st day of LMP + 1 year + 7 d – 3 mo
  - e.g. LMP = 1 Apr 2014, EDD = 8 Jan 2015 (modify if cycle >28 d by adding number of d >28)
  - EDD by LMP not reliable if irregular menstrual cycle, or if patient unsure of the LMP
- if LMP unreliable, get a dating U/S which could coincide with nuchal translucency at ~12 wk
- EDD by T1 U/S more reliable than LMP if difference is greater than 5 d from LMP due date
- history of present pregnancy (e.g. bleeding, N/V) and all previous pregnancies
- past medical, surgical, and gynecological history
- prescription and non-prescription medications
- family history: genetic diseases, birth defects, multiple gestation, and consanguinity
- social history: smoking, alcohol, drug use, and domestic violence (see Family Medicine)

In history of previous pregnancies, **ALWAYS** ask:
GTPAL
Year
Sex
Weight
Gestational age
Mode of delivery
Length of labour
Complications

Physical Exam

- complete physical exam to obtain baseline patient information – BP and weight important for interpreting subsequent changes
- BMI for risk stratification (risk of DVT, GDM, and pre-eclampsia all increase with greater BMI)

Ask every woman about abuse – not just those whose situations raise suspicion of abuse AND ask as early as possible in pregnancy

Investigations

- blood work
  - CBC, blood group and Rh status, antibody screen, and infection screening as per preconception counselling
- urine R&M, midstream urine C&S
  - screen for bacteriuria and proteinuria
- pelvic exam
  - Pap smear (only if required according to patient history and provincial screening guidelines), cervical or urine PCR for *N. gonorrhoeae* (GC) and *C. trachomatis*

Estimated Date of Delivery (EDD) Determination
- By LMP if menses regular, patient reliable historian
- By T1 U/S if irregular menses
- By embryo age and date of transfer if IVF

- T1 U/S up to 13+6/7 weeks GA is most accurate method of establishing GA
- Changes to the EDD must be documented and discussed with the patient
- Pregnancy without U/S confirming or revising the EDD prior to 22+0/7 GA is considered sub-optimally dated

Nausea and Vomiting

Epidemiology

- affects 50-90% of pregnant women
- often limited to T1 but may persist beyond this

Management
- rule out other causes of N/V especially if refractory to initial therapy
- weigh frequently, assess level of hydration, and test urine for ketones
- non-pharmacological
  - frequent small meals (bland, dry, salty are better tolerated), encourage any safe appealing foods
  - electrolyte oral solutions (Pedialyte®, Gatorade®)
  - stop prenatal vitamins and if T1, substitute with folic acid or adult/children's vitamins that are low in iron
  - increase sleep/rest
  - ginger (maximum 1000 mg/d)
  - acupuncture, acupressure, and mindfulness-based cognitive therapy
- pharmacological
  - first line: pyridoxine (B6) monotherapy or doxylamine/pyridoxine (Diclectin) combination 4 tablets PO daily (1 q am, 1 q lunch and 2 qhs) up to maximum of 8 tablets/d
  - H1 receptor antagonists should be considered for acute or chronic episodes of N/V in pregnancy
  - metoclopramide and phenothiazines can be used as an adjunctive therapy for severe N/V in pregnancy
  - Ondansetron if severe N/V and other anti-emetics have failed
- severe/refractory
  - consider homecare with IV fluids and parenteral anti-emetics, hospitalization

Hyperemesis Gravidarum

Definition
- intractable N/V, usually presents in T1 then diminishes; occasionally persists throughout pregnancy
- affects ~1% of pregnancies

Etiology
- multifactorial with hormonal, immunologic, and psychological components
- rapidly rising β-hCG ± estrogen levels may be implicated

Investigations
- rule out systemic causes: GI, pyelonephritis, thyrotoxicosis
- rule out other obstetrical causes: multiple gestation, GTN, HELLP syndrome
- CBC, electrolytes, BUN, creatinine, LFTs, urinalysis
- U/S

Management
- thiamine supplementation may be indicated
- non-pharmacological (see *Nausea and Vomiting*, OB4)
- pharmacological options
  - doxylamine/pyridoxine (for dosage, see *Nausea and Vomiting*, OB4)
  - dimenhydrinate can be safely used as an adjunct to Diclectin® (1 suppository bid or 25 mg PO qid)
  - other adjuncts: hydroxyzine, pyridoxine, phenothiazine, metoclopramide
  - also consider: ondansetron or methylprednisolone (avoid steroids in T1 due to increased risk of oral clefting)
  - if severe: admit to hospital, NPO initially then small frequent meals; correct hypovolemia, electrolyte disturbance, and ketosis; TPN (if very severe) to reverse catabolic state

Complications
- maternal
  - dehydration, electrolyte, and acid-base disturbances
  - Mallory-Weiss tear
  - Wernicke's encephalopathy, if protracted course
  - death
- fetal: usually none, IUGR is 15x more common in women losing >5% of pre-pregnancy weight

Subsequent Prenatal Visits

Timing
- for uncomplicated pregnancies, SOGC recommends q4-6 wk until 30 wk, q2-3 wk from 30 wk, and q1-2 wk from 36 wk until delivery

Assess at Every Visit
- estimated GA
- history: fetal movements, uterine bleeding, leaking, cramping, questions, concerns
- physical exam: BP, weight gain, SFH, Leopold's maneuvers (T3) for lie, position, and presentation of fetus
- investigations: urinalysis for proteinuria in high risk women; fetal heart rate starting at 10-12 wk using Doppler U/S

Symphysis Fundal Height

Symphysis Fundal Height (SFH)

12 wk	Uterine fundus at pubic symphysis
20 wk	Fundus at umbilicus
20-36 wk	SFH should be within 2 cm of GA

SFH< Dates
- Date miscalculation
- IUGR
- Fetal demise
- Oligohydramnios
- Early engagement

SFH> Dates
- Date miscalculation
- Multiple gestation
- Polyhydramnios
- large for gestational age (familial, DM)
- Fibroids

Leopold's Maneuvers
- performed after 30-32 wk gestation
- first maneuver: to determine which fetal part is lying furthest away from the pelvic inlet
- second maneuver: to determine the location of the fetal back
- third maneuver: to determine which fetal part is lying above the pelvic inlet
- fourth maneuver: to locate the fetal brow

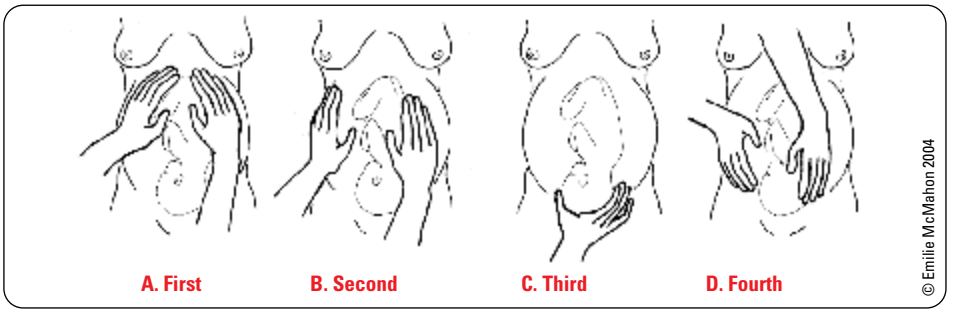

Figure 2. Leopold's maneuvers (T3)
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Prenatal Screening and Diagnostic Tests

Screening Tests
- testing should only occur following counselling and with informed consent from the patient

Table 2. High-Risk Population Screening Tests

Disease (Inheritance)	Population(s) at Risk	Screening Test(s)
Thalassemia (AR)	Mediterranean, South East Asian, Western Pacific, African, Middle Eastern, Caribbean, South American	CBC (MCV and MCH), Hb electrophoresis, or HPLC
Sickle Cell (AR)	African, Caribbean, Mediterranean, Middle Eastern, Indian, South American	CBC (MCV and MCH), Hb electrophoresis, or HPLC
Cystic Fibrosis (CF) (AR)	Family history of CF in patient or partner or medical condition linked to CF like male infertility	CFTR gene DNA analysis
Tay Sachs Disease (AR)	Ashkenazi Jewish*, French Canadians, Cajun	Enzyme assay HEXA, or DNA analysis HEXA gene
Fragile X Syndrome (X-linked)	Family history – confirmed or suspected	DNA analysis: *FMR-1* gene

AR = autosomal recessive; HEXA = hexosaminidase A; HPLC = high performance liquid chromatography
*If both partners are Ashkenazi Jewish, test for Canavan disease and Familial Dysautonomia (FD); if family history of a specific condition, look for carrier status: e.g. Gaucher, CF, Bloom syndrome, Niemann-Pick disease, etc. In all cases, if both partners are positive, refer for genetic counselling.

Table 3. Gestation-Dependent Screening Investigations

Gestational Age (wk)	Investigations	Details
8-12	Dating U/S, possible Pap smear, chlamydia/gonorrhea testing, urine C&S (detect asymptomatic bacteriuria), HIV, VDRL, HepBsAg, Rubella IgG, Parvovirus IgM or IgG if high risk (small child at home or daycare worker/primary teacher), Varicella IgG if no history of disease/immunization, CBC, blood group and screen, urine C&S (detect asymptomatic bacteriuria)	
>10	NIPT	Measures cell-free fetal DNA in maternal circulation
10-12	CVS	
11-14	Enhanced FTS IPS Part 1	Measures 1. Nuchal translucency on U/S 2. β-hCG 3. PAPP-A 4. Placental growth factor (enhanced FTS only) 5. MSAFP (enhanced FTS only)
11-14	Nuchal translucency U/S	
15-16 to term	Amniocentesis	
15-20	IPS Part 2	Measures 1. MSAFP 2. β-hCG 3. Unconjugated estrogen (estriol or μE3) 4. Inhibin A

Routine T2 U/S at 18-22 wk Helps Determine
- Number of fetuses
- GA (if no prior U/S)
- Location of placenta
- Fetal anomalies

Table 3. Gestation-Dependent Screening Investigations (continued)

Gestational Age (wk)	Investigations	Details
15-20	MSS	Measures 1. MSAFP 2. β-hCG 3. Unconjugated estrogen (estriol or μE3) 4. Inhibin A
18-20 to term	Fetal movements (quickening)	
18-20	U/S for dates, fetal growth, and anatomy assessment	
24-28	Gestational Diabetes Screen 50 g OGCT	See *Diabetes Mellitus*, OB26
28	Repeat CBC RhIG for all Rh-negative women	
35-37	GBS screen	See *Group B Streptococcus*, OB28
6 wk postpartum	Discuss contraception, menses, breastfeeding, depression, mental health, support Physical exam: breast exam, pelvic exam including Pap smear (only if due as per provincial screening)	

Maternal serum screen is also referred to as Triple Screen; if Inhibin A is also tested, it is referred to as Quadruple Screen

DDx of Increased MSAFP
- Incorrect GA
- >1 fetus (e.g. twins)
- Fetal demise
- ONTD
- Abdominal wall defects (e.g. omphalocele)

ULTRASOUND SCREENING
- 8-12 wk GA: dating U/S (most accurate form of pregnancy dating)
- measurement of crown-rump length (margin of error: ± 5 d)
- EDD should be based on T1 U/S if available
- 11-14 wk GA: NTUS
- measures the amount of fluid behind the neck of the fetus
- early screen for Trisomy 21 (may also detect cardiac and other aneuploidies like Turner syndrome)
- NT measurement is necessary for the FTS and IPS Part 1
- 18-20 wk GA: growth and anatomy U/S (margin of error: ± 10 d)
- earlier or subsequent U/S performed when medically indicated

NON-INVASIVE PRENATAL TESTING (NIPT)
- analyses maternal blood for circulating cell-free fetal DNA (ccffDNA) at 9-10 wk GA onwards. Requires dating U/S for accuracy

Advantages
- increased accuracy (high detection rate (DR), low false positive rate [FPR]) highly sensitive for Trisomy 21 (DR 99%, FPR 0.1- can also look for Trisomy 18 (DR 96%, FPR 0.1%), 13 (DR 91%, FPR 0.1%), Turner syndrome (DR 90%, FPR 0.2%), and some other disorders (DiGeorge syndrome, Cri Du Chat, Prader-Willi, Angelman syndrome, XY disorders)
- increased positive predictive value
- earlier timing with results available in 1-2 weeks where parents can potentially have a CVS at 11-13 weeks for diagnosis over an amniocentesis after 15 weeks

Disadvantages
- does not screen for ONTD
- high cost to patient (only covered in some provinces [ON and BC] in certain cases)
- need to confirm with invasive testing (it is a screening test, not a diagnostic test)
- does not test for all aneuploidies
- gives no result in 1-5% of cases (insufficient fetal fraction more common with elevated BMI)
- not applicable to donor eggs

Table 4. Comparison of FTS, MSS, and IPS

eFTS	MSS	IPS
11-14 wk	15-20 wk	11-13 wk U/S-nuchal translucency 11-14 wk: eFTS blood 15-20 wk: MSS blood including inhibin A
Risk estimate for 1. Down syndrome (Trisomy 21): increased NT, increased β-hCG, decreased PAPP-A 2. Trisomy 18: increased NT, decreased PAPP-A, decreased β-hCG Note: does not measure risk of ONTD and should be combined with MSAFP at 15-20 wk Useful when patient wants results within the T1 More accurate estimate of Down syndrome risk than MSS, sensitivity ~85% (when combined with age) 5% false positive rate Patients with positive screen should be offered CVS, amniocentesis, or NIPT (covered in some provinces, self-pay in others)	Risk estimate for 1. ONTD: increased MSAFP (sensitivity 80-90%) 2. Trisomy 21: decreased MSAFP, increased β-hCG, decreased μE3 (sensitivity 65%) 3. Trisomy 18: decreased MSAFP, decreased β-hCG, decreased μE3, decreased inhibin A (sensitivity 80%) Only offered alone if patient missed the time window for IPS or eFTS 8% baseline false positive rate for Trisomy 21, lower for NTD and Trisomy 18 Patients with positive screen should be offered U/S, amniocentesis, or NIPT (covered in some provinces, self-pay in others)	Risk estimate for ONTD, Trisomy 21, Trisomy 18 Sensitivity ~85-90% 2% false positive rate Patients with positive screen should be offered U/S and/or amniocentesis or NIPT (covered in some provinces, self-pay in others)

Note: In twins, eFTS, MSS, and IPS are not applicable; screen with NT, NIPT for chromosomal abnormalities and MSAFP for ONTDs

Diagnostic Tests
- Diagnostic tests available:
  - amniocentesis
  - chorionic villus sampling

Indications
- age >35 yr (increased risk of chromosomal anomalies)
  - risk factors in current pregnancy
  - abnormal U/S
- abnormal prenatal screen (IPS, eFTS, or MSS)
- past history/family history of:
  - chromosomal anomaly or genetic disease
  - either parent a known carrier of a genetic disorder or balanced translocation
  - consanguinity
  - >3 spontaneous abortions

AMNIOCENTESIS
- U/S-guided transabdominal extraction of amniotic fluid performed as early as 15 weeks GA

Indications
- identification of genetic and chromosomal anomalies (15-16 wk gestation) as per indications above
- confirmation of positive NIPT testing
- positive eFTS/IPS/MSS
- assessment of fetal lung maturity (T3) via the L/S ratio (lecithin:sphingomyelin)
  - if >2:1, RDS is less likely to occur

Advantages
- also screens for ONTD (acetylcholinesterase and amniotic AFP) – 96% accurate
- in women >35 yr, the risk of chromosomal anomaly (1/180) is greater than the risk of miscarriage from the procedure
- more accurate genetic testing than CVS

Disadvantages
- 1/200 to 1/900 risk of procedure-related pregnancy loss, depending on local experience
- results take 14-28 d; QF-PCR or FISH can be done on chromosomes X, Y, 13, 18, 21, 22 to give preliminary results in 48 h

Compared to CVS, amniocentesis has a higher accuracy of prenatal cytogenetic diagnosis (99.8% vs. 97.5%) and lower risk of spontaneous abortion (0.5% vs. 1-2%)

Risk Factors for Neural Tube Defects

GRIMM
Genetics: family history of NTD (risk of having second child with NTD is increased to 2-5%), consanguinity, chromosomal (characteristic of Trisomy 13, 18, and 21)
Race: European Caucasians > African Americans, 3-fold higher in Hispanics
Insufficient vitamins: zinc and folate
Maternal chronic disease (e.g. DM)
Maternal use of antiepileptic drugs

General population risk for NTD is 0.1%

CHORIONIC VILLUS SAMPLING
- biopsy of fetal-derived chorion using a transabdominal needle or transcervical catheter at 10-12 wk

Advantages
- enables pregnancy to be terminated earlier than with amniocentesis
- rapid karyotyping and biochemical assay within 48 h, including FISH analysis
- high sensitivity and specificity

Disadvantages
- 1% risk of procedure-related pregnancy loss
- does not screen for ONTD
- 1-2% incidence of genetic mosaicism "false negative" results

ISOIMMUNIZATION SCREENING

Definition
- isoimmunization: antibodies (Ab) produced against a specific RBC antigen (Ag) as a result of antigenic stimulation with RBC of another individual

Etiology
- maternal-fetal circulation normally separated by placental barrier, but sensitization can occur and can affect the current pregnancy, or more commonly, future pregnancies
- anti-Rh Ab produced by a sensitized Rh-negative mother can lead to fetal hemolytic anemia
- risk of isoimmunization of an Rh-negative mother with an Rh-positive ABO-compatible infant is 16%
- sensitization routes
  - incompatible blood transfusions
  - previous fetal-maternal transplacental hemorrhage (e.g. ectopic pregnancy, abruption)
  - invasive procedures in pregnancy (e.g. prenatal diagnosis, cerclage, D&C)
  - any type of abortion
  - labour and delivery
  - trauma (e.g. car accident, fall, etc.)

Rh Antibody Titre
A positive titre (≥1:16) indicates an increased risk of fetal hemolytic anemia

Investigations
- screening with indirect Coombs test at first visit for blood group, Rh status, and antibodies
- Kleihauer-Betke test used to determine extent of fetomaternal hemorrhage by estimating volume of fetal blood volume that entered maternal circulation
- detailed U/S for hydrops fetalis
- middle cerebral artery Dopplers are done to assess degree of fetal anemia; if not available, bilirubin is measured by serial amniocentesis to assess the severity of hemolysis
- cordocentesis for fetal Hb should be used cautiously (not first-line)

Standard dose of 300 µg of Rhogam® sufficient for 30 mL of fetal blood. Give additional 10 µg of Rhogam® for every mL of fetal blood over 30 mL

Prophylaxis
- exogenous Rh IgG (Rhogam® or WinRho®) binds to Rh antigens of fetal cells and prevents them from contacting maternal immune system
- Rhogam® (120-300 µg) given to all Rh negative and antibody screen negative women in the following scenarios:
  - routinely at 28 wk GA (provides protection for ~12 wk)
  - within 72 h of the birth of a Rh positive fetus
  - with any invasive procedure in pregnancy (CVS, amniocentesis)
  - as part of management of ectopic pregnancy
  - with miscarriage or therapeutic abortion
  - with an antepartum hemorrhage
  - with trauma
- Rhogam® 300 µg provides sufficient prophylaxis for 30 mL fetal Rh positive whole blood
- a Kleihauer-Betke test or flow cytometry can be used to measure the relative quantity of fetal blood in maternal circulation to determine if additional Rhogam® is indicated (if >30 mL fetal blood)
- if Rh negative and Ab screen positive, follow mother with serial monthly Ab titres throughout pregnancy + U/S ± serial amniocentesis as needed (Rhogam® has no benefit, as B cells sensitized antibodies already in circulation)

Treatment
- falling biliary pigment warrants no intervention (usually indicative of either unaffected or mildly affected fetus)
- intrauterine transfusion between 18-35 wk GA of O-negative packed RBCs may be required for severely affected fetus
- early delivery of the fetus for exchange transfusion following 35 wk GA

Complications
- anti-Rh IgG can cross the placenta and cause fetal RBC hemolysis resulting in fetal anemia, CHF, edema, ascites
- severe cases can lead to hydrops fetalis (edema in at least two fetal compartments due to fetal heart failure secondary to anemia) or erythroblastosis fetalis (moderate to severe immune-mediated hemolytic anemia)

Fetal Surveillance

DDx of Decreased Fetal Movements

DASH
Death of fetus
Amniotic fluid decreased
Sleep cycle of fetus
Hunger/Thirst

- patients will generally first notice fetal movement ("quickening") at 18-20 wk in primigravidas; can occur 1-2 wk earlier in multigravidas; can occur 1-2 wk later if placenta is implanted on the anterior wall of uterus
- if the patient is concerned about decreased fetal movement, she is counselled to choose a time when the fetus is normally active to count movements (usually recommended after 26 wk)
- all high-risk women should be told to do FM counts
  - ≥6 movements in 2 h expected
  - If there is a subjective decrease in fetal movement, time how long it takes to feel 10 discreet movements, laying on the left in a quiet setting may facilitate feeling subtle movements
  - if 10 movements take more than 2 h, further assessment is indicated, and patient should present to labour and delivery triage for non-stress test

NON-STRESS TEST

Normal NST: 2 accels, >15 bpm from baseline, lasting >15 s in 20 min

Definition
- FHR tracing ≥20 min using an external Doppler to assess FHR and its relationship to fetal movement (see *Fetal Monitoring in Labour*, OB33)

Describe NST: baseline rate, absent/minimal/moderate/marked variability, accelerations present/not present, decelerations early/late/variable

Indication
- any suggestion of uteroplacental insufficiency or suspected compromise in fetal well-being

Table 5. Classification of Intrapartum EFM Tracings

	Normal Tracing (Category 1)	Atypical Tracing* (Category 2)	Abnormal Tracing* (Category 3)
Baseline	110-160 bpm	100-110 bpm or >160 bpm for <30 min Rising baseline	Bradycardia <100 bpm Tachycardia >160 for >30 min Erratic baseline
Variability	6-25 bpm (moderate) ≤5 (absent or minimal) for <40 min	5 (absent or minimal) for 40-80 min	≤5 for 80 min Sinusoidal 25 bpm for >10 min
Decelerations	None or occasional variable <30 s	Variable decelerations 30-60 s duration	Variable decelerations >60 s Late deceleration(s)
Accelerations in Term Fetus	2 accelerations with acme of ≥15 bpm, lasting 15 s over <40 min of testing	2 accelerations with acme of ≥15 bpm, lasting 15 s in 40-80 min	<2 accelerations with acme (peak) of contraction of ≥15 bpm, lasting 15 s in >80 min
Accelerations in Preterm Fetus (<32 wk)	>2 accelerations with acme of >10 bpm, lasting 10 s in <40 min	<2 accelerations with acme of >10 bpm, lasting 10 s in 40-80 min	<2 accelerations with acme of >10 bpm, lasting 10 s in >80 min
Action	FURTHER ASSESSMENT OPTIONAL, based on total clinical picture	FURTHER ASSESSMENT REQUIRED	URGENT ACTION REQUIRED An overall assessment of the situation and further investigation with U/S or BPP is required; some situations will require delivery

Adapted from: SOGC, Fetal Health Surveillance: Antepartum and Intrapartum Consensus Guideline, September 2007

Reassuring BPP (8/8)

LAMB
Limb extension + flexion
AFV 2 cm x 2 cm
Movement (3 discrete)
Breathing (one episode x 30 s)

Overlap >20 mm to the internal os in the T3 of pregnancy is highly predictive of the need for a C/S. Any degree of overlap after 35 wk is an indication for a C/S

Operating Characteristics
- false positive rate depends on duration; false negative rate = 0.2-0.3%

Interpretation
- normal: at least 2 accelerations of FHR >15 bpm from the baseline lasting >15 s in 20 min
- abnormal: <2 accelerations of FHR in 40 min
- if no observed accelerations or fetal movement in the first 20 min, stimulate fetus (fundal pressure, acoustic/vibratory stimulation) and continue monitoring for 30 min

BIOPHYSICAL PROFILE

Definition
- U/S assessment of the fetus ± NST

Indications
- post-term pregnancy
- decreased fetal movement
- IUGR
- any other suggestion of fetal distress or uteroplacental insufficiency

Table 6. Scoring of the BPP

Parameter	Reassuring (2 points)
Tone	At least one episode of limb extension followed by flexion
Movement	Three discrete movements
Breathing	At least one episode of breathing lasting at least 30 s
Amniotic Fluid Volume (AFV)*	Fluid pocket of 2 cm in 2 axes

*AFV is a marker of chronic hypoxia, all other parameters indicate acute hypoxia

Interpretation
- 8: perinatal mortality rate 1:1000; repeat BPP as clinically indicated
- 6: perinatal mortality 31:1000; repeat BPP in 24 h
- 0-4: perinatal mortality rate 200:1000; deliver fetus if benefits of delivery outweigh risks

Counselling of the Pregnant Woman

Nutrition

- Canada's Food Guide to Healthy Eating suggests
  - eating a varied diet with plenty of vegetables and fruits, whole grains, dairy products, and lean meats or plant proteins
  - caloric increase of ~100 kCal/d in the T1, ~300 kCal/d in the T2 and T3, and ~450 kCal/d during lactation (less if BMI >25)
  - daily multivitamin with folic acid should be continued during pregnancy

Nutrients in Pregnancy

- folate: 0.4-1 mg/d for first 12 wk (5 mg/d if high risk)
  - supports increase in blood volume, growth of maternal and fetal tissue, and decrease in incidence of NTD
  - foods rich in folic acid include: spinach, lentils, chick peas, asparagus, broccoli, peas, brussels sprouts, corn, and oranges
- calcium: 1200-1500 mg/d
  - maintains integrity of maternal bones, skeletal development of fetus, and breast milk production
- vitamin D: 1000 IU
  - promotes calcium absorption
- iron: 0.8 mg/d in T1, 4-5 mg/d in T2, and >6 mg/d in T3
  - supports maternal increase in blood cell mass, supports fetal and placental tissue
  - required amounts exceed normal body stores and typical intake, and therefore need supplemental iron
  - iron is the only known nutrient for which requirements during pregnancy cannot be met by diet alone (see *Iron and Folate Deficiency Anemia*, OB26)
- essential fatty acids – supports fetal neural and visual development
  - contained in vegetable oils, margarines, peanuts, and fatty fish

Caffeine

- diuretic and stimulant that readily crosses placenta
- less than 300 mg/d is considered safe
- relationship between caffeine and IUGR is unknown (ACOG)
- SOGC states 1-2 cups/d are safe during pregnancy

Sources of Caffeine
- 5 oz cup coffee: 40-180 mg
- 5 oz brewed tea: 20-90 mg
- 12 oz cola: 46 mg
- Red Bull®: 67 mg
- Dark chocolate bar: 10 mg
- 8 oz hot chocolate: 5 mg

Herbal Teas and Preparations

- not enough scientific information about safety of various herbs and herbal products to recommend their use during pregnancy
- some herbal teas can have toxic or pharmacological effects on the mother or fetus
- raspberry leaf tea often used at term to promote labour
- herbal teas considered safe in moderation (2-3 cups/d): citrus peel, ginger, lemon balm, linden flower (unless cardiac condition), orange peel, and rose hip

Foodborne Illnesses

- microbiological contamination of food may occur through cross-contamination and/or improper food handling
  - listeriosis (*Listeria monocytogenes*) and toxoplasmosis (*Toxoplasma gondii*) are of concern during pregnancy
  - avoid consumption of raw meats and fish, raw hotdogs, raw eggs, raw sprouts (especially alfalfa), and unpasteurized dairy products or juices
  - avoid unpasteurized soft cheeses, deli meats, smoked salmon, and pâtés as they may be sources of Listeria
- chemical contamination of food
  - current guideline for mercury of 0.5 ppm in fish is not considered harmful for the general population, including pregnant women
  - Health Canada advises pregnant women to limit consumption of top predator fish such as shark, swordfish, king mackerel, and tilefish

Lifestyle

- exercise under physician guidance; "talk test" = should be able to speak while exercising; avoid supine position after 20 wk GA
- absolute contraindications
  - ruptured membranes, preterm labour, hypertensive disorders of pregnancy, incompetent cervix, IUGR, multiple gestations (>3), placenta previa after 28 wk, persistent T2 or T3 bleeding, uncontrolled type I DM, uncontrolled thyroid disease, serious cardiovascular or respiratory disease, and other systemic disorders

- relative contraindications
  - recurrent pregnancy loss, gestational hypertension, history of spontaneous preterm birth, mild/moderate cardiovascular or respiratory disease, symptomatic anemia, malnutrition, eating disorder, twin pregnancy after 28 wk, and other significant medical conditions
- weight gain: optimal gain depends on pre-pregnancy BMI (varies from 6.8-18.2 kg)
- work: strenuous work, extended hours and shift work during pregnancy may be associated with greater risk of low birth weight, prematurity, and spontaneous abortion
- air travel acceptable in T2; airline cut off for travel is 36-38 wk gestation depending on the airline, to avoid giving birth on the plane
- sexual intercourse: may continue, except in patients at risk for: abortion, preterm labour, or placenta previa; breast stimulation may induce uterine activity, and is discouraged in high-risk patients near term
- smoking: assist/encourage to reduce or quit smoking
  - increased risk of decreased birth weight, placenta previa/abruption, spontaneous abortion, preterm labour, and stillbirth
- alcohol: no amount of alcohol is safe in pregnancy; encourage abstinence from alcohol during pregnancy; alcohol increases incidence of abortion, stillbirth, and congenital anomalies
  - fetal alcohol syndrome (see Pediatrics, P24)
- cocaine: microcephaly, growth retardation, prematurity, and abruptio placentae
- marijuana: smoking associated with low birth weight infants
- biopsychosocial considerations: discuss birth plan, offer community maternal resources

Weight Gain in Pregnancy

BMI	Total Gain	Weekly Gain in T2 & T3
<18.5	28-40 lb	1-1.3 lb/wk
18.5-24.9	25-35 lb	1 lb/wk
>25-29.9	15-25 lb	0.5-0.7 lb/wk
>30	11-20 lb	0.4-0.6 lb/wk

Medications

- most drugs cross the placenta to some extent
- very few drugs are teratogenic, but very few drugs have proven safety in pregnancy
- use any drug with caution and only if necessary
- analgesics: acetaminophen preferable to ASA or ibuprofen

Table 7. Documented Adverse Effects, Weigh Benefits vs. Risks, and Consider Medication Change

Contraindicated Medication	Adverse Effect
ACE Inhibitor	Fetal renal defects, IUGR, oligohydramnios
Carbamazepine	ONTD in 1-2%
Chloramphenicol	Grey baby syndrome (fetal circulatory collapse 2° to toxic accumulation)
Lithium	Ebstein's cardiac anomaly, goitre, hyponatremia
Misoprostol	Mobius syndrome (congenital facial paralysis with or without limb defects), spontaneous abortion, preterm labour
NSAIDs	Premature closure of the ductus arteriosus after 30 wk GA (prior to that, indomethacin used for tocolysis)
Phenytoin	Fetal hydantoin syndrome in 5-10% (IUGR, mental retardation, facial dysmorphogenesis, congenital anomalies)
Retinoids (e.g. Accutane®)	CNS, craniofacial, cardiac, and thymic anomalies
Sulpha drugs	Anti-folate properties, therefore theoretical risk in T1; risk of kernicterus in T3
Tetracycline	Stains infant's teeth, may affect long bone development
Valproate	Congenital malformation (including ONTD) up to 9%
Warfarin	Increased incidence of spontaneous abortion, stillbirth, prematurity, IUGR, fetal warfarin syndrome (nasal hypoplasia, epiphyseal stippling, optic atrophy, mental retardation, intracranial hemorrhage)

Drug Resources During Pregnancy and Breastfeeding
- Hale T. Medications and mothers' milk, 11th ed. Pharmasoft Publishing, 2004
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

Immunizations

Intrapartum
- administration is dependent on the risk of infection vs. risk of immunization complications
- safe: tetanus toxoid, diphtheria, influenza, hepatitis B, and pertussis
- avoid live vaccines (risk of placental and fetal infection): polio, measles/mumps/rubella, and varicella
- contraindicated: oral typhoid
- the Public Health Agency of Canada recommends:
  - all pregnant women receive the influenza vaccine
  - all pregnant women should be given Tdap every pregnancy irrespective of immunization history ideally between 27-32 weeks but can be given at 13-26 weeks if high risk of preterm labour. If Tdap was given in T1 (i.e. prior to pregnancy recognition), it does not need to be repeated

Postpartum
- rubella vaccine for all non-immune mothers. If they have had an adult booster and remain non-immune, they should not be revaccinated and pregnancy should be deferred for at least 1 mo following vaccination
- hepatitis B vaccine should be given to infant within 12 h of birth if maternal status unknown or positive – follow-up doses at 1 and 6 mo
- any vaccine required/recommended is generally safe postpartum

Radiation

- ionizing radiation exposure is considered teratogenic at high doses
  - if indicated for maternal health, should be done
- imaging not involving direct abdominal/pelvic high dosage radiation is not associated with adverse effects
  - higher dosage to fetus: plain x-ray of lumbar spine/abdomen/pelvis, barium enema, CT abdomen/pelvis/lumbar spine
- radioactive isotopes of iodine are contraindicated
- no known adverse effects from U/S or MRI (long-term effects of gadolinium unknown, avoid if possible)

Table 8. Approximate Fetal Doses from Common Diagnostic Procedures

Examination	Estimated Fetal Dose (cGy)	Number of Exams Safe in Pregnancy
Plain Film		
Abdomen	0-14	35
Pelvis	0-11	45
Lumbar spine	0-17	29
Thoracic spine	0.009	555
Chest (2 views)	<0.001	5000
CT	0-8	6
Abdomen	2-5	2
Pelvis	0-24	20
Lumbar spine	0.006	833
Chest		

Adapted from: Cohen-Kerem, et al. 2005 and Valentin 2000

Radiation in Pregnancy
- Necessary amount to cause miscarriage: >5 cGy
- Necessary amount to cause malformations: >20-30 cGy

Obstetrical Hemorrhage

Definition
- vaginal bleeding from 20 wk to term

Differential Diagnosis
- bloody show (represents cervical changes/early stages of dilation) – most common etiology in T3
- placenta previa
- abruptio placentae – most common pathological etiology in T3
- vasa previa
- cervical lesion (cervicitis, polyp, ectropion, cervical cancer)
- uterine rupture
- other: bleeding from bowel or bladder, abnormal coagulation

Table 9. Comparison of Placenta Previa and Abruptio Placentae

	Placenta Previa	Abruptio Placentae
Definition	Abnormal location of the placenta near, partially, or completely over the internal cervical os	Premature separation of a normally implanted placenta after 20 wk GA
Etiology	Idiopathic	Idiopathic
Epidemiology	0.5-0.8% of all pregnancies	1-2% of all pregnancies
Risk Factors	History of placenta previa (4-8% recurrence risk) Multiparity Increased maternal age Multiple gestation Uterine tumour (e.g. fibroids) or other uterine anomalies Uterine scar due to previous abortion, C/S, D&C, myomectomy	Previous abruption (recurrence rate 5-16%) Maternal HTN (chronic or gestational HTN in 50% of abruptions) or vascular disease Cigarette smoking (>1 pack/d), excessive alcohol consumption, cocaine Multiparity and/or maternal age >35 yr PPROM Rapid decompression of a distended uterus (polyhydramnios, multiple gestation) Uterine anomaly, fibroids Trauma (e.g. motor vehicle collision, maternal battery)
Bleeding	PAINLESS	Usually PAINFUL

Placenta Previa

Definition
- placenta implanted in the lower segment of the uterus, presenting ahead of the leading pole of the fetus
- placental position is described in relation to the internal os as "mm away" or "mm of overlap"

Clinical Features
- PAINLESS bright red vaginal bleeding (recurrent), may be minimized and cease spontaneously but can become catastrophic
- mean onset of bleeding is 30 wk GA, but onset depends on degree of previa
- physical exam
  - do not perform digital vaginal exam until ruling out placenta previa
  - uterus soft and non-tender
  - presenting fetal part high or displaced
  - FHR usually normal
  - shock/anemia correspond to degree of apparent blood loss
- complications
  - fetal
    - perinatal mortality low but still higher than with a normal pregnancy
    - prematurity (bleeding often dictates early C/S)
    - intrauterine hypoxia (acute or IUGR)
    - fetal malpresentation
    - PPROM
    - risk of fetal blood loss from placenta, especially if incised during C/S
  - maternal
    - <1% maternal mortality
    - hemorrhage and hypovolemic shock, anemia, acute renal failure, and pituitary necrosis (Sheehan syndrome)
    - placenta accreta – especially if previous uterine surgery or anterior placenta previa
    - hysterectomy

Investigations
- transvaginal U/S is more accurate than transabdominal U/S at diagnosing placenta previa at any gestational age
- spontaneously resolution is likely with increasing uterine distention if the placenta obscures the internal os by less than 20 mm at 20 wk GA
- transvaginal U/S should be repeated in the T3 as continued change in the placental location is likely

Do NOT perform a vaginal exam until placenta previa has been ruled out by U/S

Management
- goal: keep pregnancy intrauterine until the risk of continuing pregnancy outweighs the risk of preterm delivery
- stabilize and monitor
  - maternal stabilization: large bore IV with hydration, O_2 for hypotensive patients
  - maternal monitoring: vitals, urine output, blood loss, blood work (hematocrit, CBC, INR/PTT, platelets, fibrinogen, FDP, type and cross match)
  - electronic fetal monitoring
  - U/S assessment: when fetal and maternal conditions permit, determine fetal viability, GA, and placental position
- Rhogam® if mother is Rhnegative
- Kleihauer-Betke test to determine extent of fetomaternal transfusion and administer Rhogam® at adequate dose
- GA <37 wk and minimal bleeding: expectant management
  - admit to hospital
  - limited physical activity, no douches, enemas, or sexual intercourse
  - consider corticosteroids for fetal lung maturity
  - delivery when fetus is mature or hemorrhage indicating maternal or fetal compromise
- GA ≥37 wk – deliver by C/S

Abruptio Placentae

Definition
- partial or total placental detachment that is premature and caused by bleeding at the decidual-placental interface
- occurring >20 wk gestation

Clinical Features
- classification
  - total (fetal death inevitable) vs. partial
  - external/revealed/apparent: blood dissects downward toward cervix
  - internal/concealed/occult (20%): blood dissects upward toward fetus, may or may not present with vaginal bleeding
  - most are mixed
- presentation
  - usually PAINFUL (80%) vaginal bleeding (bleeding not always present if abruption is concealed), uterine tenderness, uterine contractions/hypertonus
  - pain: sudden onset, constant, localized to lower back and uterus
  - shock/anemia out of proportion to apparent blood loss
  - ± fetal distress, fetal demise (15% present with demise), bloody amniotic fluid (fetal presentation typically normal)
  - ± coagulopathy

Abruptio placentae is the most common cause of DIC in pregnancy

Complications
- fetal complications: perinatal mortality 25-60%, prematurity, intrauterine hypoxia
- maternal complications: <1% maternal mortality, DIC (in 20% of abruptions), acute renal failure, anemia, hemorrhagic shock, pituitary necrosis (Sheehan syndrome), or amniotic fluid embolus

Investigations
- clinical diagnosis, U/S not sensitive for diagnosing abruption (sensitivity = 15%)

Management
- maternal stabilization: large bore IV with hydration, O_2 for hypotensive patients
- maternal monitoring: vitals, urine output, blood loss, blood work (hematocrit, CBC, PTT/PT, platelets, fibrinogen, FDP, type and cross match)
- electronic fetal monitoring
- blood products on hand (red cells, platelets, cryoprecipitate) because of DIC risk
- Rhogam® if Rh negative
  - Kleihauer-Betke test may confirm abruption
- abruption without fetal/maternal compromise (mild abruption)
  - GA <37 wk: use serial Hct to assess concealed bleeding, deliver when fetus is mature or when hemorrhage dictates
  - GA ≥37 wk: stabilize and deliver
- abruption with fetal/maternal compromise (moderate to severe abruption)
  - hydrate and restore blood loss and correct coagulation defect if present
  - vaginal delivery if no contraindication and no evidence of fetal or maternal distress
  - C/S if live fetus and fetal or maternal distress develops with fluid/blood replacement, labour fails to progress, or if vaginal delivery otherwise contraindicated

Kleihauer-Betke Test
Quantifies fetal cells in the maternal circulation

Vasa Previa

Definition
- unprotected fetal vessels pass over the cervical os; associated with velamentous insertion of cord into membranes of placenta or succenturiate (accessory) lobe

Epidemiology
- 1 in 5000 deliveries – higher in twin pregnancies

Clinical Features
- PAINLESS vaginal bleeding and fetal distress (tachy-to-bradyarrhythmia in a sinusoidal pattern)
- if undiagnosed, 50% perinatal mortality, increasing to 75% if membranes rupture (most infants die of exsanguination)
- if diagnosed antenatally on U/S without labour or symptoms, then 97% survival

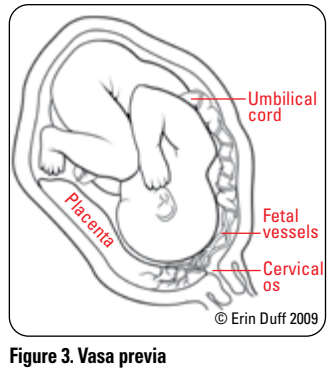


Figure 3. Vasa previa

Investigations
- Apt test (NaOH mixed with the blood) can be done immediately to determine if the source of bleeding is fetal (supernatant turns pink) or maternal (supernatant turns yellow)
- Wright's stain on blood smear and look for nucleated red blood cells (in cord, not maternal blood)

Management
- planned C/S (35-36 weeks) or if bleeding, emergency C/S (since bleeding is from fetus, a small amount of blood loss can have catastrophic consequences)

Obstetrical Complications

Preterm Labour

Definition
- labour between 20 and 37 wk gestation

Etiology
- idiopathic (most common)
- maternal: infection (recurrent pyelonephritis, untreated bacteriuria, chorioamnionitis), HTN, DM, chronic illness, mechanical factors (previous obstetric, gynecological, and abdominal surgeries); socio-environmental (poor nutrition, smoking, drugs, alcohol, stress), pre-eclampsia
- maternal-fetal: PPROM (common), polyhydramnios, placenta previa, abruptio placentae, or placental insufficiency
- fetal: multiple gestation, congenital abnormalities, fetal hydrops
- uterine: excessive enlargement (hydramnios, multiple gestation), malformations (intracavitary leiomyomas, septate uterus, and Müllerian duct abnormalities)

Epidemiology
- preterm labour complicates about 10% of pregnancies

Risk Factors
- prior history of spontaneous PTL is the most important risk factor
- prior history of large or multiple cervical excisions (cone biopsy) or mechanical dilatation (D&C)
- cervical length: measured by transvaginal U/S (cervical length >30 mm has high negative predictive value for PTL before 34 wk)
- identification of bacterial vaginosis and ureaplasma urealyticum infections
  - routine screening not supported by current data, but it is reasonable to screen high-risk women
- family history of preterm birth
- smoking
- late maternal age
- multiple gestation

Prevention of Preterm Labour
A. Cervical Cerclage
- **definition**: placement of cervical sutures at the level of the internal os, usually at the end of the T1 or in the T2 and removed in the T3
- indications: cervical incompetence (i.e. cervical dilation and effacement in the absence of increased uterine contractility)
- diagnosis of cervical incompetence
  - obstetrical Hx: silent cervical dilation, recurrent T2 losses, cervical procedures such as loop excisions
  - ability of cervix to hold an inflated Foley catheter during a hysterosonogram
  - transvaginal U/S of cervical length is recommended only for high-risk pregnancies and only before 30 wk GA
- proven benefit in the prevention of PTL in women with primary structural abnormality of the cervix (e.g. conization of the cervix, connective tissue disorders)

B. Progesterone
- progesterone thought to maintain uterine quiescence; however exact mechanism of action is unclear
- if previous PTL: 17-alphahydroxyprogesterone 250 mg IM weekly from 16+0 to 36 wk GA
- if short cervix: 200 mg daily vaginally from time of diagnosis to 36 wk GA
- superior to cerclage in preventing preterm labour of singletons not due to cervical incompetence

C. Lifestyle Modification
- smoking cessation, substance use reduction, treatment of GU infections (including asymptomatic UTIs), and patient education regarding risk factors

Predicting PTL
- fetal fibronectin: a glycoprotein in amniotic fluid and placental tissue
  - positive if >50 ng/mL; NPV > PPV
  - done if 1 or more signs of preterm labour (regular contractions >6/h, pelvic pressure, low abdominal pain and/or cramps, low backache)
  - done only if: 24-34 weeks, intact membranes, <3 cm dilated, established fetal well being
  - contraindicated as well if: cerclage, active vaginal bleeding, vaginal exam, or sex in last 24 h
  - if negative, not likely to deliver in 7-14 d (>95% accuracy); if positive increased risk of delivery, may need admission/transfer to centre that can do delivery ± tocolysis and/or corticosteroids

Clinical Features
- regular contractions (2 in 10 min, >6/h)
- cervix >1 cm dilated, >80% effaced, or length <2.5 cm

Preterm labour is the most common cause of neonatal mortality in the US

Positive fetal fibronectin in cervicovaginal fluid (>50 ng/mL) at 24 wk gestation predicted spontaneous PTL at <34 wk with sensitivity of 23%, specificity of 97%, PPV of 25%, NPV of 96%

Ultrasonographic Cervical Length Assessment in Predicting Preterm Birth in Singleton Pregnancies
J Obstet Gynaecol Can 2018;40(2);154-61
Recommendations:
1. Transabdominal ultrasonography should not be used for cervical length assessment to predict preterm birth (II-2D).
2. Transvaginal ultrasonography is the preferred route for cervical assessment to identify women at increased risk of spontaneous preterm birth and may be offered to women at increased risk of preterm birth (II-2B).
3. Transperineal ultrasonography may be offered to women at increased risk of preterm birth if transvaginal ultrasonography is either unacceptable or unavailable (II-2B).
4. Because of poor positive predictive values and sensitivities and lack of proven effective interventions, routine transvaginal cervical length assessment is not recommended in women at low risk (II-2E).
5. In women presenting with suspected preterm labour, transvaginal sonographic assessment of cervical length may be used to help in determining who is at high risk of preterm delivery and may be helpful in preventing unnecessary intervention. It is unclear whether this information results in a reduced risk of preterm birth (II-2B).
6. In asymptomatic women with a history of spontaneous preterm birth and an ultrasonographically diagnosed short cervical length (<25 mm) prior to 24 weeks of gestation, cervical cerclage should be considered to reduce the risk of preterm birth (I-B).
7. In all asymptomatic women who present with membranes at or protruding past the external cervical os, an emergency cerclage should be considered to reduce the risk of preterm delivery (I-B).

Management

A. Initial

- transfer to appropriate facility if stable
  - tocolysis and first dose of antenatal steroids prior to transfer
- hydration (normal saline at 150 mL/h)
- bed rest in left lateral decubitus position to reduce aortocaval compression and improve cardiac output
- sedation (morphine)
- avoid repeated pelvic exams (increased infection risk)
- U/S examination of fetus (GA, BPP, position, placenta location, estimated fetal weight)
- prophylactic antibiotics; (for GBS) important to consider if PPROM (e.g. erythromycin controversial, but may help to delay delivery)

B. Tocolysis (Suppression of Labour)

- does not inhibit preterm labour completely, but may delay delivery (used for <48 h) to allow for betamethasone valerate (Celestone®) and/or transfer to appropriate centre for care of the premature infant
- requirements (all must be satisfied)
  - preterm labour
  - live, immature fetus, intact membranes, cervical dilatation of <4 cm
  - absence of maternal or fetal contraindications
- contraindications
  - maternal: bleeding (placenta previa or abruption), maternal disease (HTN, DM, heart disease), preeclampsia or eclampsia, chorioamnionitis
  - fetal: erythroblastosis fetalis, severe congenital anomalies, fetal distress/demise, IUGR, multiple gestation (relative)
- agents
  - calcium channel blockers: nifedipine
    - 20 mg PO loading dose followed by 20 mg PO 90 min later
    - 20 mg can be continued q3-8h for 72 h or to a max of 180 mg
    - 10 mg PO q20min x 4 doses
    - relative contraindications: nifedipine allergy, hypotension, hepatic dysfunction, concurrent beta-mimetics or magnesium sulfate use, transdermal nitrates, or other antihypertensive medications
    - absolute contraindications: maternal congestive heart failure, aortic stenosis
  - prostaglandin synthesis inhibitors: indomethacin
    - 1st line for early preterm labour (<30 wk GA) or polyhydramnios
    - 50-100 mg PR loading dose followed by 25-50 mg q6h x 8 doses for 48 hours

C. Antenatal Corticosteroids

- betamethasone valerate (Celestone®) 12 mg IM q24h x 2 doses or dexamethasone 6 mg IM q12h x 4 doses
  - given between 24 to 33+6 wk GA if expected to deliver in the next 7 d
  - women between 22+0 and 23+6 wk GA at high risk of preterm birth within the next 7 d should be provided with multidisciplinary consultation regarding high likelihood for severe perinatal morbidity and mortality and associated maternal morbidity – consider antenatal corticosteroids therapy if early intensive care is requested and planned
  - specific maternal contraindications: active TB
- enhance fetal lung maturity, reduce perinatal death, reduce incidence of severe RDS, and intraventricular hemorrhage, necrotizing enterocolitis, and neonatal sepsis

D. Neuroprotection

- $MgSO_4$ 4 g bolus followed by 1 g/h infusion for at least 4 h if imminent delivery expected and <32 wk GA

Prognosis

- prematurity is the leading cause of perinatal morbidity and mortality
- 24 wk = 50% survival (may be higher in tertiary care centres with level 3-4 NICU)
- 30 wk or 1500 g (3.3 lb) = 90% survival
- 33 wk or 2000 g (4.4 lb) = 99% survival
- morbidity due to asphyxia, hypoxia, sepsis, RDS, intraventricular cerebral hemorrhage, thermal instability, retinopathy of prematurity, bronchopulmonary dysplasia, necrotizing enterocolitis

Cerclage for Short Cervix on Ultrasonography in Women with Singleton Gestations and Previous Preterm Birth
Obstet Gynecol 2011;117:663-71
Purpose: To determine if cerclage prevents preterm birth (<35 wk gestation) and perinatal mortality and morbidity among women with previous spontaneous preterm birth, asymptomatic singleton gestation, and short cervical length (<25 mm before 24 wk gestation) on transvaginal ultrasonography.
Methods: Meta-analysis of randomized trials identified using searches on MEDLINE, PUBMED, EMBASE, and the Cochrane Library.
Results: 5 trials included. Preterm birth was significantly lower among women receiving cerclage vs. those not receiving (RR = 0.70, 95% CI 0.55-0.89). Cerclage also significantly reduced preterm birth before 24, 28, 32, and 37 wk gestation. Perinatal mortality and morbidity were significantly lower in the cerclage group (RR = 0.64, 95% CI 0.45-0.91).
Conclusions: Cerclage significantly prevents preterm birth and perinatal mortality and morbidity in this specific group of women.

Tocolytics for Preterm Premature Rupture of Membranes
Cochrane DB Syst Rev 2014;2:CD007062
Purpose: To assess the potential benefits and harms of tocolysis in women with PPROM.
Selection Criteria: Pregnant women with singleton pregnancies and PPROM (23-36 wk and 6 d GA).
Results: 8 studies with 408 women total. Prophylactic tocolysis with PPROM was associated with increased overall latency, without additional benefits for maternal/neonatal outcomes. For women with PPROM before 34 wk, there was a significantly increased risk of chorioamnionitis in women who received tocolysis. Neonatal outcomes were not significantly different.
Conclusion: Although there are limitations to the studies, there is currently insufficient evidence to support tocolytic therapy for women with PPROM, as there was an increase in maternal chorioamnionitis without significant benefits to the infant.

Premature Rupture of Membranes

Definitions

- PROM: premature (pre-labour) rupture of membranes at any GA
- prolonged ROM: >24 h elapsed between rupture of membranes and onset of labour
- preterm ROM: ROM occurring before 37 wk gestation
- PPROM: preterm (before 37 wk) AND premature (pre-labour) rupture of membranes

Membrane status determined by

- Pooling of fluid on speculum exam
- Increased pH of vaginal fluid (nitrazine test)
- Ferning of fluid under light microscopy
- Decreased AFV on U/S

Risk Factors

- maternal: multiparity, cervical incompetence, infection (cervicitis, vaginitis, STI, UTI), family history of PROM, low socioeconomic class/poor nutrition
- fetal: congenital anomaly, multiple gestation
- other risk factors associated with PTL

Clinical Features

- history of fluid gush or continued leakage

Investigations
- sterile speculum exam (avoid introduction of infection)
  - pooling of fluid in the posterior fornix
  - cascading: fluid leaking out of cervix with cough/valsalva
- nitrazine (basic amniotic fluid turns nitrazine paper blue)
  - low specificity as it can also be positive with blood, urine, or semen
- ferning: salt in amniotic fluid evaporates, giving amniotic fluid the appearance of ferns on microscopy
- U/S to rule out fetal anomalies; assess GA, presentation, and BPP

Management
- admit for expectant management and monitor vitals q4h, daily NST, WBC count, increased surveillance
- avoid introducing infection by minimizing examinations
  - consider administration of betamethasone valerate (Celestone®) to accelerate maturity if <34 weeks if no evidence of infection
  - consider tocolysis for 48 h to permit administration of steroids if PPROM induces labour
- screen women for UTIs, STIs, GBS infection and treat with appropriate antibiotics if positive (treat GBS at time of labour)
- if not in labour or labour not indicated, consider antibiotics: penicillins or macrolide antibiotics are the antibiotics of choice
- deliver urgently if evidence of fetal distress and/or chorioamnionitis

Table 10. PROM Management

Degree of Prematurity	Management
22-25 wk	Individual consideration with counselling of parents regarding risks to preterm infants
26-34 wk	Expectant management as prematurity complications are significant
34-36 wk	"Grey zone" where risk of death from RDS and neonatal sepsis is the same
≥37 wk	Induction of labour since the risk of death from sepsis is greater than RDS

Prognosis
- varies with gestational age
- 90% of women with PROM at 28-34 wk GA go into spontaneous labour within 1 wk
- 50% of women with PROM at <26 wk GA go into spontaneous labour within 1 wk
- complications: cord prolapse, intrauterine infection (chorioamnionitis), premature delivery, limb contracture, and pulmonary hypoplasia especially at very early gestation

Antibiotic Therapy in Preterm Premature Rupture of the Membranes
J Obstet Gynaecol Can 2017;39(9):207-12
Recommendations:
1. Following PPROM at 32 weeks' gestation, antibiotics should be administered to women who are not in labour in order to prolong pregnancy and to decrease maternal and neonatal morbidity.
2. The benefit of antibiotics is greater at earlier gestational ages.
3. Antibiotics of choice are penicillins or macrolide antibiotics (erythromycin) in parenteral and/or oral forms. In patients allergic to penicillin, macrolide antibiotics should be used alone.
4. Two possible regimen options from large PPROM RCTs are: (1) ampicillin 2g IV q6h and erythromycin 250 mg IV q6h for 48 hours followed by amoxicillin 250 mg orally q8h and erythromycin 333 mg orally q8h for 5 d; (2) erythromycin 250 mg orally q6h for 10 d.
5. Amoxicillin/clavulanic acid should not be used because of an increased risk of necrotizing enterocolitis in neonates. Amoxicillin without clavulanic acid is safe.
6. Women presenting with PPROM should be screened for urinary tract infections, sexually transmitted infections, and group *B streptococcus*.

Postterm Pregnancy

Definition
- pregnancy >42 wk GA

Epidemiology
- 41 wk GA: up to 27%
- >42 wk GA: 5.5%

Etiology
- most cases idiopathic
- anencephalic fetus with no pituitary gland
- placental sulfatase deficiency (X-linked recessive condition in 1/2000-1/6000 infants) – rare

Management (for singleton, cephalic fetus, otherwise uncomplicated)
- GA 39 wk with advanced maternal age (>40 y): consideration should be given to IOL due to increased risk of stillbirth
- GA 40-41 wk: expectant management
  - no evidence to support IOL or C/S unless other risk factors for morbidity are present (see prognosis)
- GA >41 wk: offer IOL if vaginal delivery is not contraindicated
  - IOL shown to decrease C/S, fetal heart rate changes, meconium staining, macrosomia, and death when compared with expectant management
- GA >41 wk and expectant management elected: serial fetal surveillance
  - fetal movement count by the mother
  - BPP q3-4d
- if AFI is decreased, labour should be induced

Prognosis
- if >42 wk, perinatal mortality 2-3x higher (due to progressive uteroplacental insufficiency)
- with increasing GA, higher rates of: intrauterine infection, asphyxia, meconium aspiration syndrome, placental insufficiency, placental aging and infarction, macrosomia, dystocia, fetal distress, operative deliveries, pneumonia, seizures, requirement of NICU admission, stillbirth
- morbidity increased with HTN in pregnancy, DM, abruption, IUGR, and multiple gestation

Intrauterine Fetal Demise

Definition
- fetal demise in utero after 20 wk GA (before 20 wk GA called spontaneous abortion)

Epidemiology
- occurring in 1% of pregnancies

Etiology
- 50% idiopathic
- 50% secondary to HTN, DM, erythroblastosis fetalis, congenital anomalies, umbilical cord or placental complications, intrauterine infection, and APS

Clinical Features
- decreased perception of fetal movement by mother
- SFH and maternal weight not increasing
- absent fetal heart tones on Doppler (not diagnostic)
- high MSAFP
- on U/S: no fetal heart rate. Depending on timing of death, may see skull collapse, brain tissue retraction, empty fetal bladder, non-filled aorta, or poor visualization of midline flax

Management
- diagnosis: absent cardiac activity and fetal movement on U/S (required)
- determine secondary cause
  - maternal: HbA1c, fasting glucose, TSH, Kleihauer-Betke, VDRL, ANA, CBC, anticardiolipins, antibody screens, INR/PTT, serum/urine toxicology screens, cervical and vaginal cultures, and TORCH screen
  - fetal: karyotype, cord blood, skin biopsy, genetics evaluation, autopsy, amniotic fluid culture for CMV, parvovirus B19, and herpes
  - placenta: pathology, bacterial cultures

Treatment
- <12 wk: dilation and curettage
- 13-20 wk: dilation and evacuation or sometimes IOL
- >20 wk: IOL
- monitor for maternal coagulopathy (10% risk of DIC)
- parental psychological care/bereavement support as per hospital protocol
- comprehensive discussion within 3 mo about final investigation and post-mortem results, help make plans for future pregnancies

DIC: Generalized Coagulation and Fibrinolysis Leading to Depletion of Coagulation Factors

Obstetrical Causes
- Abruption
- Gestational HTN
- Fetal demise
- PPH

DIC-specific Blood Work
- Platelets
- aPTT and PT
- FDP
- Fibrinogen

Treatment
- Treat underlying cause
- Supportive
- Fluids
- Blood products
- FFP, platelets, cryoprecipitate
- Consider anti-coagulation as VTE prophylaxis

Intrauterine Growth Restriction

Definition
- estimated fetal weight <10th percentile for GA on U/S, has not reached biologically determined growth potential

Etiology/Risk Factors
- 50% unknown
- maternal causes
  - malnutrition, smoking, drug abuse, alcoholism, cyanotic heart disease, type 1 DM, SLE, pulmonary insufficiency, previous IUGR (25% risk, most important risk factor), and chronic HTN
- maternal
  - gestational HTN, chronic renal insufficiency, prolonged gestation, substance abuse, and poor nutrition
- placental
  - any disease that causes placental insufficiency
  - gross placental morphological abnormalities (infarction, hemangiomas, placenta previa, ansd abnormal cord insertion)
- fetal causes
  - TORCH infections, multiple gestation, and congenital anomalies/chromosomal abnormalities (10%)

Clinical Features
- symmetric/type I (25-30%): occurs early in pregnancy
  - reduced growth of both head and abdomen
  - head:abdomen ratio may be normal (>1 up to 32 wk; =1 at 32-34 wk; <1 after 34 wk GA)
  - usually associated with congenital anomalies or TORCH infections
- asymmetric/type II (70%): occurs late in pregnancy
  - fetal abdomen is disproportionately smaller than fetal head
  - brain is spared; therefore head:abdomen ratio increased
  - usually associated with placental insufficiency
  - more favourable prognosis than type I

TORCH
Toxoplasmosis
Others: e.g. syphilis
Rubella
CMV
HSV
• See Table 15, OB29

- complications
  - prone to meconium aspiration, asphyxia, polycythemia, hypoglycemia, hypocalcemia, hypophosphatemia, hyponatremia, and mental retardation
  - greater risk of perinatal morbidity and mortality

Investigations
- SFH measurements at every antepartum visit (ensure accurate GA)
- if mother at high risk or SFH lags >2 cm behind GA
  - U/S for biparietal diameter, head and abdominal circumference ratio, femur length, fetal weight, AFV (decrease associated with IUGR), and decrease in the rate of growth
  - ± BPP
  - Doppler analysis of umbilical cord blood flow

Management
- prevention via risk modification prior to pregnancy is ideal
- modify controllable factors: smoking, alcohol, nutrition, and treat maternal illness
- serial BPP (monitor fetal growth) and determine cause of IUGR, if possible
- delivery when extrauterine existence is less dangerous than continued intrauterine existence (abnormal function tests, absent growth, severe oligohydramnios) especially if GA >34 wk
- as IUGR fetuses are less likely to withstand stresses of labour, they are more likely to be delivered by Cesarean section

Macrosomia

Definition
- infant weight ≥90th percentile for a particular GA or >4000 g

Etiology/Risk Factors
- maternal obesity, GDM, past history of macrosomic infant, prolonged gestation, multiparity

Clinical Features
- increased risk of perinatal mortality
- CPD and birth injuries (shoulder dystocia, fetal bone fracture) more common
- complications of DM in labour (see Table 14, OB28)

Investigations
- serial SFH
- further investigations if mother at high risk or SFH >2 cm ahead of GA
- U/S predictors
  - polyhydramnios
  - T3 abdominal circumference >1.5 cm/wk
  - head circumference/abdominal circumference ratio <10th percentile
  - femur length/abdominal circumference ratio <20th percentile

Management
- prevent hyperglycemia in women with DM, optimize pre-pregnancy weight, and limit pregnancy weight gain
- prophylactic C/S is a reasonable option where EFW >5000 g in non-diabetic woman and EFW >4500 g in diabetic woman
- risks and benefits of early induction (risk of C/S vs. risk of dystocia) must be weighed in diabetic mothers, need for person-centred and shared decision-making

Polyhydramnios/Oligohydramnios

Table 11. Polyhydramnios and Oligohydramnios

	Polyhydramnios	Oligohydramnios
Definition	AFI >25 cm U/S: single deepest pocket >8 cm	AFI <5 cm U/S: single deepest pocket ≤2 cm
Etiology	Idiopathic most common Maternal Type 1 DM: abnormalities of transchorionic flow Maternal-fetal Chorioangiomas Multiple gestation Fetal hydrops (increased erythroblastosis) Fetal Chromosomal anomaly (up to 2/3 of fetuses have severe polyhydramnios) Respiratory: cystic adenomatoid malformed lung CNS: anencephaly, hydrocephalus, meningocele GI: tracheoesophageal fistula, duodenal atresia, facial clefts (interfere with swallowing)	Idiopathic most common Maternal Uteroplacental insufficiency (preeclampsia, nephropathy) Medications (ACEI) Fetal Congenital urinary tract anomalies (renal agenesis, obstruction, posterior urethral valves) Demise/chronic hypoxemia (blood shunt away from kidneys to perfuse brain) IUGR Ruptured membranes: prolonged amniotic fluid leak Amniotic fluid normally decreases after 35 wk
Epidemiology	Occur in 0.2-1.6% of all pregnancies	Occur in ~4.5% of all pregnancies Severe form in <0.7% Common in pregnancies >41 wk (~12%)
Clinical Features and Complications	Uterus large for dates, difficulty palpating fetal parts and hearing FHR Maternal complications Pressure symptoms from overdistended uterus (dyspnea, edema, hydronephrosis) Obstetrical complications Cord prolapse, placental abruption, malpresentation, preterm labour, uterine dysfunction, and PPH	Uterus small for dates Fetal complications 15-25% have fetal anomalies Amniotic fluid bands (T1) can lead to Potter's facies, limb deformities, abdominal wall defects Obstetrical complications Cord compression Increased risk of adverse fetal outcomes Pulmonary hypoplasia (late-onset) Marker for infants who may not tolerate labour well
Management	Determine underlying cause Screen for maternal disease/infection Complete fetal U/S evaluation Depends on severity Mild to moderate cases require no treatment If severe, hospitalize and consider therapeutic amniocentesis	Always warrants admission and investigation Rule out ROM Fetal monitoring (NST, BPP) U/S Doppler studies (umbilical cord and uterine artery) Maternal hydration with oral or IV fluids to help increase amniotic fluid Injection of fluid via amniocentesis will improve condition for ~1 wk – may be most helpful for visualizing any associated fetal anomalies Consider delivery if term Amnio-infusion may be considered during labour via intrauterine catheter
Prognosis	2-5 fold increase in risk of perinatal mortality	Poorer with early onset High mortality related to congenital malformations and pulmonary hypoplasia when diagnosed during T2

Multi-Fetal Gestation and Malpresentation

Epidemiology

- incidence of twins is 1/80 and triplets 1/6400 in North America
- 2/3 of twins are dizygotic (fraternal)
  - risk factors for dizygotic twins: IVF, increased maternal age, newly discontinued OCP, and ethnicity (e.g. certain African regions)
- monozygous twinning occurs at a constant rate worldwide (1/250)
- determine zygosity by number of placentas, thickness of membranes, sex, and blood type

Clinical Features

Table 12. Complications Associated with Multiple Gestation

Maternal	Uteroplacental	Fetal
Hyperemesis gravidarum GDM Gestational HTN Anemia Increased physiological stress on all systems Increased compressive symptoms C/S	Increased PROM/PTL Polyhydramnios Placenta previa Placental abruption PPH (uterine atony) Umbilical cord prolapse Cord anomalies (velamentous insertion, 2 vessel cord)	Prematurity IUGR Malpresentation Congenital anomalies Twin-twin transfusion Increased perinatal morbidity and mortality Twin interlocking (twin A breech, twin B vertex) Single fetal demise

Management
- U/S determination of chorionicity must be done within T1 (ideally 8-12 wk GA)
- increased antenatal surveillance
  - serial U/S q3-4wk from 22 wk GA to assess growth (uncomplicated diamniotic dichorionic)
  - increased frequency of U/S in monochorionic diamniotic and monochorionic monoamniotic twins
  - Doppler flow studies weekly if discordant fetal growth (>30%)
  - BPP as needed
- may attempt vaginal delivery if twin A presents as vertex, otherwise C/S (40-50% of all twin deliveries, 10% of cases have twin A delivered vaginally and twin B delivered by C/S)
- mode of delivery depends on fetal weights, GA, and presentation

The Ps of Multiple Gestation Complications

Increased rates of
Puking
Pallor (anemia)
Preeclampsia/**P**IH
Pressure (compressive symptoms)
PTL/**P**ROM/**PP**ROM
Polyhydramnios
Placenta previa/abruption
PPH/A**P**H
Prolonged labour
Cord **p**rolapse
Prematurity
Mal**p**resentation
Perinatal morbidity and mortality
Parental distress
Postpartum depression

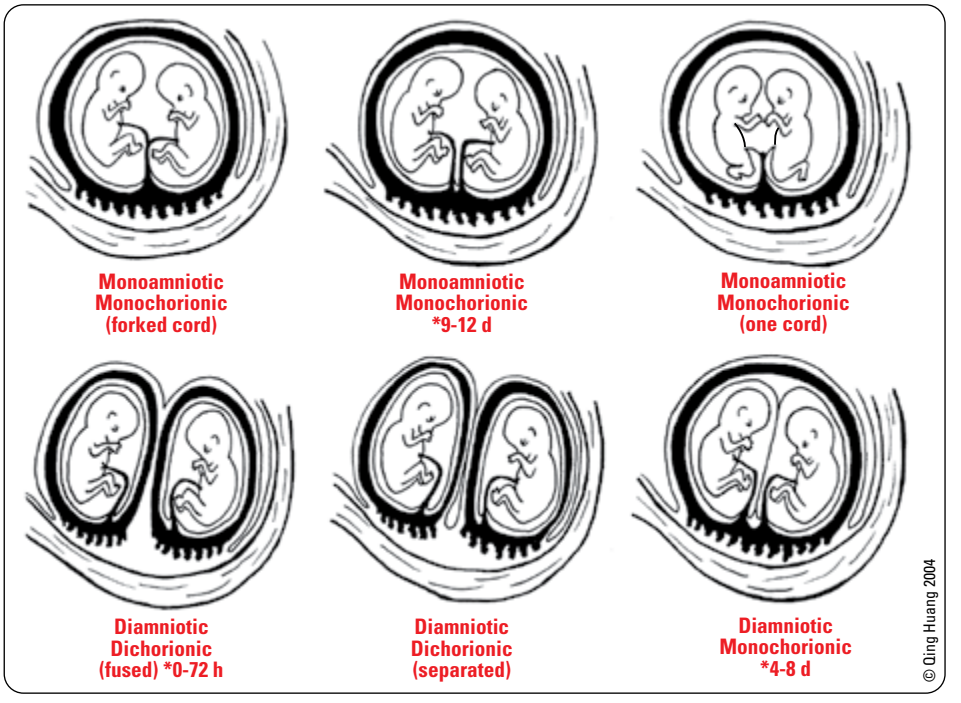


Figure 4. Classification of twin pregnancies ***Indicates time of cleavage**

Twin-Twin Transfusion Syndrome

Definition
- formation of placental intertwin vascular anastomoses causes arterial blood from donor twin to pass into veins of the recipient twin

Epidemiology
- 10% of monochorionic twins
- concern if >30% discordance in estimated fetal weight

Clinical Features
- donor twin: IUGR, hypovolemia, hypotension, anemia, and oligohydramnios
- recipient twin: hypervolemia, HTN, CHF, polycythemia, edema, polyhydramnios, and kernicterus in neonatal period

Investigations
- detected by U/S screening, Doppler flow analysis

Management
- therapeutic serial amniocentesis to decompress polyhydramnios of recipient twin and decrease pressure in cavity and on placenta
- intrauterine blood transfusion to donor twin if necessary
- laparoscopic occlusion of placental vessels
- fetoscopic laser ablation of placental vascular anastomoses when indicated and if available

Breech Presentation

Definition
- fetal buttocks or lower extremity is the presenting part as determined on U/S
- complete (10%): hips and knees both flexed
- frank (60%): hips flexed, knees extended, buttocks present at cervix
  - most common type of breech presentation
  - most common breech presentation to be delivered vaginally
- incomplete (30%): both or one hip partially flexed and both or one knee present below the buttocks, feet or knees present first (footling breech, kneeling breech)

Epidemiology
- occurs in 3-4% of pregnancies at term (25% <28 wk)

Risk Factors
- maternal: pelvis (contracted), uterus (shape abnormalities, intrauterine tumours, fibroids, previous breech), pelvic tumours causing compression, and grand multiparity
- placental: placenta previa
- fetal: prematurity, amniotic fluid (poly-/oligohydramnios), multiple gestation, congenital malformations (found in 6% of breeches; 2-3% if in vertex presentations), abnormalities in fetal tone and movement, aneuploidy, hydrocephalus, and anencephalus

Management
- ECV (external cephalic version): repositioning of singleton fetus within uterus under U/S guidance
  - overall success rate of ~60%
  - criteria: >36 wk GA, singleton, unengaged presenting part, reactive NST, not in labour
  - absolute contraindications: where C/S is required (placenta previa, previous classical C/S), previous myomectomy, PROM, uteroplacental insufficiency, nuchal cord, non-reactive NST, multiple gestation
  - relative contraindications: mild/moderate oligohydramnios, suspected IUGR, HTN, previous T3 bleed
  - risks: abruption, cord compression, cord accident, ROM, labour, fetal bradycardia requiring C/S (<1% risk), alloimmunization, fetal death (1:5000)
  - method: tocometry, followed by U/S guided transabdominal manipulation of fetus with constant fetal heart monitoring
  - if patient Rh negative, give Rhogam® after the procedure
  - better prognosis if multiparous, good fluid volume, small baby, skilled obstetrician, and posterior placenta
- pre-or early-labour U/S to assess type of breech presentation, fetal growth, estimated weight, placenta position, attitude of fetal head (flexed is preferable); if U/S unavailable, recommend C/S
- ECV and elective C/S should be presented as options with the risks and benefits outlined; obtain informed consent
- method for vaginal breech delivery
  - encourage effective maternal pushing efforts
  - at delivery of head (after feet), assistant must apply suprapubic pressure to flex and engage fetal head
  - delivery can be spontaneous or assisted; avoid fetal traction
  - apply fetal manipulation only after spontaneous delivery to level of umbilicus
- contraindications to vaginal breech delivery
  - cord presentation
  - clinically inadequate maternal pelvis
  - fetal factors incompatible with vaginal delivery (e.g. hydrocephalus, macrosomia, fetal growth restriction)
- C/S recommended if: the breech has not descended to the perineum in the second stage of labour after 2 h, in the absence of active pushing, or if vaginal delivery is not imminent after 1 h of active pushing

Prognosis
- regardless of route of delivery, breech infants have lower birth weights and higher rates of perinatal mortality, congenital anomalies, abruption, and cord prolapse

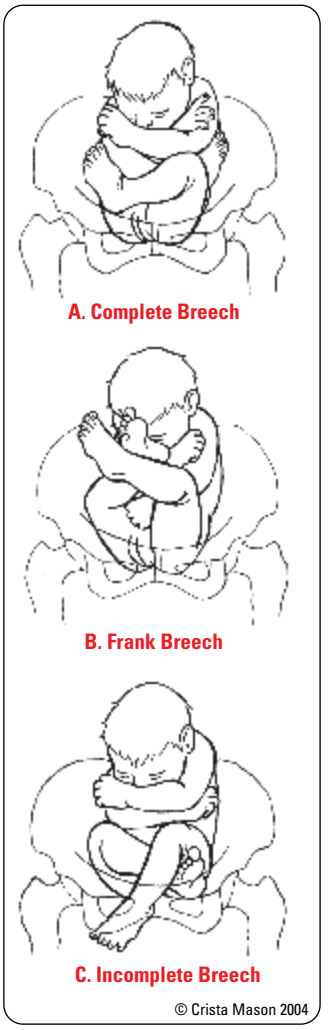


Figure 5. Types of breech presentation

Criteria for Vaginal Breech Delivery
- Frank or complete breech, GA >36 wk
- EFW 2500-3800 g based on clinical and U/S assessment (5.5–8.5 lb)
- Fetal head flexed
- Continuous fetal monitoring
- 2 experienced obstetricians, assistant, and anesthetist present
- Ability to perform emergency C/S within 30 min if required

Hypertensive Disorders of Pregnancy

Hypertension in Pregnancy

- hypertensive disorders of pregnancy are classified as either pre-existing or gestational HTN. Pre-eclampsia and eclampsia are included in the spectrum of hypertensive disorders of pregnancy

Ominous Symptoms of HTN in Pregnancy
RUQ pain, headache, and visual disturbances

PRE-EXISTING HYPERTENSION

Definition
- BP ≥140/90 prior to 20 wk GA; BP should be elevated on ≥2 occasions at least 15 minutes apart
- essential HTN is associated with an increased risk of gestational HTN, abruptio placentae, IUGR, and IUFD

GESTATIONAL HTN

Definition
- sBP ≥140 or dBP ≥90 after 20 wk GA without proteinuria in a woman known to be normotensive before pregnancy

PREECLAMPSIA
Definition
- pre-existing or gestational HTN with new onset proteinuria or adverse conditions (end organ dysfunction)

ECLAMPSIA
Definition
- the occurrence of ≥1 generalized convulsions and/or coma in the setting of preeclampsia and in the absence of other neurologic conditions

Note
Eclampsia prior to 20 wk of gestation is rare and should raise the possibility of an underlying molar pregnancy or antiphospholipid syndrome

Epidemiology of Eclampsia
- an eclamptic seizure occurs in approximately 0.5% of mildly preeclamptic women and 2-3% of severely preeclamptic women

Clinical Manifestation of Eclampsia
- eclampsia is a clinical diagnosis
- typically tonic-clonic and lasting 60-75 s
- symptoms that may occur before the seizure include persistent frontal or occipital headache, blurred vision, photophobia, right upper quadrant or epigastric pain, and altered mental status
- in up to one third of cases, there is no proteinuria or blood pressure >140/90 mmHg prior to the seizure
- in general, women with typical eclamptic seizures who do not have focal neurologic deficits or prolonged coma do not require diagnostic evaluation including imaging

Risk Factors for Hypertensive Disorders in Pregnancy
- maternal factors
  - primigravida (80-90% of gestational HTN), first conception with a new partner, PMHx or FHx of gestational HTN, or preeclampsia/eclampsia
  - DM, chronic HTN, or renal insufficiency
  - obesity
  - antiphospholipid syndrome or inherited thrombophilia
  - extremes of maternal age (<18 or >35 yr)
  - previous stillbirth or IUFD
  - vascular or connective tissue disease
- fetal factors
  - IUGR or oligohydramnios
  - GTN
  - multiple gestation
  - fetal hydrops "mirror syndrome"
  - abruptio placentae

Hypertension in Pregnancy

Adverse Maternal Conditions
- sBP >160 mmHg
- dBP >100 mmHg
- HELLP
- Cerebral hemorrhage
- Renal dysfunction: oliguria <500 mL/d
- Left ventricular failure, pulmonary edema
- Placental abruption, DIC
- **Symptoms**
  - Abdominal pain, N/V
  - Headaches, visual problems
  - SOB, chest pain
  - Eclampsia: convulsions

Adverse Fetal Conditions
- IUGR
- Oligohydramnios
- Absent/reversed umbilical artery end diastolic flow
- **Can result in:**
  - Fetal disability and/or death

Clinical Evaluation of Hypertensive Disorders in Pregnancy
- in general, clinical evaluation should include the mother and fetus
- evaluation of mother:
  - body weight
  - central nervous system
    - presence and severity of headache
    - visual disturbances – blurring, scotomata

        - tremulousness, irritability,and somnolence
        - hyperreflexia
    - hematologic
        - bleeding, petechiae
    - hepatic
        - RUQ or epigastric pain
        - severe N/V
    - renal
        - urine output and colour
- evaluation of fetus:
    - fetal movement
    - fetal heart rate tracing – NST
    - U/S for growth
    - BPP
    - Doppler flow studies

Laboratory Evaluation of Hypertensive Disorders in Pregnancy

- CBC
- PTT, INR, fibrinogen – if abnormal LFTs or bleeding
- ALT, AST
- creatinine, uric acid
- 24 h urine collection for protein or albumin:creatinine ratio
- may consider placental growth factor (PlGF) testing as an early screening test for suspected preeclampsia

Complications of Hypertensive Disorders in Pregnancy

- maternal
    - liver and renal dysfunction
    - seizure - "eclampsia"
    - abruptio placentae
    - left ventricular failure/pulmonary edema
    - DIC (release of placental thromboplastin consumptive coagulopathy)
    - HELLP syndrome
    - hemorrhagic stroke (50% of deaths)
- fetal (2° to placental insufficiency)
    - IUGR, prematurity, abruptio placentae, IUFD

Management of HTN

- for non-severe HTN (149-159/90-105) target a BP of 130-155/80-105 in women without comorbidities or <140/90 in women with comorbidities
- for both pre-existing and gestational HTN, labetalol 100-400 mg PO bid-tid, nifedipine XL preparation 20-60 mg PO od, or α-methyldopa 250-500 mg PO bid-qid
- for severe HTN (BP>160/110), give one of:
    - labetalol 20 mg IV then 20-80 mg IV q30min (max 300 mg) (then switch to oral)
    - nifedipine 5-10 mg capsule q30min
        - hydralazine 5 mg IV, repeat 5-10 mg IV q30min or 0.5 to 10 mg/h IV, to a maximum of 20 mg IV (or 30 mg IM)
- no ACEI, ARBs, diuretics (in cases of pulmonary edema or cardiac failure, may be used), prazosin, or atenolol
- pre-existing HTN and gestational HTN without any deterioration can be followed until 37 wk, then decide to induce shortly thereafter

Management of Preeclampsia

- if stable and no adverse factors (GA 24-33+6 wk), expectant management, ± delivery as approaching 34-36 wk (must weigh risks of fetal prematurity vs. risks of developing severe preeclampsia/eclampsia)
- antenatal corticosteroids should be considered if GA ≤ 34 wk
- if >37 wk, immediate delivery is recommended
- for severe preeclampsia, stabilize and deliver, regardless of GA
- if severe preeclampsia during labour, increase maternal monitoring: hourly input and output, urine dip q12h, hourly neurological vitals, and increase fetal monitoring (continuous FHR monitoring)
- antihypertensive therapy
    - labetalol 20 mg IV, then 20-80 mg IV q30min (max 300 mg) (then switch to oral)
    - nifedipine 5-10 mg capsule q30min
        - hydralazine 5 mg IV, repeat 5-10 mg IV q30min or 0.5-10 mg/h IV, to a maximum of 20 mg IV (or 30 mg IM)

I-A Evidence-Recommendation Highlights of SOGC Clinical Practice Guidelines Diagnosis, Evaluation, and Management of the Hypertensive Disorders of Pregnancy
J Obstet Gynaecol Can 2014;36(5):416-38

- For BP measurement, Korotkoff phase V should be used to designate the dBP.
- Calcium supplementation (of at least 1g/d, orally) is recommended for women with low dietary intake of calcium (<600 mg/d). (I-A)
- For preeclampsia prevention among increased risk women, low-dose ASA (75-100 mg/d) is recommended until delivery.
- Umbilical artery Doppler velocimetry should be part of the antenatal fetal surveillance in preeclampsia.
- Initial antihypertensive therapy for severe HTN (sBP >160 or dBP ≥110) should be with labetalol, nifedipine, or hydralazine.
- Initial antihypertensive therapy for non-severe HTN (BP 140-159/90-109 mmHg) should be with methyldopa, β-blockers, or calcium channel blockers.
- Antenatal corticosteroids for fetal lung maturation should be considered for all women with preeclampsia before 34 wk gestation.
- In a planned vaginal delivery with an unfavourable cervix, cervical ripening should be used.
- Oxytocin 5 units IV or 10 units IM should be used as part of the management during the third stage of labour, particularly in the presence of thrombocytopenia or coagulopathy.
- Magnesium sulfate is the recommended first-line treatment for eclampsia.
- Magnesium sulfate is the recommended eclampsia prophylaxis in severe preeclampsia.

Preeclampsia Investigations

- CBC
- AST, ALT
- INR and aPTT (if abn LFTs or bleeding)
- Cr
- Urine (24 h protein collection or albumin/creatinine ratio)
- Uric acid

- seizure prevention
  - magnesium sulfate: 4 g IV loading dose, followed by 1g/h
  - postpartum management
  - risk of seizure highest in first 24 h postpartum – continue $MgSO_4$ for 12-24 h after delivery
  - vitals q1h
  - consider HELLP syndrome
  - most return to a normotensive BP within 2 wk

Management of Eclampsia

- ABCs
- roll patient into LLDP
- supplemental O_2 via face mask to treat hypoxemia due to hypoventilation during convulsive episode
- aggressive antihypertensive therapy for sustained dBP ≥105 mmHg or sBP ≥160 mmHg with hydralazine or labetalol
- prevention of recurrent convulsions: to prevent further seizures and the possible complications of repeated seizure activity (e.g. rhabdomyolysis, metabolic acidosis, aspiration pneumonitis, etc.)
- $MgSO_4$ is now the drug of choice
- the definitive treatment of eclampsia is DELIVERY, irrespective of gestational age, to reduce the risk of maternal morbidity and mortality from complications of the disease
- mode of delivery is dependent on clinical situation and fetal-maternal condition

HELLP Syndrome
Hemolysis
Elevated **L**iver Enzymes
Low Platelets

Differential Diagnosis of Cause for Seizure in a Pregnant Woman
- Stroke
- Hypertensive disease (hypertensive encephalopathy, pheochromocytoma)
- Space-occupying lesion of the CNS
- Metabolic disorders (hypoglycemia, SIADH)
- Infection (meningitis, encephalitis)
- TTP or thrombophilia
- Idiopathic epilepsy
- Use of illicit drugs
- Cerebral vasculitis

Medical Complications of Pregnancy

Iron and Folate Deficiency Anemia

Table 13. Iron Deficiency and Folate Deficiency Anemia

	Iron Deficiency Anemia	Folate Deficiency Anemia
Etiology	See Hematology, H15	See Hematology, H25
Epidemiology	Responsible for 80% of non-physiologic anemia during pregnancy	Incidence varies from 0.5-25% depending on region, population, and diet
Clinical Features	See Hematology, H15	See Hematology, H25
Investigations	See Hematology, H15	See Hematology, H25
Management	Prevention (non-anemic): 30 mg elemental iron/d (met by most prenatal vitamins) Treatment (anemic): 30-120 mg elemental iron/d 325 mg ferrous fumarate = 106 mg elemental Fe; 325 mg ferrous sulfate = 65 mg elemental Fe; 325 mg ferrous gluconate = 36 mg elemental Fe Polysaccharide-Iron Complex = 150 mg elemental Fe/capsule	Prevention: 0.4-1 mg folic acid PO daily for 1-3 mo preconceptually and throughout T1, or 5 mg folic acid/d with past history of ONTD, DM, or antiepileptic medication use
Complications	Maternal: angina, CHF, infection, slower recuperation, preterm labour Fetal: decreased oxygen carrying capacity leading to fetal distress, IUGR, and low birth weight	Maternal: decreased blood volume, N/V, and anorexia Fetal: neural tube defects in T1, low birth weight, and prematurity
Notes	Mother needs 1 g of elemental iron per fetus; this amount exceeds normal stores + dietary intake Iron requirements increase during pregnancy due to fetal/placental growth (500 mg), increased maternal RBC mass (500 mg), and losses (200 mg) – more needed for multiple gestations	Minimum daily requirement is 0.4 mg Most often associated with iron deficiency anemia Folic acid is necessary for closure of neural tube during early fetal development (by day 28 of gestation)

Diabetes Mellitus

Epidemiology

- 2-4% of pregnancies are complicated by DM

Classification of Diabetes Mellitus

- type 1 and type 2 DM (see Endocrinology, E7)
- GDM: onset of DM during pregnancy (usually tested for around 24-28 wk GA)

Etiology

- type 1 and type 2 DM
- GDM: anti-insulin factors produced by placenta and high maternal cortisol levels create increased peripheral insulin resistance → leading to GDM and/or exacerbating pre-existing DM

MANAGEMENT

A. TYPE 1 and TYPE 2 DM

Preconception
- pre-plan and refer to high-risk clinic
- commence folic acid 3 mo prior
- optimize glycemic control (HbA1c <6%)
- counsel patient on potential risks and complications
- evaluate for diabetic retinopathy, neuropathy, and CAD

Pregnancy
- for Type 2 DM, if already on oral medication, generally switch to insulin therapy
  - continuing glyburide or metformin controversial
  - teratogenicity unknown for other oral anti-hyperglycemics
- tight glycemic control
  - insulin dosage may need to be adjusted in T2 due to increased demand and increased insulin resistance
- monitor as for normal pregnancy, plus initial 24 h urine protein and creatinine clearance, retinal exam, and HbA1c
  - HbA1c: >140% of pre-pregnancy value associated with increased risk of spontaneous abortion and congenital malformations
- increased fetal surveillance (fetal growth, BPP, NST) starting in the late T2 and T3, consider fetal ECHO in the T2 (if high HbA1c in T1 or just prior to pregnancy) to look for cardiac abnormalities

Monitoring Glucose Levels
- Frequent measurements of blood glucose during pregnancy are advised for women with type 1 or 2 DM to help prevent or treat both hypoglycemia and hyperglycemia, and also improves neonatal outcome
- Aim for:
  - FPG ≤5.3 mmol/L (95 mg/dL)
  - 1 h post prandial PG ≤7.8 mmol/L (140 mg/dL), 2 h post prandial PG ≤6.7 mmol/L (120 mg/dL)
- Most women can be followed with monthly HbA1c determinations

Labour
- timing of delivery depends on fetal and maternal health and risk factors (i.e. must consider size of baby, lung maturity, maternal blood glucose)
- induce by 38-39 wk, depending on glycemic control and presence of end-organ involvment
- type of delivery
  - increased risk of cephalopelvic disproportion (CPD) and shoulder dystocia with babies >4000 g (8.8 lbs)
  - consider elective C/S for predicted birthweight >4500 g (9.9 lbs) (controversial)
- monitoring
  - during labour, monitor blood glucose q1h with patient on insulin and dextrose drip
  - aim for blood glucose between 3.9-7 mmol/L to reduce the risk of neonatal hypoglycemia

Post-prandial blood glucose values seem to be the most effective at determining the likelihood of macrosomia or other adverse pregnancy outcomes

Postpartum
- insulin requirements dramatically drop with expulsion of placenta (source of insulin antagonists)
- monitor glucose q6h, restart insulin at two-thirds of pre-pregnancy dosage when glucose >8 mmol/L

B. GESTATIONAL DM

Screening and Diagnosis
- all pregnant women between 24-28 wk GA (or at any stage if high risk)
- 2 screening options
  - 2-step screening (recommended by the Canadian Diabetes Association)
    - Step 1: perform a random non-fasting 50 g OGCT
      - 1 h PG <7.8 mmol/L is normal
      - 1 h PG ≥11.1 mmol/L is GDM
      - if 1 h PG 7.8-11.0 mmol/L, proceed to Step 2
    - Step 2: perform a fasting 75 g OGTT, GDM if ≥1 of:
      - FPG ≥5.3 mmol/L
      - 1 h PG ≥10.6 mmol/L
      - 2 h PG ≥9.0 mmol/L
  - Alternative 1-step screening with fasting 75 g OGTT; GDM if ≥1 of:
    - FPG ≥5.1 mmol/L
    - 1 h PG ≥10.0 mmol/L
    - 2 h PG ≥8.5 mmol/L

Risk Factors for GDM
- Age >25 yr
- Obesity
- Ethnicity (Aboriginal, Hispanic, Asian, and African)
- FHx of DM
- Previous history of GDM
- Previous child with birthweight >4.0 kg
- Polycystic ovarian syndrome
- Current use of glucocorticoids
- Essential HTN or pregnancy-related HTN

Management
- first line: diet modification and increased physical activity
- initiate insulin therapy if glycemic targets not achieved within 2 wk of lifestyle modification alone
- glycemic targets: FPG <5.3 mmol/L, 1 h PG <7.8 mmol/L, 2 h PG <6.7 mmol/L
- oral agents can be used in pregnancy but is off-label and should be discussed with patient
- stop insulin and diabetic diet postpartum
- follow-up with 75 g OGTT between 6 wk-6 mo postpartum, counsel about lifestyle modifications

Prognosis
- most maternal and fetal complications are related to hyperglycemia and its effects

Table 14. Complications of DM in Pregnancy

Maternal	Fetal
Obstetric HTN/preeclampsia (especially if pre-existing nephropathy/proteinuria): insulin resistance is implicated in etiology of HTN Polyhydramnios: maternal hyperglycemia leads to fetal hyperglycemia, which leads to fetal polyuria (a major source of amniotic fluid)	**Growth Abnormalities** Macrosomia: maternal hyperglycemia leads to fetal hyperinsulinism resulting in accelerated anabolism IUGR: due to placental vascular insufficiency
Diabetic Emergencies Hypoglycemia Ketoacidosis Diabetic coma	**Delayed Organ Maturity** Fetal lung immaturity: hyperglycemia interferes with surfactant synthesis (respiratory distress syndrome)
End-Organ Involvement or Deterioration (occur in type 1 DM and type 2 DM, not in GDM) Retinopathy Nephropathy	**Congenital Anomalies (occur in type 1 DM and type 2 DM, not in GDM)** 2-7x increased risk of cardiac (ventricular septal defect), NTD, GU (cystic kidneys), GI (anal atresia), and MSK (sacral agenesis) anomalies due to hyperglycemia Note: Pregnancies complicated by GDM do not manifest an increased risk of congenital anomalies because GDM develops after the critical period of organogenesis (in T1)
Other Pyelonephritis/UTI: glucosuria provides a culture medium for *E. coli* and other bacteria Increased incidence of spontaneous abortion (in type 1 DM and type 2 DM, not in GDM): related to pre-conception glycemic control	**Labour and Delivery** Preterm labour/prematurity: most commonly in patients with HTN/preeclampsia Preterm labour is associated with poor glycemic control but the exact mechanism is unknown Increased incidence of stillbirth Birth trauma: due to macrosomia, can lead to difficult vaginal delivery and shoulder dystocia **Neonatal** Hypoglycemia: due to pancreatic hyperplasia and excess insulin secretion in the neonate Hyperbilirubinemia and jaundice: due to prematurity and polycythemia Hypocalcemia: exact pathophysiology not understood, may be related to functional hypoparathyroidism Polycythemia: hyperglycemia stimulates fetal erythropoietin production

Long-Term Maternal Complications
- type 1 and type 2 DM: risk of progressive retinopathy and nephropathy
- GDM: 50% risk of developing type 2 DM in next 20 yr

Early-Onset Group B *Streptococcus*

Epidemiology
- 15-40% recto-vaginal carrier rate

Risk Factors (for neonatal disease)
- maternal intrapartum GBS colonization during current pregnancy
- GBS bacteria at any time during the current pregnancy
- previous infant with invasive GBS disease
- prolonged rupture of membranes ≥18 h
- maternal fever (temperature ≥38°C)

Clinical Features
- not harmful to mother
- risk of vertical transmission (neonatal sepsis, meningitis or pneumonia, and death)

Investigations
- offer screening to all women at 35-37 wk with vaginal and anorectal swabs for GBS culture

Treatment
- prophylactic treatment of maternal GBS at delivery decreases neonatal morbidity and mortality
- indications for antibiotic prophylaxis: positive GBS screen, GBS in urine, previous infant with GBS disease, or GBS status unknown + one of the other risk factors
- antibiotics for GBS prophylaxis (should be given 4 h prior to delivery to be considered adequate)
  - penicillin G, 5 million IU IV, then 2.5 million IU IV q4h until delivery
  - penicillin allergic but not at risk for anaphylaxis: cefazolin 2 g IV then 1 g q8h
  - penicillin allergic and at risk of anaphylaxis: vancomycin 1 g IV q12h until delivery (vancomycin and clindamycin levels in amniotic fluid do not reach therapeutic levels, all babies should be screened for GBS despite treatment)
- if maternal fever, broad spectrum antibiotic coverage is advised

Indications for Intrapartum Antibiotic GBS Prophylaxis
Centres for Disease Control and Prevention. Prevention of Perinatal Group B Streptococcal Disease. MMWR 2010;59(RR-10):14
- Previous infant with invasive GBS disease
- GBS bacteriuria during any trimester of the current pregnancy
- Positive GBS vaginal-rectal screening culture in late gestation during current pregnancy
- Unknown GBS status at the onset of labour (culture not done, incomplete, or results unknown) and any of the following:
  - Delivery at <37 wk gestation
  - Amniotic membrane rupture ≥18 h
  - Intrapartum temperature ≥38.0 °C (≥100.4 °F)
  - Intrapartum nucleic-acid amplification test positive for GBS

Urinary Tract Infection

Epidemiology
- most common medical complication of pregnancy
- asymptomatic bacteriuria in 2-7% of pregnant women, more frequently in multiparous women
- note: asymptomatic bacteriuria should be treated in pregnancy due to increased risk of pyelonephritis and preterm labour

Treat asymptomatic bacteriuria in pregnancy because of increased risk of progression to cystitis, pyelonephritis, and probable increased risk of preterm labour

Etiology
- increased urinary stasis from mechanical and hormonal (progesterone) factors
- organisms include GBS as well as those that occur in non-pregnant women

Clinical Features
- may be asymptomatic
- dysuria, urgency, and frequency in cystitis
- fever, flank pain, and costovertebral angle tenderness in pyelonephritis

Investigations
- urinalysis, urine C&S
- cystoscopy and renal function tests in recurrent infections

Management
- uncomplicated UTI
  - first line: amoxicillin (250-500 mg PO q8h x 7 d)
  - alternatives: nitrofurantoin (100 mg PO bid x 7 d) or cephalosporins
  - follow with monthly urine cultures
- pyelonephritis
  - hospitalization and IV antibiotics

Prognosis
- complications if untreated: acute cystitis, pyelonephritis, and possible preterm labour
- recurrence is common

Infections During Pregnancy

Table 15. Infections During Pregnancy

Infection	Agent	Source of Transmission	Greatest Transmission Risk to Fetus	Effects on Fetus	Effects on Mother	Diagnosis	Management
Chicken Pox	Varicella zoster virus (herpes family)	To mother: direct, respiratory To baby: transplacental	13-30 wk GA, and 5 d pre- to 2 d post-delivery	Congenital varicella syndrome (limb aplasia, chorioretinitis, cataracts, cutaneous scars, cortical atrophy, IUGR, hydrops), preterm labour	Fever, malaise, vesicular pruritic lesions	Clinical, ± vesicle fluid culture, ± serology	Varicella-zoster immune globulin for mother if exposed, decreases congenital varicella syndrome Note: do not administer vaccine during pregnancy (live attenuated vaccine)
***Cytomegalovirus**	DNA virus (herpes family)	To mother: blood/ organ transfusion, sexual contact To baby: transplacental, during delivery, breast milk	T1-T3	5-10% develop CNS involvement (mental retardation, cerebral calcification, hydrocephalus, microcephaly, deafness, chorioretinitis)	Asymptomatic or flu-like	Serologic screen; isolate virus from urine or secretion culture	No specific treatment; maintain good hygiene and avoid high risk situations
Erythema Infectiosum (Fifth Disease)	Parvovirus B19	To mother: respiratory, infected blood products To baby: transplacental	10-20 wk GA	Spontaneous abortion (SA), stillbirth, hydrops *in utero*	Flu-like, rash, arthritis; often asymptomatic	Serology, viral PCR, maternal AFP; if IgM present, follow fetus with U/S for hydrops	If hydrops occurs, consider fetal transfusion
Hepatitis B	DNA virus	To mother: blood, saliva, semen, vaginal secretions To baby: transplacental, breast milk	T3 10% vertical transmission if asymptomatic and HBsAg +ve; 85-90% if HBsAg and HBeAg +ve	Prematurity, low birth weight, neonatal death	Fever, N/V, fatigue, jaundice, elevated liver enzymes	Serologic screening for all pregnancies	Rx neonate with HBIG and vaccine (at birth, 1, 6 mo); 90% effective
***Herpes Simplex Virus**	DNA virus	To mother: intimate mucocutaneous contact To baby: transplacental, during delivery	Delivery (if genital lesions present); less commonly *in utero*	Disseminated herpes (20%); CNS sequelae (35%); self-limited infection	Painful vesicular lesions	Clinical diagnosis	Acyclovir for symptomatic women, suppressive therapy at 36 wk controversial Suggested C/S if active genital lesions, even if remote from vulva

Table 15. Infections During Pregnancy (continued)

Infection	Agent	Source of Transmission	Greatest Transmission Risk to Fetus	Effects on Fetus	Effects on Mother	Diagnosis	Management
HIV	RNA retrovirus	To mother: blood, semen, vaginal secretions To baby: in utero, during delivery, breast milk	1/3 *in utero*, 1/3 at delivery, 1/3 breastfeeding	IUGR, preterm labour, PROM	See Infectious Diseases, ID25	Serology, viral PCR All pregnant women are offered screening	Triple anti-retroviral therapy decreases transmission to <1% Elective C/S: no previous antiviral Rx or monotherapy only, viral load unknown or >500 RNA copies/mL, unknown prenatal care, patient request
***Rubella**	ssRNA togavirus	To mother: respiratory droplets (highly contagious) To baby: transplacental	T1	SA or congenital rubella syndrome (hearing loss, cataracts, CV lesions, mitral regurgitation, IUGR, hepatitis, CNS defects, osseous changes)	Rash (50%), fever, posterior auricular or occipital lymphadenopathy, arthralgia	Serologic testing; all pregnant women screened (immune if titre >1:16); infection if IgM present or >4x increase in IgG	No specific treatment; offer vaccine following pregnancy Do not administer during pregnancy (live attenuated)
Syphilis	Spirochete (*Treponema pallidum*)	To mother: sexual contact To baby: transplacental	T1-T3	Risk of preterm labour, multisystem involvement, fetal death	See Infectious Diseases, ID23	VDRL screening for all pregnancies; if positive, requires confirmatory testing	Penicillin G 2.4 million IU IM x 1 dose if early syphilis, 3 doses if late syphilis, monitor VDRL monthly If penicillin G allergic: clindamycin 900 mg IV q8h
***Toxoplasmosis**	Protozoa (*Toxoplasma gondii*)	To mother: raw meat, unpasteurized goat's milk, cat feces/urine To baby: transplacental	T3 (but most severe if infected in T1); only concern if primary infection during pregnancy	Congenital toxoplasmosis (chorioretinitis, hydrocephaly, intracranial calcification, mitral regurgitation, microcephaly) NB: 75% initially asymptomatic at birth	Majority subclinical; may have flu-like symptoms	IgM and IgG serology; PCR of amniotic fluid	Self-limiting in mother; spiramycin decreases fetal morbidity but not rate of transmission

* Indicates TORCH infection

Venous Thromboembolism

Epidemiology

- incidence of 12.1/10,000 (DVT), and 5.4/10,000 (PE)
- increased risk of VTE throughout pregnancy with highest risk of DVT in T3 and post-partum period; highest risk of PE post-partum (first 6 wk)

Risk Factors

- previous VTE, age >35, obesity, infection, bedrest/immobility, shock/dehydration, and thrombophilias (see Hematology, H35)

Table 16. Risk Factors for VTE Specific to Pregnancy

Hypercoagulability	Stasis	Endothelial
Increased Factors: II, V, VII, VIII, IX, X, XII, fibrinogen Increased platelet aggregation Decreased protein S, tPA, factors XI, XIII Increased resistance to activated protein C Antithrombin can be normal or reduced	Increased venous distensibility Decreased venous tone 50% decrease in venous flow in lower extremity by T3 Uterus is mechanical impediment to venous return	Vascular damage at delivery (C/S or SVD) Uterine instrumentation Peripartum pelvic surgery

Virchow's Triad for VTE
- Hypercoagulable state
- Stasis
- Endothelial damage

Clinical Features

- most DVTs occur in the iliofemoral or calf veins with a predilection for the left leg
- signs of a pulmonary embolism are non-specific

Investigations

- duplex venous Doppler sonography for DVT
- CXR and V/Q scan or spiral CT for PE

Management

- before initiating treatment, obtain a baseline CBC including platelets and aPTT
- treatment with LMWH preferred
  - dosing varies depending on specific LMWH used
  - should be discontinued at least 24 h prior to delivery

- unfractionated heparin
  - bolus of 5000 IU followed by an infusion of ~30,000 IU/24h
  - measure aPTT 6 h after the bolus
  - maintain aPTT at a therapeutic level (1.5-2x normal)
  - repeat q24h once therapeutic
  - heparin-induced thrombocytopenia (HIT) uncommon (3%), but serious complication
- warfarin is contraindicated during pregnancy due to its potential teratogenic effects
- compression stockings
- poor evidence to support a recommendation for or against avoidance of prolonged sitting
- VTE prophylaxis
  - women on long-term anticoagulation: full therapeutic anticoagulation throughout pregnancy and for 6-12 wk postpartum
  - women with a non-active PMHx of VTE: unfractionated heparin regimens suggested
  - insufficient evidence in pregnancy to recommend routine use of LMWH for all patients
  - current prophylaxis regimens for acquired thrombophilias (e.g. APS) include low dose ASA in conjunction with prophylactic heparin

Normal Labour and Delivery

Definition of Labour

- true labour: regular, painful contractions of increasing intensity associated with progressive dilatation and effacement of cervix and descent of presenting part, or progression of station
  - preterm (≥20 to ≤36+6 wk GA)
  - term (37-41+6 wk GA)
  - postterm (≥42 wk GA)
- false labour (Braxton-Hicks contractions): irregular contractions, with unchanged intensity and long intervals, occur throughout pregnancy and not associated with any cervical dilatation, effacement, or descent
  - often relieved by rest or sedation

The Cervix

- see Bishop Score (see Table 21, OB37)
  - dilatation: latent phase (0-4 cm, variable time); active phase (4-10 cm)
  - effacement: thinning of the cervix by percentage or length of cervix (cm)
  - consistency: firm, medium, or soft
  - position: posterior, mid, or anterior
- other consideration:
  - application: contact between the cervix and presenting part (i.e. well or poorly applied)

The Fetus

- **fetal lie**: orientation of the long axis of the fetus with respect to the long axis of the uterus (longitudinal, transverse, and oblique)
- **fetal presentation**: fetal body part closest to the birth canal
  - breech (complete, frank, and incomplete) (see Figure 5, OB23)
  - cephalic (vertex/occiput, face, or brow)
  - transverse (shoulder)
  - compound (fetal extremity prolapses along with presenting part)
  - all except vertex are considered malpresentations (see *Obstetrical Complications*, OB16)
- **fetal position**: position of presenting part of the fetus relative to the maternal pelvis
  - OA: most common presentation ("normal") – left OA most common
  - OP: most rotate spontaneously to OA; may cause prolonged second stage of labour
  - OT: leads to arrest of dilatation
    - normally, fetal head enters maternal pelvis and engages in OT position
    - subsequently rotates to OA position (or OP in a small percentage of cases)
- **attitude**: flexion/extension of fetal head relative to shoulders
  - brow presentation: head partially extended (requires C/S)
  - face presentation: head fully extended
    - mentum posterior always requires C/S, mentum anterior can deliver vaginally
- **station**: position of presenting bony part relative to ischial spines – determined by vaginal exam
  - at ischial spines = station 0 = engaged
  - –5 to –1 cm above ischial spines
  - +1 to +5 cm below ischial spines
- **asynclitism**: alignment of the sagittal suture relative to the axis of the birth canal
  - lateral tilt seen with either anterior or posterior asynclitism and may impact descent

Maternal Triage Assessment
ID: Age, GPA, EDD, GA, GBS, Rh, Serology
CC
HPI: 4 key questions:
- Contractions: Since when, how close (q x min), how long (x s), how painful
- Bleeding: Since when, how much (pads), colour (pinky vs. brownish vs. bright red), pain, last U/S, trauma/intercourse
- Fluid (ROM): Since when, large gush vs. trickle, soaked pants, clear vs. green vs. red, continuous
- FM: As much as usual?, When last movement?, Kick counts (lie still for 1-2 h, cold juice, feel FM – should have 6 movements in 2 h)

PregHx: Any complications (HTN, GDM, infections), IPS/FTS screening, last U/S (BPP score, growth/estimated fetal weight, position), last vaginal exam
POBHx: Every previous pregnancy and outcome: year, SVD/C-section/miscarriage/abortion, baby size, length of labour, use of vacuum or forceps, complications
PMHx, Meds, Allergies, SHx
O/E: Maternal vitals, fetal heart tracing (baseline, variability, presence of accelerations/decelerations), Leopold's, vaginal exam, U/S

Reference Point for Describing Fetal Position
- Occiput for cephalic presentation
- Sacrum for breech presentation
- Mentum for face presentation

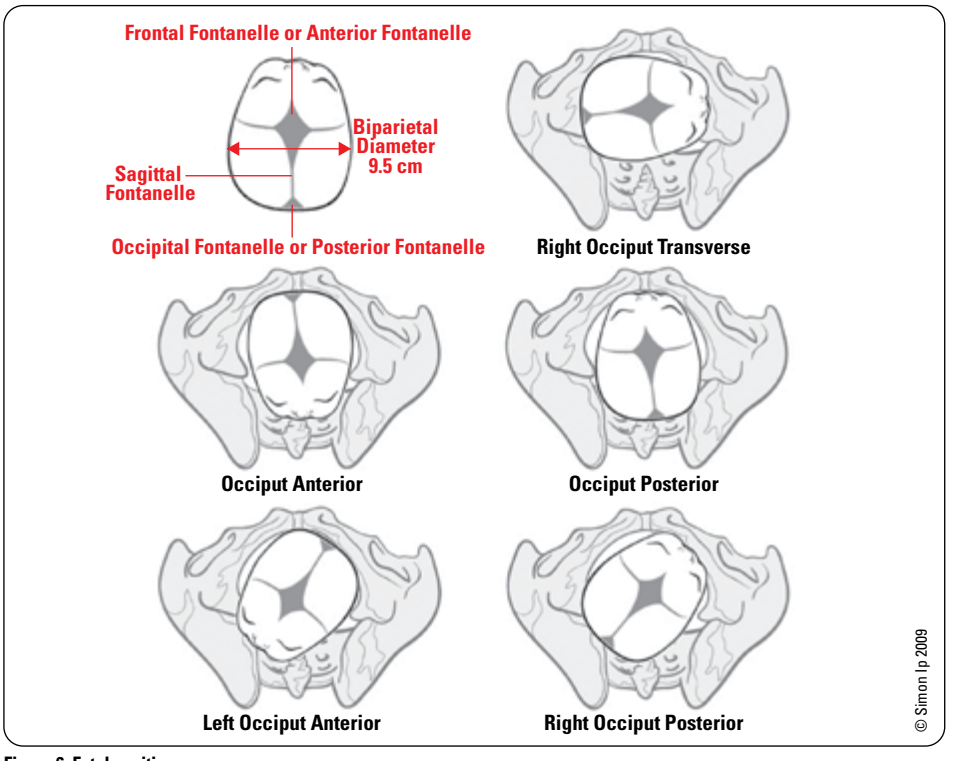


Figure 6. Fetal positions

Four Stages of Labour

First Stage of Labour (0 – 10 cm cervical dilation)

- latent phase
  - uterine contractions typically infrequent and irregular
  - slow cervical dilatation (usually to 4 cm) and effacement
- active phase
  - rapid cervical dilatation to full dilatation (nulliparous ≥1.0 cm/h, multiparous ≥1.2 cm/h)
  - phase of maximum slope on cervical dilatation curve
  - painful, regular contractions q2-3min, lasting 45-60 s
  - contractions strongest at fundus

Second Stage of Labour (10 cm dilation – delivery of the baby)

- from full dilatation to delivery of the baby; duration varies based on parity, contraction quality, and type of analgesia
- mother feels a desire to bear down and push with each contraction
- women may choose a comfortable position that enhances pushing efforts and delivery
  - upright (semi-sitting, squatting) and LLDP are supported in the literature
- progress measured by descent

Third Stage of Labour (delivery of the baby – delivery of the placenta)

- from baby's birth to separation and expulsion of the placenta
- can last up to 30 min before intervention is indicated
- demonstrated by gush of fresh blood, umbilical cord lengthening, uterine fundus changing shape (firm and globular), and rising upward
- active management: start oxytocin IV drip, or give 10 IU IM or 5 mg IV push, after delivery of anterior shoulder in anticipation of placental delivery, otherwise give after delivery of placenta
- routine oxytocin administration in third stage of labour can reduce the risk of PPH by >40%

Fourth Stage of Labour

- first postpartum hour
- monitor vital signs and bleeding, repair lacerations
- ensure uterus is contracted (palpate uterus and monitor uterine bleeding)
- inspect placenta for completeness and umbilical cord for presence of 2 arteries and 1 vein
- 3rd and 4th stages of labour most dangerous to the mother (i.e. hemorrhage)

Course of Normal Labour*

Stage	Nulliparous	Multiparous
First	6-18 h	2-10 h
Second	30 min-3 h	5-30 min
Third	5-30 min	5-30 min

*without epidural

Signs of Placental Separation

- Gush of blood
- Lengthening of cord
- Uterus becomes globular
- Fundus rises

Continuous Support for Women During Childbirth
Cochrane DB Syst Rev 2011;16:CD003766
Study: Systematic review of 21 RCTs from 11 countries, 15,061 women in labour.
Intervention: Continuous support during labour vs. usual care.
Outcome: Effects on mothers and their babies.
Results: Continuous intrapartum support increased likelihood of shorter labour, spontaneous vaginal birth, decrease in analgesia use, and a decrease in dissatisfaction with childbirth experience. Greatest benefit when provider is not a health care professional. Continuous support was also associated with decreased likelihood to have a Cesarean or instrumental vaginal birth, regional analgesia, or a baby with a low 5 min APGAR score.

The Cardinal Movements of the Fetus During Delivery

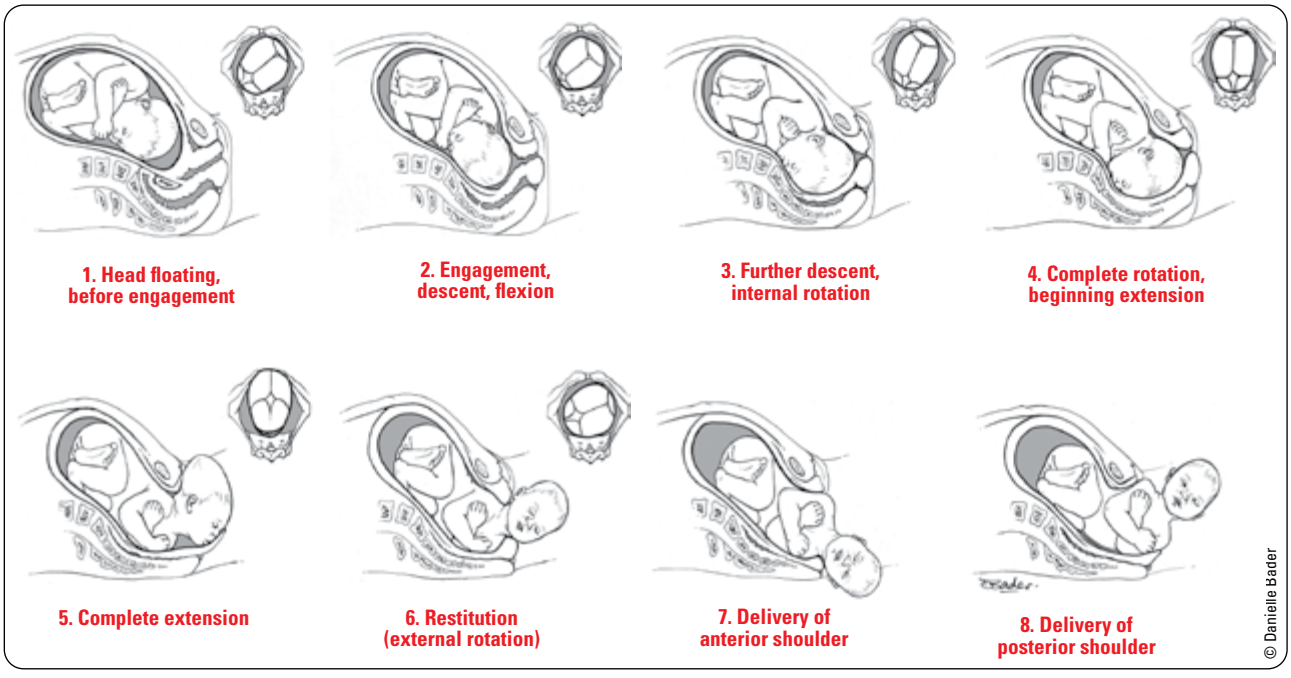


Figure 7. Cardinal movements of fetus during delivery
Adapted from illustration in Williams Obstetrics, 19th ed

Analgesic and Anesthetic Techniques in Labour and Birth

- pain or anxiety leads to high endogenous catecholamines, which produce a direct inhibitory effect on uterine contractility

Non-Pharmacologic Pain Relief Techniques

- reduction of painful stimuli
  - maternal movement, position change, counter-pressure, and abdominal compression
- activation of peripheral sensory receptors
  - superficial heat and cold
  - immersion in water during labour
  - touch and massage, acupuncture, and acupressure
  - TENS
  - intradermal injection of sterile water
  - aromatherapy
- enhancement of descending inhibitory pathways
  - attention focusing and distraction
  - hypnosis
  - music and audio analgesia
  - biofeedback

Pharmacologic Methods (see Anesthesia and Perioperative Medicine, A27)

- nitrous oxide (e.g. self-administered Entonox®)
- narcotics (usually combined with anti-emetic)
- pudendal nerve block
- perineal infiltration with local anesthetic
- regional anesthesia (epidural block, combined spinal-epidural, and spinal)

Fetal Monitoring in Labour


- see online **Fetal Heart Rate Tutorial**

Vaginal Exam

- membrane status, as indicated by amniotic fluid (clear, pink, bloody, and meconium)
- cervical effacement (thinning), dilatation, consistency, position, and application
- fetal presenting part, position, and station
- bony pelvis size and shape
- monitor progress of labour at regular intervals and document in a partogram

Intrapartum Fetal Monitoring

- intermittent fetal auscultation with Doppler device q15-30min for 1 min in first stage active phase following a contraction, q5min during second stage when pushing has begun
- continuous electronic FHR monitoring reserved for abnormal auscultation, prolonged labour, labour which is induced or augmented, meconium present, multiple gestation/fetal complication, and concerns about the fetus tolerating labour
  - use of continuous electronic monitoring shown to lead to higher intervention rates and no improvement in outcome for the neonate when used routinely in all patients (i.e. no risk factors)
  - techniques for continuous monitoring include external (Doppler) vs. internal (fetal scalp electrode) monitoring
- fetal scalp sampling should be used in conjunction with electronic FHR monitoring and contraction monitoring (CTG) to resolve the interpretation of abnormal or atypical patterns

Electronic FHR Monitoring

- FHR measured by Doppler; contractions measured by tocometer
- described in terms of baseline FHR, variability (short-term, long-term), and periodicity (accelerations, decelerations)
- **Baseline FHR**
  - normal range is 110-160 bpm
  - parameter of fetal well-being vs. distress
- **Variability**
  - physiologic variability is a normal characteristic of FHR
  - variability is measured over a 15 min period and is described as: absent, minimal (<6 bpm), moderate (6-25 bpm), or marked (>25 bpm)
  - normal variability indicates fetal acid-base status is acceptable
  - can only be assessed by electronic contraction monitoring (CTG)
  - variability decreases intermittently even in healthy fetus
  - see Table 19, OB35
- **Periodicity**
  - accelerations: increase of ≥15 bpm for ≥15 s, (or ≥10 bpm for ≥10 s if <32 wk GA)
  - decelerations: 3 types, described in terms of shape, onset, depth, duration recovery, occurrence, and impact on baseline FHR and variability

Table 17. Factors Affecting Fetal Heart Rate

	Fetal Tachycardia (FHR >160 bpm)	Fetal Bradycardia (FHR <110 bpm)	Decreased Variability
Maternal Factors	Fever, hyperthyroidism, anemia, dehydration	Hypothermia, hypotension, hypoglycemia, position, umbilical cord occlusion	Infection Dehydration
Fetal Factors	Arrhythmia, anemia, infection, prolonged activity, chronic hypoxemia, congenital anomalies	Rapid descent, dysrhythmia, heart block, hyopoxia, vagal stimulation (head compression), hypothermia, acidosis	CNS anomalies Dysrhythmia Inactivity/sleep cycle, preterm fetus
Drugs	Sympathomimetics	β-blockers Anesthetics	Narcotics, sedatives Magnesium sulphate, β-blockers
Uteroplacental	Early hypoxia (abruption, HTN) Chorioamnionitis	Late hypoxia (abruption, HTN) Acute cord prolapse Hypercontractility	Hypoxia

Approach to the Management of Abnormal FHR

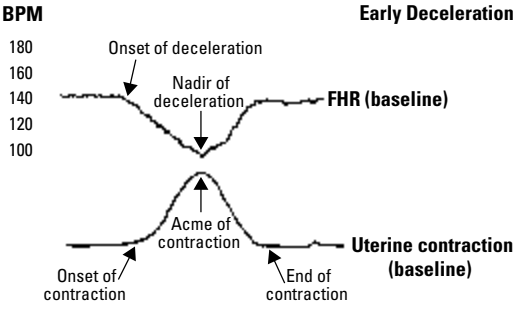
POISON – ER
Position (LLDP)
O$_2$ (100% by mask)
IV fluids (corrects maternal hypotension)
Fetal **s**calp stimulation
Fetal **s**calp electrode
Fetal **s**calp pH
Stop **o**xytocin
Notify MD
Vaginal **e**xam to rule out cord prolapse
Rule out fever, dehydration, drug effects, prematurity
- If above fails, consider C/S

Continuous CTG as a Form of EFM for Fetal Assessment During Labour
Cochrane DB Syst Rev 2013;5:CD006066
Purpose: To examine the effectiveness of continuous electronic fetal monitoring or cardiotocography during labour.
Selection Criteria: Randomized and quasi-randomized controlled trials comparing continuous CTG (with and without fetal blood sampling) to a) no fetal monitoring, b) intermittent auscultation, or c) intermittent CTG.
Results: 13 trials, 37,000 women. Continuous CTG compared with intermittent auscultation showed no difference in overall perinatal death rate or cerebral palsy rates. Nonetheless, neonatal seizures were halved (RR 0.50, 95% CI 0.31-0.80) and there was a significant increase in C/S (RR 1.63, 95% CI 1.29-2.07) and instrumental vaginal birth (RR 1.15, 95% CI 1.01-1.33) with CTG.
Conclusion: Continuous CTG may reduce the incidence of neonatal seizures, but has no effect on cerebral palsy rates, infant mortality, or other measures of neonatal well-being. Continuous CTG was also associated with an increase in C/S and instrumental deliveries.

Table 18. Comparison of Decelerations

Early Decelerations

- Uniform shape with onset early in contraction, returns to baseline by end of contraction, mirrors contraction (nadir occurs at peak of contraction)
- Gradual deceleration and return to baseline
- Often repetitive; no effect on baseline FHR or variability
- Benign, due to vagal response to head compression

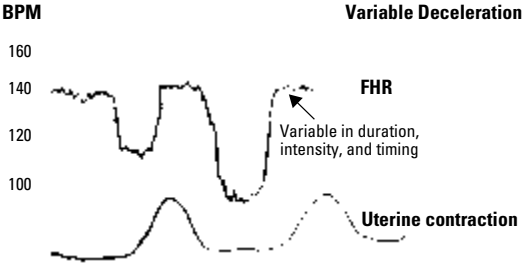


Variable Decelerations

- Variable in shape, onset, and duration
- Most common type of periodicity seen during labour
- Often with abrupt drop in FHR >15 bpm below baseline (>15 s, <2 min); usually no effect on baseline FHR or variability
- Due to cord compression or, in second stage, forceful pushing with contractions

Complicated Variable Decelerations

- FHR drop <70 bpm for >60 s
- Loss of variability or decrease in baseline after deceleration
- Biphasic deceleration
- Slow return to baseline
- Baseline tachycardia or bradycardia
- May be associated with fetal acidemia



Rule of 60s Suggesting Severe Variable Decelerations
Deceleration to <60 bpm
>60 bpm below baseline
>60 s in duration with slow return to baseline

Late Decelerations

- Uniform shape with onset, nadir, and recovery occurring after peak of contraction, slow return to baseline
- May cause decreased variability and change in baseline FHR
- Due to fetal hypoxia and acidemia, maternal hypotension, or uterine hypertonus
- Usually a sign of uteroplacental insufficiency (an ominous sign)

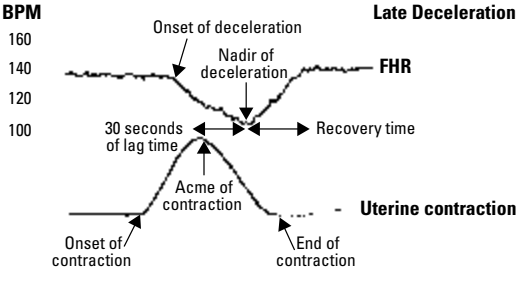


Table 19. Classification of Intrapartum EFM Tracings

	Normal Tracing (Category 1)	Atypical Tracing* (Category 2)	Abnormal Tracing* (Category 3)
Baseline	110-160 bpm	Bradycardia 100-110 bpm Tachycardia >160 for 30-80 min Rising baseline	Bradycardia <100 bpm Tachycardia >160 bpm for >80 min Erratic baseline
Variability	6-25 bpm ≤5 bpm for <40 min	≤5 bpm for 40-80 min	<5 bpm for >80 min ≥25 bpm for >10 min
Decelerations	None Early decelerations Occasional uncomplicated variable decelerations	Repetitive (≥3) uncomplicated variable decelerations Occasional late decelerations Any prolonged deceleration (2-3 min)	Repetitive (≥3) complicated variable decelerations Repetitive late decelerations Any prolonged deceleration (≥3 min)
Accelerations	Accelerations spontaneous or during scalp stimulation	Absent with scalp stimulation	Nearly absent
Action	EFM may be interrupted for ≤30 min if mother/fetus stable	Further assessment required	Action required: review clinical situation, obtain scalp pH, prepare for possible delivery

Adapted from SOGC Guidelines, September 2008
*Previous classification was "reassuring" vs. "non-reassuring", but distinction is now made between tracings that have some concerning changes but do not require immediate action (atypical) versus those with major concerns requiring immediate intervention (abnormal)

Fetal Scalp Blood Sampling

- cervix must be adequately dilated
- indicated when atypical or abnormal fetal heart rate is suggested by clinical parameters including heavy meconium or moderately to severely abnormal FHR patterns (including unexplained low variability, repetitive late decelerations, complex variable decelerations, and fetal cardiac arrhythmias)

- done by measuring pH or more recently fetal lactate
  - pH ≥7.25, lactate <4.2 mmol/L: normal, repeat if abnormal FHR persists
  - pH 7.21-7.24, lactate 4.2-4.8 mmol/L: repeat assessment in 30 min or consider delivery if rapid fall since last sample
  - pH ≤7.20, lactate >4.8 mmol/L indicates fetal acidosis, delivery is indicated
- contraindications
  - known or suspected fetal blood dyscrasia (hemophilia, vWD)
  - active maternal infection (HIV, genital herpes)

Fetal Oxygenation

- uterine contractions during labour decrease uteroplacental blood flow, which results in reduced oxygen delivery to the fetus
- most fetuses tolerate this reduction in flow and have no adverse effects
- distribution of oxygen to the fetus depends on maternal, uteroplacental, and fetal factors
- fetal response to hypoxia/asphyxia:
  - decreased movement, tone, and breathing activities
  - anaerobic metabolism (decreased pH)
  - transient fetal bradycardia followed by fetal tachycardia
  - redistribution of fetal blood flow
- increased flow to brain, heart, and adrenals
- decreased flow to kidneys, lungs, gut, liver, and peripheral tissues
- increase in blood pressure

Table 20. Factors Affecting Fetal Oxygenation

Factor	Mechanism	Example
Maternal	Decreased maternal oxygen carrying capacity	Significant anemia (iron deficiency, hemoglobinopathies), carboxyhemoglobin (smokers)
	Decreased uterine blood flow	Hypotension (blood loss, sepsis), regional anesthesia, maternal positioning
	Chronic maternal conditions	Vasculopathies (SLE, type 1 DM, chronic HTN), APS, cyanotic heart disease, COPD
Uteroplacental	Uterine hypertonus	Placental abruption, hyperstimulation secondary to oxytocin, prostaglandins, or normal labour
	Uteroplacental dysfunction	Placental abruption, placental infarction (dysfunction marked by IUGR, oligohydramnios, abnormal Doppler studies), chorioamnionitis, placental edema (DM, hydrops), placental senescence (post-dates)
Fetal	Cord compression	Oligohydramnios, cord prolapse, or entanglement
	Decreased fetal oxygen carrying capacity	Significant anemia (isoimmunization, feto-maternal bleed), carboxyhemoglobin (exposure to smokers)

Induction of Labour

Definition

- artificial initiation of labour in a pregnant woman prior to spontaneous initiation to deliver the fetus and placenta

Prerequisites for Labour Induction

- capability for C/S if necessary
- maternal
  - inducible/ripe cervix: short, thin, soft, anterior cervix with open os
  - if cervix is not ripe, use prostaglandin vaginal insert (Cervidil®), prostaglandin gel (Prepidil®), misoprostol (Cytotec®), or Foley catheter
- fetal
  - normal fetal heart tracing
  - cephalic presentation
  - adequate fetal monitoring available
- likelihood of success determined by Bishop score
  - cervix considered unfavourable if <6
  - cervix favourable if ≥6
  - score of 9-13 associated with high likelihood of vaginal delivery

Induction is indicated when the risk of continuing pregnancy exceeds the risks associated with induced labour and delivery

Table 21. Bishop Score

Cervical Characteristic	0	1	2	3
Position	Posterior	Mid	Anterior	–
Consistency	Firm	Medium	Soft	–
Effacement (%)	0-30	40-50	60-70	≥80
Dilatation (cm)	0	1-2	3-4	≥5
Station of Fetal Head	-3	-2	-1, 0	+1, +2, +3

Induction vs. Augmentation
Induction is the artificial initiation of labour
Augmentation promotes contractions when spontaneous contractions are inadequate

Indications
- post-dates pregnancy (generally >41 wk) = most common reason for induction
- maternal factors
  - DM = second most common reason for induction
  - gestational HTN ≥37 wk
  - preeclampsia
  - other maternal medical problems, e.g. renal or lung disease, chronic hypertension, and cholestasis
  - maternal age over 40
- maternal-fetal factors
  - isoimmunization, PROM, chorioamnionitis
- fetal factors
  - suspected fetal jeopardy as evidenced by biochemical or biophysical indications
  - macrosomia, fetal demise, IUGR, oligo/polyhydramnios, anomalies requiring surgical intervention, and twins
  - previous stillbirth or low PAPP-A

Consider the Following Before Induction
- Indication for induction
- Contraindications
- GA
- Cervical favourability
- Fetal presentation
- Potential for CPD
- Fetal well-being/FHR
- Membrane status

Risks
- failure to achieve labour and/or vaginal birth
- uterine hyperstimulation with fetal compromise or uterine rupture
- maternal side effects to medications
- uterine atony and PPH

Contraindications
- maternal
  - prior classical or inverted T-incision C/S or uterine surgery (e.g. myomectomy)
  - unstable maternal condition
  - active maternal genital herpes
  - invasive cervical carcinoma
  - pelvic structure deformities
- maternal-fetal
  - placenta previa or vasa previa
  - cord presentation
- fetal
  - fetal distress, malpresentation/abnormal lie, or preterm fetus without lung maturity

Induction Methods

CERVICAL RIPENING

Definition
- use of medications or other means to soften, efface, and dilate the cervix; increases likelihood of successful induction
- ripening of an unfavourable cervix (Bishop score <6) is warranted prior to induction of labour

Methods
- intravaginal prostaglandin PGE2 gel (Prostin® gel): long and closed cervix
  - recommended dosing interval of prostaglandin gel is every 6-12 h up to 3 doses
- intravaginal PGE2 (Cervidil®): long and closed cervix, may use if ROM
  - continuous release, can be removed if needed
  - controlled release PGE2
- intracervical PGE2 (Prepidil®)
- intravaginal PGE1 misoprostol (Cytotec®): long and closed cervix
  - inexpensive, stored at room temperature
  - more effective than PGE2 for achieving vaginal delivery and less epidural use
- Foley catheter placement to mechanically dilate the cervix

Evidence for Cervical Ripening Methods (SOGC Guidelines)
- Meta-analysis of five trials has concluded that the use of oxytocin to ripen the cervix is not effective
- Since the best dose and route of misoprostol for labour induction with a live fetus are not known and there are concerns regarding hyperstimulation, the use of misoprostol for induction of labour should be within clinical trials only (Level Ib evidence) or in cases of intrauterine fetal death to initiate labour

Intravaginal PGE2 (Cervidil®) Compared to Intravaginal Prostaglandin Gel
4 RCTs have compared the two with varying results, depending on the dosing regime of gel used.
Theoretical advantages of Cervidil®:
- Slow, continuous release
- Only one dose required
- Ability to use oxytocin 30 min after removal vs. 6 hours for gel
- Ability to remove insert if required (i.e. excessive uterine activity)

INDUCTION OF LABOUR

Amniotomy

- artificial ROM (amniotomy) to stimulate prostaglandin synthesis and secretion; may try this as initial measure if cervix is open and soft, the membranes can be felt, and if the head is present at the cervix
- few studies address the value of amniotomy alone for induction of labour
- amniotomy plus intravenous oxytocin: more women delivered vaginally at 24 h than amniotomy alone (relative risk = 0.03) and had fewer instrumental vaginal deliveries (relative risk = 5.5)

Oxytocin

- oxytocin (Pitocin®): 10 U in 1L NS, run at 0.5-2 mU/min IV increasing by 1-2 mU/min q20-60min
- reduces rate of unsuccessful vaginal deliveries within 24 h when used alone (8.3% vs. 54%, RR 0.16)
- ideal dosing regimen of oxytocin is not known
- current recommendations: use the minimum dose to achieve active labour and increase q30min as needed
- reassessment should occur once a dose of 20 mU/min is reached
- potential complications
  - hyperstimulation/tetanic contraction (may cause fetal distress or uterine rupture)
  - uterine muscle fatigue, uterine atony (may result in PPH)
  - vasopressin-like action causing anti-diuresis

Oxytocin t1/2 = 3-5 min

Augmentation of Labour

- augmentation of labour with oxytocin is used to promote adequate contractions when spontaneous contractions are inadequate and cervical dilatation or descent of fetus fails to occur

Provided there are no contraindications, oxytocin is utilized to improve uterine contraction strength and/or frequency

Abnormalities and Complications of Labour and Delivery

Abnormal Progression of Labour (Dystocia)

Definition

- expected patterns of descent of the presenting part and cervical dilatation fail to occur in the appropriate time frame; can occur in all stages of labour
- during active phase: >4 h of <0.5 cm/h
- during 2nd stage: >1 h with no descent during active pushing

Etiology

- Power (leading cause): contractions (hypotonic, uncoordinated), inadequate maternal expulsive efforts
- Passenger: fetal position, attitude, size, anomalies (hydrocephalus)
- Passage: pelvic structure (CPD), maternal soft tissue factors (tumours, full bladder or rectum, vaginal septum)
- Psyche: hormones released in response to stress may contribute to dystocia; psychological and physiological stress should be evaluated as part of the management once dystocia has been diagnosed

The 4 Ps of Dystocia
Power
Passenger
Passage
Psyche

Management

- confirm diagnosis of labour (rule out false labour)
- search for factors of CPD
- concern for dystocia if adequate contractions measured by intrauterine pressure catheter (IUPC) with no descent/dilatation for >2 h
- management: if CPD ruled out, IV oxytocin augmentation ± amniotomy

Risks of Dystocia

- inadequate progression of labour is associated with an increased incidence of:
  - maternal stress
  - maternal infection
  - PPH
  - need for neonatal resuscitation
  - fetal compromise (from uterine hyperstimulation)
  - uterine rupture
  - hypotension

Shoulder Dystocia

Definition
- fetal anterior shoulder impacted above pubic symphysis after fetal head has been delivered
- life threatening emergency

Etiology/Epidemiology
- incidence 0.15-1.4% of deliveries
- occurs when breadth of shoulders is greater than biparietal diameter of the head

Risk Factors
- maternal: obesity, DM, multiparity, and previous shoulder dystocia
- fetal: prolonged gestation or macrosomia (especially if associated with GDM)
- labour
  - prolonged 2nd stage
  - instrumental midpelvic delivery

Presentation
- "turtle sign": head delivered but retracts against inferior portion of pubic symphysis
- complications
  - fetal
    - hypoxic ischemic encephalopathy (chest compression by vagina or cord compression by pelvis can lead to hypoxia)
    - brachial plexus injury (Erb's palsy: C5-C7; Klumpke's palsy: C8-T1), 90% resolve within 6 mo
    - fracture (clavicle, humerus, and cervical spine)
    - death
  - maternal
    - perineal injury
    - PPH (uterine atony or lacerations)
    - uterine rupture

Treatment
- goal: to displace anterior shoulder from behind symphysis pubis; follow a stepwise approach of maneuvers until goal achieved (see sidebar)
- other options
  - cleidotomy (deliberate fracture of neonatal clavicle)
  - Zavanelli maneuver: replacement of fetus into uterine cavity and emergent C/S
  - symphysiotomy

Prognosis
- 1% risk of long-term disability for infant

Approach to the Management of Shoulder Dystocia

ALARMER
Apply suprapubic pressure and ask for help
Legs in full flexion (McRobert's maneuver)
Anterior shoulder disimpaction (suprapubic pressure)
Release posterior shoulder by rotating it anteriorly with hand in the vagina under adequate anesthesia
Manual corkscrew i.e. rotate the fetus by the posterior shoulder until the anterior shoulder emerges from behind the maternal symphysis
Episiotomy
Rollover (on hands and knees)
*Note that suprapubic pressure and McRobert's maneuver together will resolve 90% of cases

Umbilical Cord Prolapse

Definition
- descent of the cord to a level adjacent to or below the presenting part, causing cord compression between presenting part and pelvis

Etiology/Epidemiology
- increased incidence with prematurity/PROM, fetal malpresentation (~50% of cases), low-lying placenta, polyhydramnios, multiple gestation, and CPD
- incidence: 1/200-1/400 deliveries

Presentation
- visible or palpable cord
- FHR changes (variable decelerations, bradycardia, or both)

Treatment
- emergency C/S if not fully dilated and vaginal delivery not imminent
- O_2 to mother, monitor fetal heart
- alleviate pressure of the presenting part on the cord by elevating fetal head with a pelvic exam (maintain this position until C/S)
- keep cord warm and moist by replacing it into the vagina ± applying warm saline soaks
- roll mother onto all fours or position mother in Trendelenburg or knee-to-chest position
- if fetal demise or too premature (<22 wk), allow labour and delivery

Umbilical Cord Accident Causes
- Nuchal cord
  - Type A (looped)
  - Type B (hitched)
- Body loop
- Single artery
- True knot
- Torsion
- Velamentous
- Short cord <35 cm
- Long cord >80 cm

- 1/3 of protraction disorders develop into 2° arrest of dilatation due to CPD
- 2/3 of protraction disorders progress through labour to vaginal delivery

Uterine Rupture

Definition
- associated with previous uterine scar (in 40% of cases), hyperstimulation with oxytocin, grand multiparity, and previous intrauterine manipulation
- generally occurs during labour, but can occur earlier with a classical incision
- 0.5-0.8% incidence, up to 12% with classical incision

Presentation
- prolonged fetal bradycardia – most common presentation
- acute onset of constant lower abdominal pain, may not have pain if receiving epidural analgesia
- hyper/hypotonic uterine contractions
- abnormal progress in labour
- vaginal bleeding
- intra-abdominal hemorrhage
- loss of station of the presenting fetal part
- maternal tachycardia, hypotension, or shock

Risk Factors
- uterine scarring (i.e. previous uterine surgeries including C/S (especially classical incision), perforation with D&C, and myomectomy)
- excessive uterine stimulation (i.e. protracted labour, oxytocin, prostaglandins)
- uterine trauma (i.e. operative equipment, ECV)
- multiparity
- uterine abnormalities
- malpresentation
- placenta accreta

Treatment
- rule out placental abruption
- maternal stabilization (may require hysterectomy), treat hypovolemia
- immediate delivery for fetal survival

Complications
- maternal mortality 1-10%
- maternal hemorrhage, shock, DIC
- amniotic fluid embolus
- hysterectomy if uncontrollable hemorrhage
- fetal distress, associated with infant mortality as high as 15%

Maternal Mortality Causes
- Thromboembolism
- Cardiac event
- Suicide
- Sepsis
- Ectopic pregnancy
- HTN
- Amniotic fluid embolism
- Hemorrhage

* In Canada (2013), lifetime risk of maternal death is 1 in 5200

Amniotic Fluid Embolus

Definition
- amniotic fluid debris in maternal circulation triggering an anaphylactoid immunologic response

Etiology/Epidemiology
- rare intrapartum or immediate postpartum complication
- 13-30% maternal mortality rate
- leading cause of maternal death in induced abortions and miscarriages
- 1/8000-1/80,000 births

Risk Factors
- placental abruption
- rapid labour
- multiparity
- uterine rupture
- uterine manipulation
- induction medication and procedures

Differential Diagnosis
- pulmonary embolus, drug-induced anaphylaxis, septic shock, eclampsia, HELLP syndrome, abruption, and chronic coagulopathy

Presentation
- sudden onset of respiratory distress, cardiovascular collapse (hypotension, hypoxia), and coagulopathy
- seizure in 10%
- ARDS and left ventricular dysfunction seen in survivors

Management
- should be managed in the ICU by a multidisciplinary team
- supportive measures (high flow O_2, ventilation support, fluid resuscitation, inotropic support, ± intubation) and coagulopathy correction

Chorioamnionitis

Definition
- infection of the chorion, amnion, and amniotic fluid

Etiology/Epidemiology
- incidence 1-5% of term pregnancies and up to 25% in preterm deliveries
- ascending infection (microorganisms from vagina)
- predominant microorganisms include: GBS, *Bacteroides* and *Prevotella* species, *E. coli*, and anaerobic *Streptococcus*

Clinical Features of Chorioamnionitis
- Temperature
- Tachycardia (maternal or fetal)
- Tenderness (uterine)
- Foul discharge

Risk Factors
- low parity, prolonged ROM, long labour, multiple vaginal exams during labour, and internal monitoring
- bacterial vaginosis and other vaginal infections

Clinical Features
- maternal fever ≥38° C, maternal or fetal tachycardia, uterine tenderness, and foul and purulent cervical discharge

Investigations
- CBC: leukocytosis
- amniotic fluid: Gram stain, glucose, or culture results consistent with infection

Treatment
- IV antibiotics
  - ampicillin 2 g IV q6h + gentamicin 2 mg/kg load, then 1.5 mg/kg IV q8h
  - anaerobic coverage (i.e. clindamycin 900 mg IV q8h)
  - if at risk for endometritis, continue treatment post-partum especially if C/S delivery
- antipyretics
- proper labour progression (not an indication for immediate delivery or C/S)

Complications
- bacteremia of mother or fetus, wound infection if C/S, pelvic abscess, neonatal meningitis, neonatal sepsis, and neonatal death
- long-term infant complications: cerebral palsy and bronchopulmonary dysplasia

Meconium

Epidemiology
- present early in labour in 10% of pregnancies, more common in postdate pregnancies
- in general, meconium may be present in up to 25% of all labours; usually NOT associated with poor outcome
- concern if fluid changes from clear to meconium-stained
- always abnormal if seen in preterm fetus

Particulate (thickened) meconium is associated with lower APGARs, an increased risk of meconium aspiration, and perinatal death. Particulate meconium generally has a darker green or black colour, whereas thin meconium is usually yellow to light green

Etiology
- likely cord compression ± uterine hypertonia
- may indicate undiagnosed breech
- increasing meconium during labour may be a sign of fetal distress

Features
- may be watery or thicker (particulate)
- light yellow/green or dark green-black in colour

Treatment
- call respiratory therapy, neonatology, or pediatrics to delivery room
- closely monitor FHR for signs of fetal distress

Operative Obstetrics

Operative Vaginal Delivery

Definition
- forceps or vacuum extraction

Indications
- fetal
  - atypical or abnormal fetal heart rate tracing, evidence of fetal compromise
  - consider if second stage is prolonged, as this may be due to poor contractions or failure of fetal head to rotate
- maternal
  - need to avoid voluntary expulsive effort (e.g. cardiac/cerebrovascular disease)
  - exhaustion, lack of cooperation, and excessive analgesia may impair pushing effort

Contraindications
- unknown fetal head presentation
- unengaged head
- fetal bone demineralization disorder (e.g. osteogenesis imperfecta)
- fetal bleeding disorder (e.g. hemophilia or vWD)

Prerequisites for Operative Vaginal Delivery

ABCDEFGHIJK
Anesthesia (adequate)
Bladder empty
Cervix fully dilated and effaced with ROM
Determine position of fetal head
Equipment ready (including facilities for emergent C/S)
Fontanelle (posterior fontanelle midway between thighs)
Gentle traction
Handle elevated
Incision (episiotomy)
Once **j**aw visible remove forceps
Knowledgeable operator

Forceps

Outlet Forceps Position
- head visible between labia in between contractions
- sagittal suture in or close to AP diameter
- rotation cannot exceed 45°

Low Forceps Position
- presenting part at station +2 or greater
- subdivided based on whether rotation less than or greater than 45°

Mid Forceps Position
- presenting part below spines but above station +2

Types of Forceps
- Simpson or Tucker-McLane forceps for OA presentations
- Kielland (rotational) forceps when rotation of head or correction of asynclitism is required
- Piper forceps for after-coming head in breech delivery
- Wrigley's for preterm babies

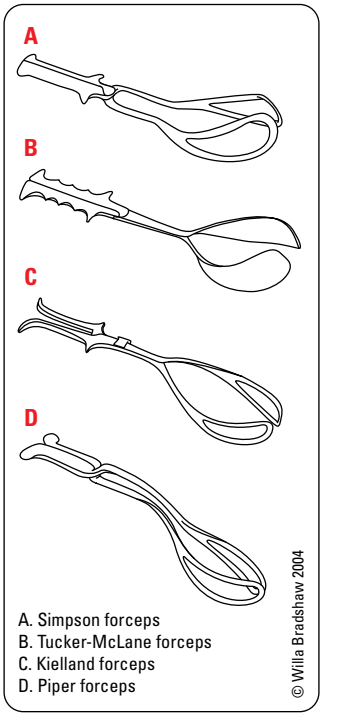


Figure 8. Types of forceps

Vacuum Extraction

- traction instrument used as alternative to forceps delivery; aids maternal pushing
- contraindications: <34 wk GA (<2500 g), fetal head deflexed, fetus requires rotation, fetal condition (e.g. bleeding disorder)

Limits for Trial of Vacuum
- After 3 pulls over 3 contractions with no progress
- After 3 pop-offs with no obvious cause
- 20 min and delivery is not imminent

Table 22. Advantages and Disadvantages of Forceps vs. Vacuum Extraction

	Forceps	Vacuum Extraction
Advantages	Higher overall success rate for vaginal delivery Decreased incidence of fetal morbidity	Easier to apply Less anesthesia required Less maternal soft-tissue injury compared to forceps
Disadvantages	Greater incidence of maternal injury	Suitable only for vertex presentations Maternal pushing required Contraindicated in preterm delivery
Complications	Maternal: anesthesia risk, lacerations, injury to bladder, uterus, or bone, pelvic nerve damage, PPH, and infections Fetal: fractures, facial nerve palsy, trauma to face/scalp, intracerebral hemorrhage, cephalohematoma, and cord compression	Increased incidence of cephalohematoma and retinal hemorrhages, and jaundice compared to forceps Subgaleal hemorrhage Subaponeurotic hemorrhage Soft tissue trauma

Lacerations

- first degree: involves skin and vaginal mucosa but not underlying fascia and muscle
- second degree: involves fascia and muscles of the perineal body but not the anal sphincter
- third degree: involves the anal sphincter (partial IIIa or complete IIIb)
- fourth degree: extends through the anal sphincter into the rectal mucosa
- for third and fourth degree tears, a single prophylactic dose of IV antibiotics (2nd generation cephalosporin, e.g. cefoxitin or cefotetan) should be administered to reduce perineal wound complications; laxatives should also be prescribed and constipation should be avoided

Episiotomy

Definition

- incision in the perineal body at the time of delivery
- essentially a controlled second degree laceration
- midline: incision through central tendinous portion of perineal body and insertions of superficial transverse perineal and bulbocavernosus muscles
  - heals better, but increases risk of 3rd/4th degree tears
- mediolateral: incision through bulbocavernosus, superficial transverse perineal muscle, and levator ani
  - reduced risk of extensive tear but more painful

Indications

- to relieve obstruction of the unyielding perineum
- to expedite delivery (e.g. abnormal FHR pattern)
- instrumental delivery
- controversial between practitioners as to whether it is preferable to make a cut or let the perineum tear as needed
- current evidence suggests letting perineum tear and then repair as needed (restricted use)

Complications

- infection, hematoma, extension into anal musculature or rectal mucosa, fistula formation, and incontinence

Risk Factors for the Development of Obstetric Anal Sphincter Injuries in Modern Obstetric Practice
Obstet Gynecol 2018;131(2):290-96
Objective: To characterize the rate of obstetric anal sphincter injuries and identify key risk factors of obstetric anal sphincter injuries, including duration of the second stage of labour.
Methods: Retrospective cohort study including all singleton, term, cephalic vaginal deliveries from 2013 to 2014.
Results: The overall incidence rate of obstetric anal sphincter injuries was 4.9% (3.6% of women who delivered spontaneously vs 24.0% of women who had a vacuum-assisted vaginal delivery, P<.001, CI 18.1–22.6%). In bivariate and multivariate analyses, obstetric anal sphincter injury incidence was higher among women with second stage of labour longer than 2 hours, Asian race, nulliparity, vaginal birth after cesarean delivery, episiotomy, and vacuum delivery. Women with a vacuum-assisted vaginal delivery had four times the odds of obstetric anal sphincter injury (adjusted odds ratio [OR] 4.23, 95% CI 3.59-4.98) and those whose second stage of labour lasted at least 180 minutes vs less than 60 minutes had three times the odds of incurring obstetric anal sphincter injury (adjusted OR 3.20, 95% CI 2.62-3.89).

Cesarean Delivery

Epidemiology

- overall 28% rate in Canada (range 18.5-35.3% by province/territory)

Indications

- maternal: obstruction, active herpetic lesion on vulva, invasive cervical cancer, previous uterine surgery (past C/S is most common), and underlying maternal illness (eclampsia, HELLP syndrome, heart disease)
- maternal-fetal: failure to progress, placental abruption or previa, and vasa previa
- fetal: abnormal fetal heart tracing, malpresentation, cord prolapse, and certain congenital anomalies

Types of Cesarean Incisions

- skin
  - transverse (Pfannenstiel)
  - decreased exposure and slower entry
  - improved strength and cosmesis
  - vertical midline
  - rapid peritoneal entry and increased exposure
  - increased dehiscence
- uterine
  - low transverse (most common): in non-contractile lower segment
- decreased chance for rupture in subsequent pregnancies
  - low vertical
  - used for very preterm infants or poorly developed maternal lower uterine segment
  - classical (rare): in thick, contractile segment
  - used for transverse lie, preterm breech, fetal anomaly, >2 fetuses, lower segment adhesions, obstructing fibroid, and inaccessible lower uterine segment (e.g. morbid obesity)

Risks/Complications

- anaesthetic complications (e.g. aspiration)
- hemorrhage (average blood loss ~1000 cc)
- infection (UTI, wound, and endometritis)
  - single dose prophylactic antibiotic should be used (e.g. cefazolin 1-2 g)
- injury to surrounding structures (bowel, bladder, ureter, and uterus)
- thromboembolism (DVT, PE)
- increased recovery time/hospital stay
- maternal mortality (<0.1%)

Common OR Questions

7 Layers to Dissect
Skin, fatty layer, fascia, muscle separation (rectus abdominis), peritoneum, bladder flap, uterus

Layers of the Rectus Sheath
Above the arcuate line: external oblique, external internal oblique, internal oblique, rectus abdominis, internal internal oblique, transversus abdominis
Below the arcuate line: external oblique, internal oblique, transversus abdominis, rectus abdominis

Name of the Obliterated Umbilical Ligament Urachus

Most C/S performed with regional analgesia

Trial of Labour after Cesarean Section (TOLAC)

- should be recommended if no contraindications after previous low transverse incision
- success rate varies with indication for previous C/S (generally 60-80%)
- risk of uterine rupture (<1% with low transverse incision), increased by interval <18 mo and one layer closure

Contraindications
- previous classical, inverted T, or unknown uterine incision, or complete transection of uterus (6% risk of rupture)
- history of uterine surgery (e.g. myomectomy) or previous uterine rupture
- multiple gestation
- non-vertex presentation or placenta previa
- inadequate facilities or personnel for emergency C/S

VBAC*
- Rate of successful VBAC ranges from 60-82%
- No significant difference in maternal deaths or hysterectomies between VBAC or C/S
- Uterine rupture more common in VBAC group
- Evidence regarding fetal outcome is lacking

*Safety of vaginal birth after Cesarean section: A systematic review. *Obstet Gynecol* 2004;103:420-9

Puerperal Complications

- puerperium: 6 wk period of adjustment after pregnancy when pregnancy-induced anatomic and physiologic changes are reversed

Postpartum Hemorrhage

Definition
- loss of >1000 ml of blood or bleeding associated with signs/symptoms of hypovolemia within 24 hours of birthing process regardless of mode of delivery
- primary – within first 24 h postpartum
- secondary – after 24 h but within first 12 wk

Epidemiology
- incidence 5-15%

Etiology (4 Ts)
1. Tone (uterine atony)
- most common cause of PPH (70-80%)
- avoid with active management of 3rd stage of labour with 1) oxytocin administration 2) uterine massage 3) umbilical cord traction
- due to:
  - overdistended uterus (polyhydramnios, multiple gestations, and macrosomia)
  - uterine muscle exhaustion (prolonged or rapid labour, grand multiparity, oxytocin use, and general anesthetic)
  - uterine distortion (fibroids)
  - intra-amniotic infection (fever or prolonged ROM)
  - bladder distension (preventing uterine contraction)

2. Tissue
- retained placental products (membranes, cotyledon, or succenturiate lobe)
- retained blood clots in an atonic uterus
- gestational trophoblastic neoplasia
- abnormal placentation (e.g. placenta previa or placental abruption)

3. Trauma
- laceration (vagina, cervix, or uterus), episiotomy, hematoma (vaginal, vulvar, or retroperitoneal), uterine rupture, and uterine inversion

4. Thrombin
- coagulopathy (pre-existing or acquired)
  - most identified prior to delivery (low platelets increases risk)
  - includes hemophilia, DIC, ITP, TTP, and vWD (most common)
  - therapeutic anti-coagulation

Uterine atony is the most common cause of PPH

DDx of Early PPH – 4 Ts
Tone (atony)
Tissue (retained placenta, clots)
Trauma (laceration, inversion)
Thrombin (coagulopathy)

DDx of Late PPH
Retained products
± endometritis
Sub-involution of uterus

Investigations
- assess degree of blood loss and shock by clinical exam
- explore uterus and lower genital tract for evidence of atony, retained tissue, or trauma
- may be helpful to observe red-topped tube of blood – no clot in 7-10 min indicates coagulation problem

Management
- ABCs, call for help
- 2 large bore IVs, run crystalloids wide open
- CBC, coagulation profile, cross and type pRBCs
- treat underlying cause
- Foley catheter to empty bladder and monitor urine output

Medical Therapy
- oxytocin 10 IU IM is preferred in low-risk vaginal deliveries, oxytocin IV infusion (20-40 IU in 1000 mL crystalloid at 150 mL/h) is an acceptable alternative. Oxytocin 5-10 IU IV bolus (20-40 IU in 250 mL crystalloid) can be used after vaginal birth, but not with elective C/S
- carbetocin, a long-acting oxytocin, 100 μg IV bolus over 1 min for elective C/S or 100 ug IM for vaginal deliveries with 1 risk factor for PPH (instead of a continuous oxytocin infusion)
- methylergonavine maleate (ergotamine) 0.25 mg IM/IMM q15min up to 1.25 mg; can be given as IV bolus of 0.125 mg (may exacerbate HTN)
- carboprost (Hemabate®), a synthetic PGF-1α analog, 250 μg IM/IMM q15min to max 2 mg (major prostaglandin side effects and contraindicated in cardiovascular, pulmonary, renal, and hepatic dysfunction)
- misoprostol 600-800 μg PO/SL (faster) or PR/PV (side effect: pyrexia if >600 μg)
- tranexamic acid (Cyklokapron®), an antifibrinolytic, 1 g IV

Local Control
- bimanual massage: elevate the uterus and massage through patient's abdomen
- uterine packing (mesh with antibiotic treatment)
- Bakri Balloon for tamponade: may slow hemorrhage enough to allow time for correction of coagulopathy or for preparation of an OR

Surgical Therapy (Intractable PPH)
- D&C (beware of vigorous scraping, which can lead to Asherman's syndrome)
- embolization of uterine artery or internal iliac artery by interventional radiologist
- laparotomy with bilateral ligation of uterine artery (may be effective), ovarian artery, or hypogastric artery, compression sutures (B-Lynch or Cho sutures)
- hysterectomy last option, with angiographic embolization if post-hysterectomy bleeding

Retained Placenta

Definition
- placenta undelivered after 30 min postpartum

Etiology
- placenta separated but not delivered
- abnormal placental implantation (placenta accreta, placenta increta, and placenta percreta)

Risk Factors
- placenta previa, prior C/S, post-pregnancy curettage, prior manual placental removal, and uterine infection

Clinical Features
- risk of PPH and infection

Investigations
- explore uterus
- assess degree of blood loss

Management
- 2 large bore IVs, type and screen
- Brandt maneuver (firm traction on umbilical cord with one hand applying suprapubic pressure cephalad to avoid uterine inversion by holding uterus in place)
- oxytocin 10 IU in 20 mL NS into umbilical vein
- manual removal if above fails
- D&C if required (U/S guidance if available)
- cefazolin 2 g IV if manual removal or D&C

Uterine Inversion

Definition
- inversion of the uterus through cervix ± vaginal introitus

Etiology/Epidemiology
- often iatrogenic (excess cord traction with fundal placenta)
- excessive use of uterine tocolytics
- more common in grand multiparous women (lax uterine ligaments)
- 1/1500-1/2000 deliveries

Clinical Features
- can cause profound vasovagal response with bradycardia, vasodilation, and hypovolemic shock
- shock may be disproportionate to maternal blood loss

Management
- urgent management essential, call anesthesia
- ABCs: initiate IV crystalloids
- can use tocolytic drug (see *Preterm Labour*, OB16) or nitroglycerin IV to relax uterus and aid replacement
- replace uterus without removing placenta
- remove placenta manually and withdraw slowly
- IV oxytocin infusion (only after uterus replaced)
- re-explore uterus
- may require general anesthetic ± laparotomy

Postpartum Pyrexia

Definition
- fever >38°C on any 2 of the first 10 d postpartum, except the 1st day

Etiology
- endometritis
- wound infection (check C/S and episiotomy sites)
- mastitis/engorgement
- UTI
- atelectasis
- pneumonia
- DVT or pelvic thrombophlebitis

Etiology of Postpartum Pyrexia

B-5W
Breast: engorgement, mastitis
Wind: atelectasis, pneumonia
Water: UTI
Wound: episiotomy, C/S site infection
Walking: DVT, thrombophlebitis
Womb: endometritis

Investigations
- detailed history and physical exam, relevant cultures
- for endometritis: blood and genital cultures
- serum lactic acid for early detection of sepsis

Treatment
- depends on etiology
  - infection: empiric antibiotics, adjust when sensitivities available
- endometritis: clindamycin + gentamicin IV
- mastitis: cloxacillin or cephalexin
- wound infection: cephalexin + frequent sitz baths for episiotomy site infection
  - DVT: anticoagulants
- prophylaxis against post-C/S endometritis: administer 2 g cefazolin IV 30 min prior to skin incision

Risk Factors for Endometritis
C/S, intrapartum chorioamnionitis, prolonged labour, prolonged ROM, multiple vaginal examinations

ENDOMETRITIS
- definition: inflammation of the endometrium most commonly due to infection
- clinical features: fever, chills, abdominal pain, uterine tenderness, foul-smelling vaginal discharge, or lochia
- treatment: depends on infection severity; oral antibiotics if well, IV antibiotics with hospitalization in moderate to severe cases

VENOUS THROMBOEMBOLISM
- see *Venous Thromboembolism*, OB30

Mastitis

- **definition**: inflammation of mammary glands
- must rule out inflammatory carcinoma, as indicated
- differentiate from mammary duct ectasia: mammary duct(s) beneath nipple clogged and dilated ± ductal inflammation ± nipple discharge (thick, grey to green), often postmenopausal women

Table 23. Lactational vs. Non-Lactational Mastitis

	Lactational	Non-Lactational
Epidemiology	More common than non-lactational Often 2-3 wk postpartum	Periductal mastitis most common Mean age 32 yr
Etiology	*S. aureus*	May be sterile May be infected with *S. aureus* or other anaerobes Smoking is risk factor May be associated with mammary duct ectasia
Symptoms	Unilateral localized pain Tenderness Erythema	Subareolar pain May have subareolar mass Discharge (variable colour) Nipple inversion
Treatment	Heat or ice packs Continued nursing/pumping Antibiotics (cloxacillin/cephalexin) (erythromycin if penicillin-allergic)	Broad-spectrum antibiotics and I&D Total duct excision (definitive)
Abscess	Fluctuant mass Purulent nipple discharge Fever, leukocytosis Discontinue nursing, IV antibiotics (nafcillin/oxacillin), I&D usually required	If mass does not resolve, fine-needle aspiration to exclude cancer and U/S to assess presence of abscess Treatment includes antibiotics, aspiration, or I&D (tends to recur) May develop mammary duct fistula A minority of non-lactational abscesses may occur peripherally in breast with no associated periductal mastitis (usually *S. aureus*)

Postpartum Mood Alterations

POSTPARTUM BLUES

- 40-80% of new mothers, onset day 3-10; extension of the "normal" hormonal changes and adjustment to a new baby
- self-limited, should resolve by 2 wk
- manifested by mood lability, depressed affect, increased sensitivity to criticism, tearfulness, fatigue, irritability, poor concentration/despondency, anxiety, and insomnia

POSTPARTUM DEPRESSION

- **definition**: major depression occurring in a woman within 6 mo of childbirth (see Psychiatry, PS12)
- **epidemiology**: 10-15%, risk of recurrence 50%
- **risk factors**
  - personal or family history of depression (including PPD)
  - prenatal depression or anxiety
  - stressful life situation
  - poor support system
  - unwanted pregnancy
  - colicky or sick infant
- **clinical features**: suspect if the "blues" last beyond 2 wk, or if the symptoms in the first 2 wk are severe (e.g. extreme disinterest in the baby, suicidal or homicidal/infanticidal ideation)
- **assessment**: Edinburgh Postnatal Depression Scale or others
- **treatment**: antidepressants, psychotherapy, supportive care, and ECT if refractory
- **prognosis**: interferes with bonding and attachment between mother and baby, so it can have long-term effects

POSTPARTUM PSYCHOSIS

- **definition**: onset of psychotic symptoms over 24-72 h within first month postpartum, can present in the context of depression
- **epidemiology**: rare (0.2%)

Postpartum Care

Postpartum Office Visit at 6 Weeks

Care of Mother (The 10 Bs)

- **B**e careful: do not use douches or tampons for 4-6 wk post-delivery
- **B**e fit: encourage gradual increases in walking, Kegel exercises
- **B**irth control: assess for use of contraceptives
- **B**reastfeeding is NOT an effective method of birth control (see Gynecology, GY15, for more detail about different contraceptive options postpartum)
- **B**ladder: assess for urinary incontinence, maintain high fluid intake
- **B**lood pressure: especially if gestational HTN
- **B**lood tests: CBC (for anemia if had PPH)
- **B**lues: (see *Postpartum Mood Alterations*, OB47)
- **B**owel: fluids and high-fibre foods, bulk laxatives; for hemorrhoids/perineal tenderness: pain meds, doughnut cushion, sitz baths, and ice compresses
- **B**reast and pelvic exam: watch for Staphylococcal or Streptococcal mastitis/abscess, ± Pap smear at 6 wk if due for screening

The acronym "**BUBBLES**" for what to ask about when rounding on postpartum care. Modify this for C/S or vaginal delivery

Baby care and breastfeeding-- Latch? Amount?
Uterus – firm or boggy?
Bladder function – Voiding well? Dysuria?
Bowel function – Passing gas or stool? Constipated?
Lochia or discharge – Any blood?
Episiotomy/laceration/incision – Pain controlled?
Symptoms of VTE – Dyspnea? Calf pain?

Physiological Changes Postpartum

- uterus weight rapidly diminishes through catabolism, cervix loses its elasticity and regains firmness
  - should involute ~1 cm below umbilicus per day in first 4-5 d, reaches non-pregnant state in 4-6 wk postpartum
- ovulation resumes in ~45 d after giving birth, non-lactating women usually ovulate sooner than lactating women
- lochia: normal vaginal discharge postpartum, uterine decidual tissue sloughing
  - decreases and changes in colour from red (lochia rubra; presence of erythrocytes, 3-4 d) → pale (lochia serosa) → white/yellow (lochia alba; residual leukorrhea) over 3-6 wk
- foul-smelling lochia suggests endometritis

Breastfeeding Problems

- inadequate milk: consider domperidone
- breast engorgement: cool compress, manual expression/pumping
- nipple pain: clean milk off nipple after feeds, moisturizer, topical steroid if needed
- mastitis: treat promptly (see *Postpartum Pyrexia*, OB46)
- inverted nipples: makes feeding difficult
- maternal medications: may require pediatric consultation (see *Breastfeeding and Drugs*, OB48)

Bladder Dysfunction

- pelvic floor prolapse can occur after vaginal delivery
- stress or urge urinary incontinence common
- increased risk with instrumental delivery or prolonged second stage
- conservative management for stress and urge incontinence: pelvic floor retraining with Kegel exercises/pelvic physiotherapy, vaginal cones or pessaries, and lifestyle modifications (e.g. limit fluid, caffeine intake)
- surgical management for stress incontinence: midurethral slings including retropubic tension free vaginal tape (TVT) or transobturator tape (TOT), retropubic urethropexy (Burch), urethral bulking

Puerperal Pain

- "after pains" common in first 3 d due to uterine contractions; encourage simple analgesia
- ice packs can be used on perineum if painful
- encourage regular analgesia and stool softener

Breastfeeding and Drugs

Table 24. Drug Safety During Breastfeeding

Safe During Breastfeeding	Contraindicated When Breastfeeding
Analgesics (e.g. acetaminophen, NSAIDs)	Chloramphenicol (bone marrow suppression)
Anticoagulants (e.g. heparin)	Cyclophosphamide (immune system suppression)
Antidepressants (e.g. sertraline, fluoxetine, tricyclic antidepressants)	Sulphonamides (in G6PD deficiency, can lead to hemolysis)
Antiepileptics (e.g. phenytoin, carbamazepine, valproic acid)	Nitrofurantoin (in G6PD deficiency, can lead to hemolysis)
Antihistamines	Tetracycline
Antimicrobials (e.g. penicillins, aminoglycosides, cephalosporins)	Lithium
β-adrenergics (e.g. propanolol, labetalol)	Phenindione
Insulin	Bromocriptine
Steroids	Anti-neoplastics and immunosuppresants
OCP (low dose) – although may decrease breast milk production	Psychotropic drugs (relative contraindication)

Common Medications

Table 25. Common Medications

Drug Name (Brand Name)	Dosing Schedule	Indications/Comments
betamethasone valerate (Celestone®)	12 mg IM q24h x 2 doses	Enhancement of fetal pulmonary maturity for PTL
carboprost (Hemabate®)	0.25 mg IM/IMM q15min Max 2 mg	Treatment of uterine atony
cefazolin	2 g IV then 1 g q8h	GBS prophylaxis (penicillin allergic and not at risk for anaphylaxis)
clindamycin	900 mg IV q8h	Used in endometritis
dexamethasone	6 mg IM q12h x 4 doses	Enhancement of fetal pulmonary maturity for PTL
dinoprostone (Cervidil®: PGE2 impregnated thread)	10 mg PV (remove after 12 h) Max 3 doses	Induction of labour Advantage: can remove if uterine hyperstimulation
doxylamine succinate (Diclectin®)	2 tabs qhs + 1 tab qam + 1 tab qpm Max 8 tabs/d	Each tablet contains 10 mg doxylamine succinate with vitamin B6 Used first-line for N/V in pregnancy, including hyperemesis gravidarum
erythromycin	500 mg IV q6h	GBS prophylaxis (penicillin allergic and at risk for anaphylaxis)
folic acid	0.4-1 mg PO OD x 1-3 mo preconception and T1 5 mg PO OD with past Hx of NTD/risks for NTD	Prevention of ONTD
methotrexate	50 mg/mL IM or 50 mg PO x 1 dose	For ectopic pregnancy or medical abortion
methylergonavine maleate (Ergotamine®)	0.25 mg IM/IMM q15min up to 1.25 mg or IV bolus 0.125 mg	Treatment of uterine atony
misoprostol (Cytotec®)	600-1000 µg PR x 1 dose 400 µg PO/SL x 1 dose or 800 µg PV x 1 dose 3-7 d after methotrexate	For treatment of PPH For medical abortion/retained products of conception
oxytocin (Pitocin®)	0.5-2.0 mU/min IV or 10 U/L NS increase by 1-2 mU/min q20-60min Max 36-48 mU/min 10 IU IM at delivery of anterior shoulder and of placenta 20 IU/L NS or RL IV continuous infusion	Augmentation of labour (also induction of labour) Prevention of uterine atony Treatment of uterine atony
Penicillin G	5 million IU IV, then 2.5 million IU IV q4h until delivery	GBS prophylaxis
PGE2 gel (Prostin® gel)	0.5 mg PV q6-12h; max 3 doses	Induction of labour
Rh IgG (Rhogam®)	300 µg IM x 1 dose	Given to Rh-negative women Routinely at 28 wk GA Within 72 h of birth of Rh+ fetus Positive Kleihauer-Betke test With any invasive procedure in pregnancy Ectopic pregnancy Antepartum hemorrhage Miscarriage or therapeutic abortion (dose: 50 µg IM only)

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GY Gynecology

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Acronyms

β-hCG	beta-human chorionic gonadotropin
ACEI	angiotensin converting enzyme inhibitors
AFP	alpha-fetoprotein
AIS	androgen insensitivity syndrome
ARB	angiotensin II receptor blockers
ASCUS	atypical squamous cells of undetermined significance
AUB	abnormal uterine bleeding
BMD	Bone mineral density
BMI	body mass index
BSO	bilateral salpingo-oophorectomy
BV	bacterial vaginosis
CAH	congenital adrenal hyperplasia
CHC	combined hormonal contraception
CMV	cytomegalovirus
D&C	dilatation and curettage
DES	diethylstilbestrol
DHEA	dehydroepiandrosterone
DM	diabetes mellitus
DMPA	depot medroxyprogesterone acetate or Depo-Provera®
DUB	dysfunctional uterine bleeding
DVT	deep venous thrombosis
EPC	emergency postcoital contraception
FSH	follicle stimulating hormone
GA	gestational age
GIFT	gamete intrafallopian transfer
GnRH	gonadotropin-releasing hormone
GTD	gestational trophoblastic disease
GTN	gestational trophoblastic neoplasia
HERS	heart and estrogen/progestin replacement study
HMG	human menopausal gonadotropin
HPO	hypothalamic-pituitary-ovarian
HPV	human papillomavirus
HRT	hormone replacement therapy
HSG	hysterosalpingography
HSIL	high grade squamous intraepithelial lesion
HSV	herpes simplex virus
IBD	inflammatory bowel disease
ICSI	intracytoplasmic sperm injection
ITP	immune thrombocytopenic purpura
IUD	intrauterine device
IUI	intrauterine insemination
IUS	interauterine system
IVDU	intravenous drug use
IVF	*in vitro* fertilization
IVM	*in vitro* maturation
JRA	juvenile rheumatoid arthritis
LDH	lactate dehydrogenase
LEEP	loop electrosurgical excision procedure
LH	luteinizing hormone
LHRH	luteinizing hormone-releasing hormone
LMP	last menstrual period
LN	lymph node
LNMP	last normal menstrual period
LSIL	low grade squamous intraepithelial lesion
LVSI	lymphovascular space involvement
MRKH	Mayer-Rokitansky-Küster-Hauser
NK	natural killer
N/V	nausea/vomiting
OCP	oral contraceptive pill
OGTT	oral glucose tolerance test
PCOS	polycystic ovarian syndrome
PCR	polymerase chain reaction
PG	prostaglandin
PID	pelvic inflammatory disease
PMB	postmenopausal bleeding
PMDD	premenstrual dysphoric disorder
PMN	polymorphonuclear neutrophils
PMS	premenstrual syndrome
RPR	rapid plasma reagin
SCC	squamous cell carcinoma
SERMs	selective estrogen receptor modulator
SHBG	sex hormone binding globulin
SHG	sonohysterography
SPERM	selective progesterone receptor modulator
SSRIs	selective serotonin reuptake inhibitors
STI	sexually transmitted infections
TAH	total abdominal hysterectomy
TET	tubal embryo transfer
TH	total hysterectomy
TOT	tension-free transobturator tape
TSH	thyroid-stimulating hormone
TVT	tension-free vaginal tape
TZ	transformation zone
UAE	uterine artery embolization
U/S	ultrasound
UTI	urinary tract infection
VDRL	venereal disease research laboratory
VIN	vulvar intraepithelial neoplasia
VTE	venous thromboembolism
vWD	von Willebrand disease
W/D	withdrawal
WHI	Women's Health Initiative
ZIFT	zygote intrafallopian transfer

Basic Anatomy Review

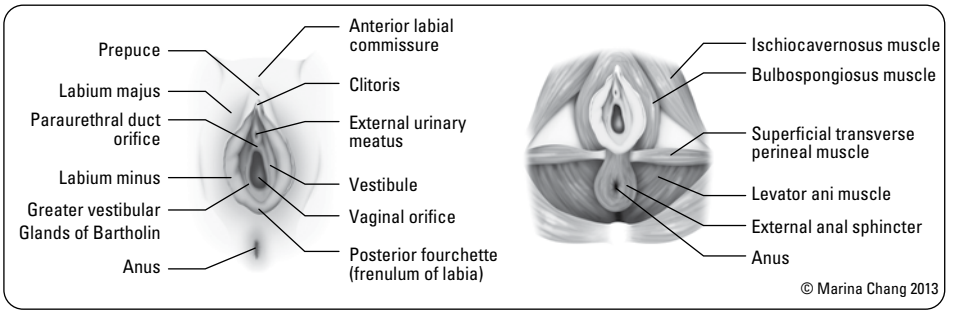


Figure 1. Vulva and perineum

A. EXTERNAL GENITALIA

- blood supply: internal pudendal artery
- sensory innervation: pudendal nerve
- lymphatic drainage: inguinal nodes

B. VAGINA

- muscular canal extending from cervix to vulva, anterior to rectum and posterior to bladder
- lined by rugated, stratified squamous epithelium
- upper vagina separated by cervix into anterior, posterior, and lateral fornices
- blood supply: vaginal branch of internal pudendal artery with anastamoses from uterine, inferior vesical, and middle rectal arteries

C. UTERUS

- thick walled, muscular organ between bladder and rectum, consisting of two major parts:
  - uterine corpus
    - blood supply: uterine artery (branch of the internal iliac artery, anterior division)
  - cervix
    - blood supply: cervical branch of uterine artery
- supported by the pelvic diaphragm, the pelvic organs, and 4 paired sets of ligaments
  - round ligaments: travel from anterior surface of uterus, through broad ligaments, and inguinal canals then terminate in the labia majora
    - function: anteversion
    - blood supply: Sampson's artery (branch of uterine artery running through round ligament)
  - uterosacral ligaments: arise from sacral fascia and insert into posterior inferior uterus
    - function: mechanical support for uterus, prevent prolapse and contain autonomic nerve fibres
  - cardinal ligaments: extend from lateral pelvic walls and insert into lateral cervix and vagina
    - function: mechanical support, prevent prolapse
  - broad ligaments: pass from lateral pelvic wall to sides of uterus; contain fallopian tube, round ligament, ovarian ligament, nerves, vessels, and lymphatics

- infundibulopelvic ligament (suspensory ligament of the ovary): continuous tissue that connects ovary to pelvic wall
  - contains the ovarian artery, ovarian vein, ovarian plexus, and lymphatic vessels
- position of the uterus
  - anteverted (majority), retroverted, neutral

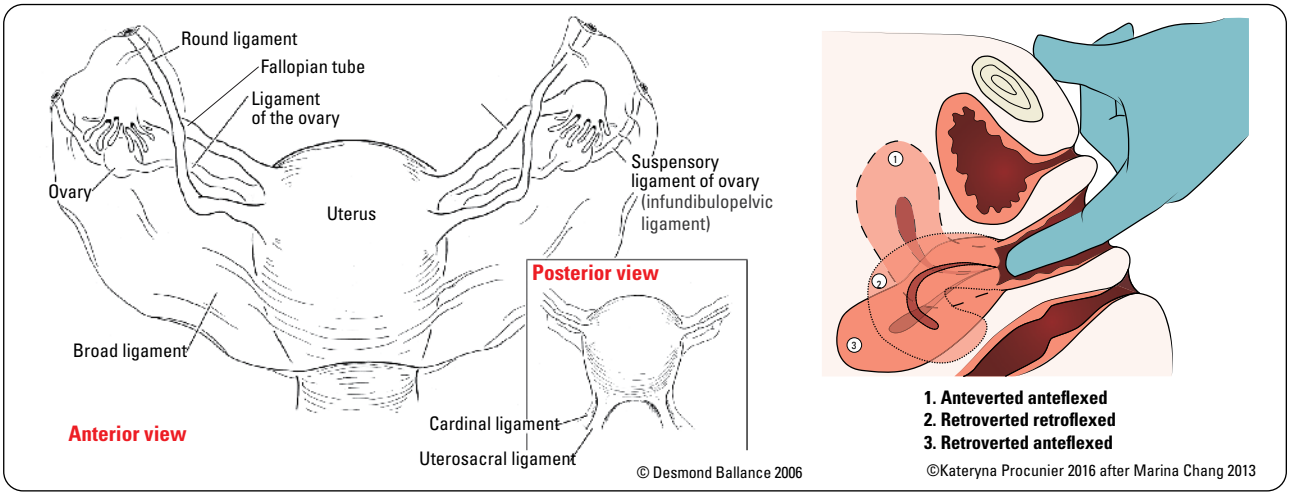


Figure 2. Genital organs and positioning of the uterus

D. FALLOPIAN TUBES

- 8-14 cm muscular tubes extending laterally from the uterus to the ovary
- interstitial, isthmic, ampullary, and infundibular segments; terminates at fimbriae
- mesosalpinx: peritoneal fold that attaches fallopian tube to broad ligament
- blood supply: uterine and ovarian arteries

E. OVARIES

- consist of cortex with ova and medulla with blood supply
- supported by infundibulopelvic ligament (suspensory ligament of ovary)
- mesovarium: peritoneal fold that attaches ovary to broad ligament
- blood supply: ovarian arteries (branches off of aorta), left ovarian vein (drains into left renal vein), right ovarian vein (drains into inferior vena cava)

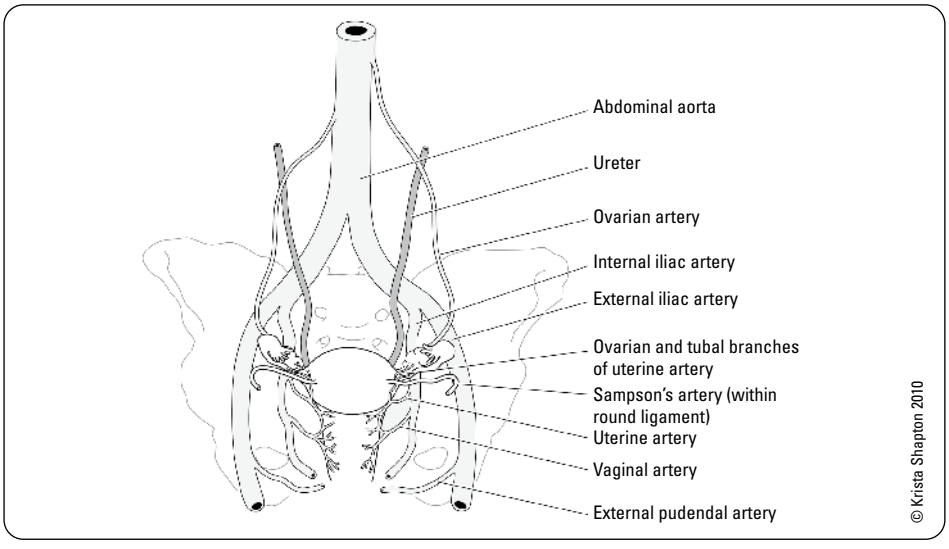


Figure 3. Vascular supply

Determination of Uterine Position by Clinical Exam

- If cervix faces anteriorly (under the urethra and less easily accessible), i.e. toward vaginal orifice, more likely RETROVERTED UTERUS
- If cervix faces posteriorly (easily accessible), i.e. toward sacrum or rectum, more likely ANTEVERTED UTERUS
- If uterus palpable on bimanual exam, more likely ANTEVERTED UTERUS

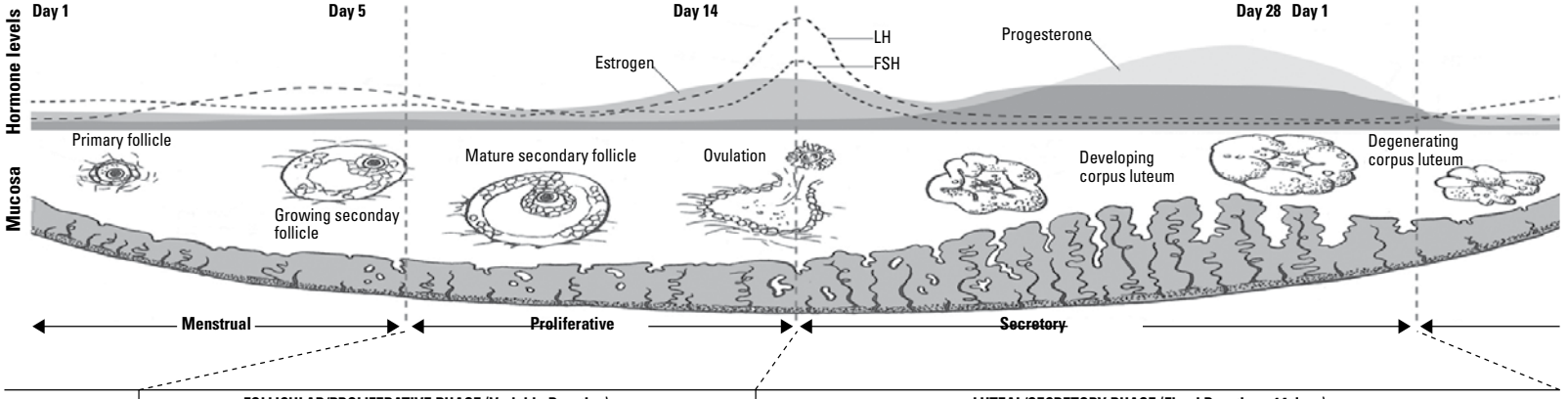
"Water Under the Bridge"
The ureters run posterior to the uterine arteries

Common Anatomy Questions in the OR

- **What is the origin of the left and right ovarian arteries?**
  Descending aorta
- **What are the drainage sites for the left and right ovarian veins?**
  Left to left renal vein, right to inferior vena cava
- **What is the most common place to locate the ureter?**
  Pelvic brim, medial leaf of the broad ligament as it passes under the uterine artery
- **Which artery runs under the round ligament?**
  Sampson's artery

Menstruation

Menstrual Cycle



	FOLLICULAR/PROLIFERATIVE PHASE (Variable Duration)			LUTEAL/SECRETORY PHASE (Fixed Duration - 14 days)		
	Early	**Mid**	**Late**	**OVULATION**	**Early-Mid**	**Late**
Initiating Events	↓ E and ↓ P (from end of previous cycle)	↑ FSH acts on ovarian granulosa cells	Growing follicles continue to secrete E	Sudden switch from negative to positive feedback (E and P now ↑ FSH & LH)	Switch back to negative feedback	No fertilized oocyte
HPO Axis	↑ GnRH pulse frequency ↑ FSH ↑ LH pulse frequency	↑ E from follicles (ovary)		↑↑ LH pulse amplitude (LH surge)	↓ LH	
Hormones			↑ E from follicles, especially from dominant follicle	E peaks → LH surge → ovulation	↑ P from corpus luteum	↓ P secondary to degeneration of corpus luteum
Feedback on HPO Axis		Negative feedback E → ↓ FSH, ↓ LH		Positive feedback: E and P → ↑ FSH, ↑ LH	Negative feedback P → ↓ FSH, ↓ LH	
Ovaries	↑ FSH → follicular growth in 3-30 follicles	↑ follicular growth (by reducing atresia) → ↑ E	Dominant follicle persists, remainder undergo atresia Granulosa cells luteinize → produce P	~36 h after LH surge, dominant follicle releases oocyte; corpus luteum (remnant of dominant follicle) produces P		Cessation of P from corpus luteum
Endometrium	Menses from P withdrawal (from end of previous cycle)		E builds up endometrium		P stabilizes endometrium	Withdrawal of P → menses
Cervical Mucus		Cervical mucus: Clear, ↑ amount, Spinnbarkeit 8-10 cm, more stringy				Cervical mucus: Opaque, scant amount, Spinnbarkeit 1-2 cm

E = estrogen; FSH = follicle-stimulating hormone; GnRH = gondatropin-releasing hormone; HPO = hypothalamic pituitary-ovarian; LH = lutenizing hormone; P = progesterone

Figure 4. Events of the normal menstrual cycle

CHARACTERISTICS
- Menarche 10-15 yr
- Average 12.2 yr
- Entire cycle 28 ± 7 d with bleeding for 1-6 d
- 25-80 mL blood loss per cycle

ESTROGEN
ESTROGEN is the main hormone in the follicular/proliferative phase and is stimulated by FSH. As the level increases it acts negatively on FSH. The majority of estrogen is secreted by the dominant follicle

Estrogen effects
- On the follicles in the ovaries
  - Reduces atresia
- On the endometrium
  - Proliferation of glandular and stromal tissue
- On all target tissues
  - Decreases E receptors

PROGESTERONE
PROGESTERONE is the main hormone in the luteal/secretory phase and is stimulated by LH. Increased progesterone acts negatively on LH and is secreted by the corpus luteum (remnant of dominant follicle)

Progesterone effects
- On the endometrium
  - Cessation of mitoses (stops building endometrium up)
  - "Organization" of glands (initiates secretions from glands)
  - Inhibits macrophages, interleukin-8, and enzymes from degrading endometrium
- On all target tissues
  - Decrease E receptors (the "anti-estrogen" effect)
  - Decrease P receptors

Stages of Puberty

- see Pediatrics, P31
- adrenarche: increased secretion of adrenal androgens; usually precedes gonadarche by 2 yr
- gonadarche: increased secretion of gonadal sex steroids; ~age 8 yr
- thelarche: breast development
- pubarche: pubic and axillary hair development
- menarche: onset of menses, usually following peak height velocity and/or 2 yr following breast budding

Stages of Puberty

"Boobs, Pubes, Grow, Flow"
Thelarche, Pubarche, Growth spurt, Menarche

Tanner Stage

Thelarche
1. None
2. Breast bud
3. Further enlargement of areolae and breasts with no separation of contours
4. 2º mound of areolae and papilla
5. Areolae recessed to general contour of breast – adult

Pubarche
1. None
2. Downy hair along labia only
3. Darker/coarse hair extends over pubis
4. Adult-type hair with no thigh involvement
5. Adult hair in distribution and type; extends over thighs. Not all patients achieve Tanner Stage 5. For image see Pediatrics, P32

Premenstrual Syndrome

- synonyms: "ovarian cycle syndrome," "menstrual molimina" (moodiness)

Etiology
- multifactorial: not completely understood; genetics likely play a role
- CNS-mediated neurotransmitter (serotonin, dopamine, GABA) interactions with sex steroids (P, E, and T)
- serotonergic dysregulation – currently most plausible theory

Diagnostic Criteria for Premenstrual Syndrome
- at least one affective and one somatic symptom during the 5 d before menses in each of the three prior menstrual cycles
  - affective: depression, angry outbursts, irritability, anxiety, confusion, social withdrawal
  - somatic: breast tenderness or swelling, abdominal bloating, headache, swelling of extremities, joint or muscle pain, or weight gain
- symptoms relieved within 4 d of onset of menses and do not recur until at least day 13 of cycle
- symptoms present in the absence of any pharmacologic therapy, hormone ingestion, drug or alcohol use
- symptoms occur reproducibly during 2 cycles of prospective recording
- patient suffers from identifiable dysfunction in social or occupational performance

Premenstrual Syndrome
Physiological and emotional disturbances that occur 1-2 wk prior to menses and last until a few days after onset of menses; common symptoms include depression, irritability, tearfulness, and mood swings

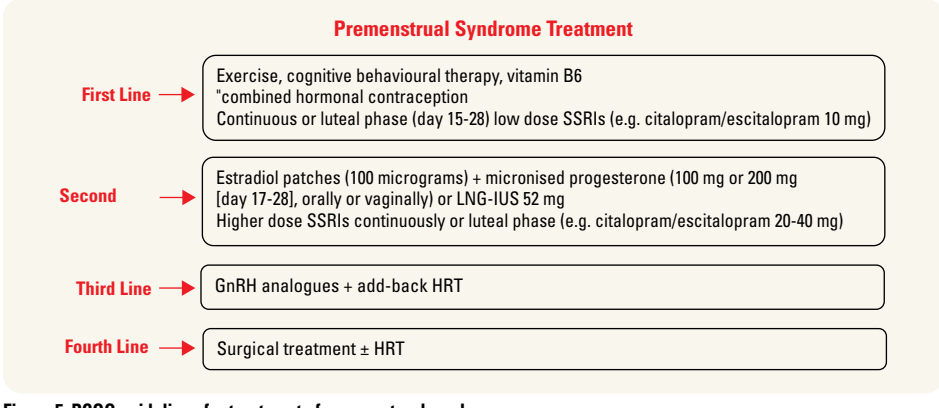


Figure 5. RCOG guidelines for treatment of premenstrual syndrome
Adapted from source: https://www.rcog.org.uk/globalassets/documents/guidelines/gt48managementpremensturalsyndrome.pdf

Premenstrual Dysphoric Disorder

Clinical Feature
- irritability, depressed mood
- breast pain and bloating

Diagnostic Criteria for Premenstrual Dysphoric Disorder
- at least 5 of the following 11 symptoms during most menstrual cycles of the last year (with at least 1 of the first 4)
  - depressed mood or hopelessness
  - anxiety or tension
  - affective instability
  - anger or irritability
  - decreased interest in activities
  - difficulty concentrating
  - lethargy
  - change in appetite
  - hypersomnia or insomnia
  - feeling overwhelmed
  - physical symptoms: breast tenderness/swelling, headaches, joint/muscle pain, bloating, or weight gain
- symptoms cause significant distress and/or interfere with social or occupational functioning
- symptoms must be present during the week prior to menses and resolve within a few days after onset of menses
- may be superimposed on other psychiatric disorders, provided it is not merely an exacerbation of another disorder

Common Investigations and Procedures

Imaging

Ultrasound (U/S)

- transabdominal or transvaginal U/S is the imaging modality of choice for pelvic structures
- transvaginal U/S provides better resolution of uterus and adnexal structures
  - detects early pregnancy if β-hCG ≥1500 (β-hCG must be ≥6500 for transabdominal U/S)
- may be used to identify pelvic pathology
  - identify ectopic pregnancy, intrauterine pregnancy
  - assess uterine, adnexal, cul-de-sac, and ovarian masses (e.g. solid or cystic)
  - determine endometrial thickness, locate/characterize fibroids
  - monitor follicles during assisted reproduction
  - assess endometrial lining in postmenopausal women

Every woman of childbearing age presenting to ER with abdominal or pelvic pain should have β-hCG measured

Endometrial Biopsy

- performed in the office using an endometrial suction curette (pipelle) guided through the cervix to aspirate fragments of endometrium
  - pre-treatment with misoprostol (Cytotec®) is optional
- more invasive procedure (i.e. D&C) may be done in the office or operating room ± hysteroscopy. This may be required if endometrial biopsy is not possible in the office setting or if there is suspicion for an endometrial polyp
- indications
  - AUB/PMB
    - age >40
    - risk factors for or history of endometrial cancer
    - failure of medical treatment
    - significant intermenstrual bleeding
    - consider in women with infrequent menses suggesting anovulatory cycles

Hysterectomy

Indications

- uterine fibroids
- endometriosis, adenomyosis
- uterine prolapse
- pelvic pain
- AUB
- cancer (endometrium, ovaries, fallopian tubes, cervix)

Complications

- general anesthetic
- bleeding
- infection
- injury to other organs (ureter, bladder, rectum)
- loss of ovarian function (if ovaries removed, iatrogenic menopause)

Approaches

1. Open (abdominal approach): uterus removed via transverse (Pfannenstiel) or midline laparotomy
2. Minimally invasive approaches
   - vaginal hysterectomy: entire procedure performed through the vagina. No abdominal incisions
   - laparoscopic-assisted vaginal hysterectomy: vascular pedicles are divided by a combination of laparoscopic and vaginal approaches
   - total laparoscopic hysterectomy: all vascular pedicles including the colpotomy approached laparoscopically and removed through the vagina
   - robotic: a type of laparoscopic approach. May be advantageous in high BMI patients. More costly

No. 377 – Hysterectomy for Benign Gynaecological Indications
J Obstet Gynaecol Can 2019;41(4):543-557
Summary:

1. Hysterectomy should be approached by either vaginal, laparoscopic, or open routes
2. Correction of preoperative anemia (hemoglobin <120 g/L), preoperative antibiotic prophylaxis, and measures to decrease risk of venous thromboembolism are recommended
3. In patients with endometriosis, full excision of local endometriosis should be performed concurrently
4. Opportunistic salpingectomy can be considered at the time of hysterectomy, but the planned surgical approach should not be changed for this sole purpose
5. Urinary tract injury is a known complication of hysterectomy and there should be a low threshold for further investigation in cases where injury is suspected- consider routine cystoscopy

Women should be counselled about the benefits and risks of removing the ovaries, the risk of ovarian cancer versus the long-term health implications of earlier menopause

Table 1. Classification of Hysterectomy

Classification	Tissues Removed	Indications
Subtotal Hysterectomy	Uterus	Inaccessible cervix (e.g. adhesions) Patient choice/preference Severe endometriosis
Total Hysterectomy (extrafascial simple hysterectomy/type 1)	Uterus, cervix, uterine artery ligated at uterus	Uterine fibroids Endometriosis Adenomyosis Heavy menstrual bleeding DUB
Total Hysterectomy (extrafasical simple hysterectomy/type 1) + Bilateral Salpingo-Oophorectomy	Uterus, cervix, uterine artery ligated at uterus, fallopian tubes, ovaries	Endometrial cancer Malignant adnexal masses Consider for endometriosis
Modified Radical Hysterectomy (type 2)	Uterus, cervix, proximal 1/3 parametria, uterine artery ligated medial to the ureter, mid point of uterosacral ligaments, and upper 1-2 cm vagina	Cervical cancer (up to stage 1B1)
Radical Hysterectomy (type 3)	Uterus, cervix, entire parametria, uterine artery ligated at its origin from internal iliac artery, uterosacral ligament at most distal attachment (rectum), and upper 1/3-1/2 vagina	Cervical cancer

Disorders of Menstruation

Amenorrhea

Differential Diagnosis of Amenorrhea

Table 2. Differential Diagnosis of Primary Amenorrhea

With Secondary Sexual Development		Without Secondary Sexual Development	
Normal breast and pelvic development	**Normal breast, abnormal uterine development**	**High FSH (hypergonadotropic hypogonadism)**	**Low FSH (hypogonadotropic hypogonadism)**
Hypothyroidism Hyperprolactinemia PCOS Hypothalamic dysfunction	Androgen insensitivity Anatomic abnormalities Müllerian agenesis, uterovaginal septum, imperforate hymen	Gonadal dysgenesis Abnormal sex chromosome (Turner's XO) Normal sex chromosome (46XX, 46XY)	Constitutional delay (rare in girls) Congenital abnormalities Isolated GnRH deficiency Pituitary failure (Kallman syndrome, head injury, pituitary adenoma, etc.) Acquired endocrine disorders (type 1 DM) Pituitary tumours Systemic disorders (IBD, JRA, chronic infections, etc.) Functional hypothalamic amenorrhea

Most Common Causes of Primary Amenorrhea
1. Müllerian agenesis
2. Abnormal sex chromosomes (Turner's syndrome)
3. Functional hypothalamic amenorrhea

Table 3. Differential Diagnosis of Secondary Amenorrhea

With Hyperandrogenism	Without Hyperandrogenism
PCOS Autonomous hyperandrogenism (androgen secretion independent of the HPO axis) Ovarian: tumour, hyperthecosis Adrenal androgen-secreting tumour Late onset or mild congenital adrenal hyperplasia (rare)	Hypergonadotropic hypogonadism (i.e. primary ovarian insufficiency: high FSH, low estradiol) Idiopathic Autoimmune: type 1 DM, autoimmune thyroid disease, Addison's disease Iatrogenic: cyclophosphamide drugs, radiation Hyperprolactinemia Endocrinopathies: most commonly hyper or hypothyroidism Hypogonadotropic hypogonadism (low FSH): Pituitary compression or destruction: pituitary adenoma, craniopharyngioma, lymphocytic hypophysitis, infiltration (sarcoidosis), head injury, Sheehan's syndrome Functional hypothalamic amenorrhea (often related to stress excessive exercise and/or anorexia)

Functional hypothalamic amenorrhea is the most common cause of secondary amenorrhea

Investigations

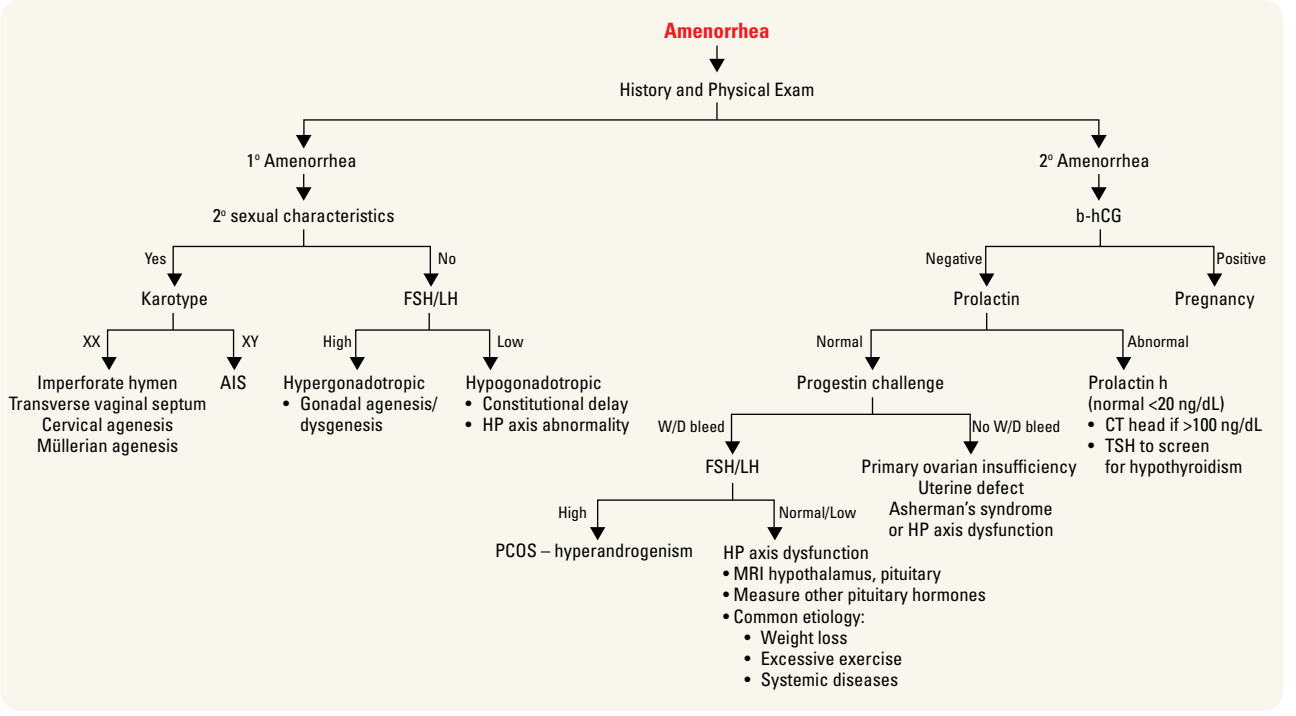


Figure 6. Diagnostic approach to amenorrhea

- β-hCG, hormonal workup (TSH, prolactin, FSH, LH, androgens, estradiol)
- progesterone challenge to assess estrogen status
  - medroxyprogesterone acetate (Provera®) 10 mg PO OD for 10-14 d
  - any uterine bleed within 2-7 d after completion of Provera® is considered to be a positive test/ withdrawal bleed
    - withdrawal bleed suggests presence of adequate estrogen to thicken the endometrium; thus withdrawal of progesterone results in bleeding
    - if no bleeding occurs, this may be secondary to inadequate estrogen (hypoestrogenism), excessive androgens, or progesterones (decidualization) or pregnancy
- karyotype: indicated if primary ovarian insufficiency or absent puberty
- U/S to confirm normal anatomy, identify PCOS

Prolactinoma Symptoms
Galactorrhea, visual changes, headache

Treatment

Table 4. Management of Amenorrhea

Etiology	Management
1° AMENORRHEA	
Androgen insensitivity syndrome	Gonadal resection after puberty
	Psychological counselling
	Creation of neo-vagina with dilation
Anatomical	
Imperforate hymen	Surgical management
Transverse vaginal septum	Surgical management
Cervical agenesis	Suppression and ultimately hysterectomy
Müllerian dysgenesis (MRKH syndrome)	Psychological counselling
	Creation of neo-vagina with dilation
	Diagnostic study to confirm normal urinary system and spine

Primary Amenorrhea
No menses by age 13 in absence of 2° sexual characteristics, or no menses by age 15 with 2° sexual characteristics, or no menses 2 yr after thelarche

Secondary Amenorrhea
No menses for >6 mo or 3 cycles after documented menarche

Table 4. Management of Amenorrhea (continued)

Etiology	Management
2° AMENORRHEA	
HP-axis dysfunction	**Identify modifiable underlying cause** Combined OCP to decrease risk of osteoporosis, maintain normal vaginal and breast development (NOT proven to work)
Hyperprolactinemia	MRI/CT head to rule out lesion If no demonstrable lesions by MRI Bromocriptine, cabergoline if fertility desired Combined OCPs if no fertility desired Demonstrable lesions by MRI: surgical management
Polycystic ovarian syndrome	See *Polycystic Ovarian Syndrome*, GY23
Premature ovarian failure	Screen for DM, hypothyroidism, hypoparathyroidism, hypocorticolism Hormonal therapy with estrogen + progestin to decrease risk of osteoporosis; can use OCP after induction of puberty
Uterine defect	Evaluation with hysterosalpingography or sonohysterography
Asherman's syndrome	Hysteroscopy: excision of synechiae

2° amenorrhea is pregnancy until proven otherwise

Abnormal Uterine Bleeding

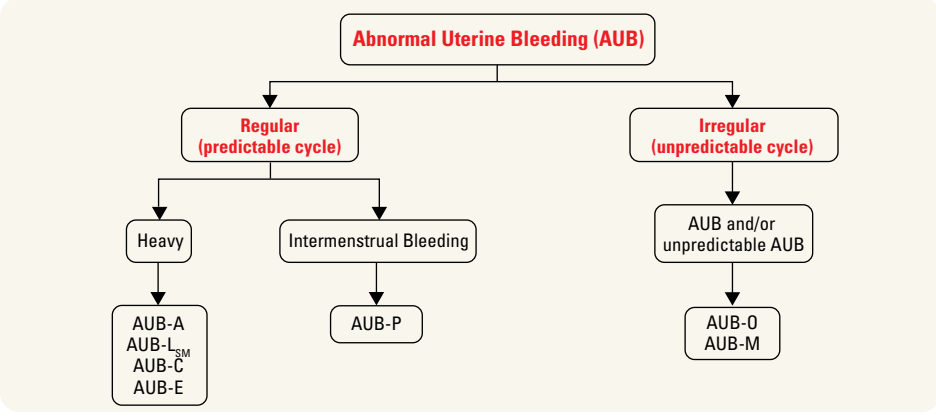


Figure 7. Diagnostic approach to abnormal uterine bleeding

Approach

- menstrual bleeding should be evaluated by ascertaining: frequency/regularity of menses, duration, volume of flow, impact on quality of life, and timing (inter or premenstrual or breakthrough)
- is it regular?
  - regular: cycle to cycle variability of <20 d – "Can you predict your menses within 20 days?"
  - irregular: cycle to cycle variability of ≥20 d
- is it heavy?
  - ≥80 cc of blood loss per cycle or
  - ≥8 d of bleeding per cycle or
  - bleeding that significantly affects quality of life
- is it structural?
  - PALM
- is it non-structural?
  - COEIN

Postmenopausal bleeding is endometrial cancer until proven otherwise

Abnormal Uterine Bleeding
Change in frequency, duration, or amount of menstrual flow that affects quality of life

Table 5. AUB – Etiologies, Investigations, and Management

Etiology	Investigations	Management
	STRUCTURAL	
Polyps (AUB-P)	Transvaginal sonography Saline infusion sonohysterography	Polypectomy (triage based on symptoms,polyp size, histopathology and patient age)
Adenomyosis (AUB-A)	Transvaginal sonography MRI	See *Adenomyosis*, GY13
Leiomyoma (AUB-L) **Submucosal (AUB-Lsm)** **Other (AUB-Lo)**	Transvaginal sonography Saline infusion sonohysterography Diagnostic hysteroscopy	See *Fibroids (Leiomyomata)*, GY13
Malignancy and Hyperplasia (AUB-M)	Transvaginal sonography Endometrial biopsy for all women >40 yr with AUB, for women <40 yr with persistent AUB or endometrial cancer risk factors	Dependent on diagnosis
	NON-STRUCTURAL	
Coagulopathy (AUB-C)	CBC, coagulation profile (especially in adolescents), vWF, Ristocetin cofactor, factor VIII	Dependent on diagnosis (hormonal modulation (e.g. OCP), Mirena IUS, endometrial ablation)
Ovulatory dysfunction (AUB-O)	Bloodwork: β-hCG, ferritin, prolactin, FSH, LH, serum androgens (free testosterone, DHEA), progesterone, 17-hydroxy progesterone, TSH, free T4 pelvic ultrasound	See *Infertility*, GY22
Endometrial (AUB-E)	Endometrial biopsy	Tranexamic acid Hormonal modulation (e.g. OCP) Mirena IUS Endometrial ablation
Iatrogenic (AUB-I)	Transvaginal sonography (rule out forgotten IUD) Review OCP/HRT use Review meds (especially neuroleptic use)	Remove offending agent
Not yet classified (AUB-N)	—	—

Treatment

- resuscitate patient if hemodynamically unstable
- treat underlying disorders
  - if anatomic lesions and systemic disease have been ruled out, consider AUB
- medical
  - mild AUB
    - NSAIDs
    - anti-fibrinolytic (e.g. Cyklokapron®) at time of menses
    - combined hormonal contraceptive
    - progestins (Provera®) on first 10-14 d of each month or every 3 mo if AUB-O
    - Mirena® IUD
    - correct anemia - iron
  - acute, severe AUB
    - replace fluid losses, consider admission

    a) estrogen (Premarin®) 25 mg IV q4h x 24 h with Gravol® 50 mg IV/PO q4h or anti-fibrinolytic (e.g. Cyklokapron®) 10 mg/kg IV q8h (rarely used)

    b) tapering OCP regimen, 35 μg pill tid x7d then taper to 1 pill/d for 3wk with Gravol® 50 mg IV/PO q4h
      - or taper to 1 tab tid x 2 d → bid x 2 d → OD (more commonly used)
    - after (a) or (b), maintain patient on monophasic OCP for next several months or consider alternative medical treatment
      - medical (can also consider):
        - high dose progestins
        - danazol (Danocrine®)
        - GnRH agonsits (e.g. Lupron ®) with add-back if taken for >6 mo
        - ulipristal acetate
- surgical
  - endometrial ablation
    - if finished childbearing
    - repeat procedure may be required if symptom recur, especially if <40 yr
  - hysterectomy: definitive treatment

Dysmenorrhea

Etiology
- primary/idiopathic
- secondary (acquired)
  - endometriosis
  - adenomyosis
  - uterine polyps
  - uterine anomalies (e.g. non-communicating uterine horn)
  - leiomyoma
  - intrauterine synechiae
  - ovarian cysts
  - cervical stenosis
  - imperforate hymen, transverse vaginal septum
  - pelvic inflammatory disease
  - IUD (copper)
  - foreign body

Primary Dysmenorrhea
Recurrent crampy lower abdominal pain during menses in the absence of demonstrable disease

Secondary Dysmenorrhea
Pain during menses that can be attributed to an underlying disorder (endometriosis, adenomyosis, fibroids)

Table 6. Comparison of Primary and Secondary Dysmenorrhea

	Primary Dysmenorrhea	Secondary Dysmenorrhea
Features	Recurrent, crampy lower abdominal pain that occurs during menses in the absence of demonstrable disease	Similar features as primary dysmenorrhea but with an underlying disorder that can account for the symptoms, such as endometriosis, adenomyosis or uterine fibroids
Signs and Symptoms	Colicky pain in abdomen, radiating to the lower back, labia, and inner thighs beginning hours before onset of bleeding and persisting for hours or days (48-72 h) Associated symptoms: N/V, altered bowel habits, headaches, fatigue (prostaglandin-associated)	Associated dyspareunia, abnormal bleeding, infertility
Diagnosis	Assess for associated dyspareunia, abnormal bleeding, infertility (signs of 2° dysmenorrhea) Rule out underlying pelvic pathology and confirm cyclic nature of pain Pelvic examination not required; indicated for patients not responding to therapy or with signs of organic pathology	Bimanual exam: uterine or adnexal tenderness, fixed uterine retroflexion, uterosacral nodularity, pelvic mass, or enlarged irregular uterus (findings are rare in women <20 yr) U/S, laparoscopy and hysteroscopy may be necessary to establish the diagnosis Vaginal and cervical cultures may be required
Treatment	Regular exercise, local heat NSAIDs: should be started before onset of pain Combined hormonal contraceptives with continuous or extended use: suppress ovulation/ reduce menstrual flow	Treat underlying cause

Endometriosis

Definition
- the presence of endometrial tissue (glands and stroma) outside of the uterine cavity
- chronic condition, resolving only with menopause

Etiology
- not fully understood; proposed mechanisms include (combination likely involved):
  - retrograde menstruation (Sampson's theory)
  - immunologic: decreased NK cell activity limiting clearance of transplanted endometrial cells from pelvic cavity (may be due to decreased NK cell activity)
  - metaplasia of coelomic epithelium
  - extrapelvic disease may be due to aberrant vascular or lymphatic dissemination of cells
    - e.g. ovarian endometriosis may be due to direct lymphatic flow from uterus to ovaries

Differential Diagnoses
- Chronic PID, recurrent acute salpingitis
- Hemorrhagic corpus luteum
- Benign/malignant ovarian neoplasm
- Ectopic pregnancy

Classic Triad of Endometriosis
- Dysmenorrhea
- Dyspareunia (cul-de-sac, uterosacral ligament)
- Dyschezia (uterosacral ligament, cul-de-sac, rectosigmoid attachment)

Epidemiology
- incidence: 15-30% of pre-menopausal women
- mean age at presentation: 25-30 yr
- regresses after menopause

Risk Factors
- family history (7-10x increased risk if affected 1st degree relative)
- obstructive anomalies of the genital tract (earlier onset) – resolves with treatment of anomaly
- nulliparity
- age >25 yr

Sites of Occurrence

- ovaries: 60% patients have ovarian involvement
- broad ligament, vesicoperitoneal fold
- peritoneal surface of the cul-de-sac, uterosacral ligaments
- rectosigmoid colon, appendix
- rarely may occur in sites outside abdomen/pelvis, including lungs

Clinical Features

- may be asymptomatic and can occur with one of 3 presentations

1. pain

- menstrual symptoms
  - cyclic symptoms due to growth and bleeding of ectopic endometrium, usually precede menses (24-48 h) and continue throughout and after flow
  - secondary dysmenorrhea
  - sacral backache with menses
  - pain may eventually become chronic, worsening perimenstrually
  - deep dyspareunia
- bowel and bladder symptoms
  - frequency, dysuria, hematuria
  - cyclic diarrhea/constipation, hematochezia, dyschezia (suggestive of deeply infiltrating disease)

2. infertility

- 30-40% of patients with endometriosis will be infertile
- 15-30% of those who are infertile will have endometriosis

3. mass (endometrioma)

- ovarian mass can present with any of above symptoms or be asymptomatic
- physical examination:
  - tender nodularity of uterine ligaments and cul-de-sac felt on rectovaginal exam
  - fixed retroversion of uterus
  - firm, fixed adnexal mass (endometrioma: an endometriotic cyst encompassing ovary)

Investigations

- definitive diagnosis can be made based on:
  - direct visualization of lesions typical of endometriosis at laparoscopy
  - biopsy and histologic exam of specimens (2 or more of: endometrial epithelium, glands, stroma, hemosiderin-laden macrophages)
- laparoscopy
  - mulberry spots: dark blue or brownish-black implants on the uterosacral ligaments, cul-de-sac, or anywhere in the pelvis
  - endometrioma: "chocolate" cysts on the ovaries
  - "powder-burn" lesions on the peritoneal surface
  - early white lesions and clear blebs
  - peritoneal "pockets"
- CA-125 (cancer antigen 125)
  - may be elevated in patients with endometriosis but should NOT be used as a diagnostic test

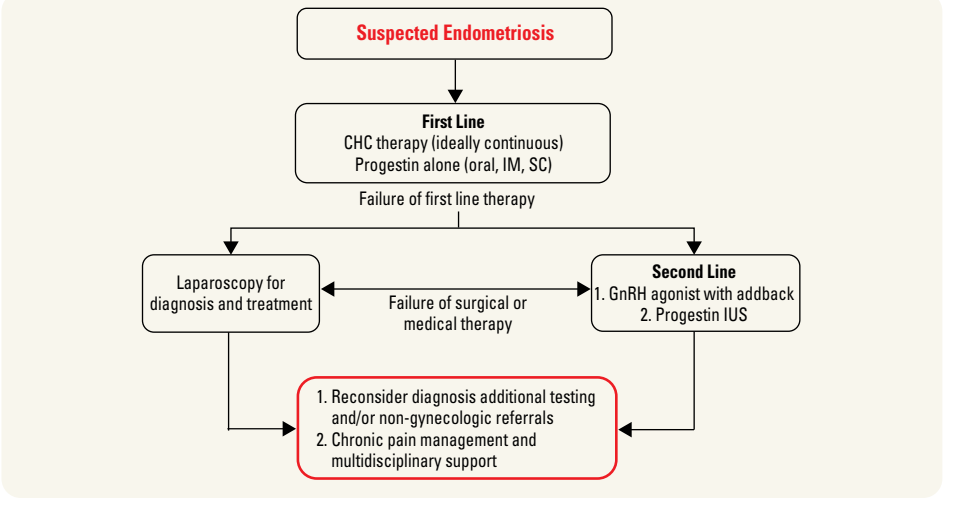


Figure 8. SOGC guidelines for treatment of endometriosis

Endometriosis – Take Home Points

- Suggestive history even with a negative exam should be considered adequate for a presumptive diagnosis
- Pelvic pain that is not primary dysmenorrhea should be considered endometriosis until proven otherwise
- Medical management is the mainstay of endometriosis

Treatment

- surgical confirmation of disease is NOT required prior to starting medical management. Asymptomatic endometriosis does not require treatment. Management depends on certainty of the diagnosis, severity of symptoms, extent of disease, desire for future fertility, and impact to GI/GU systems (e.g. intestinal obstruction)

- medical
  - NSAIDs (e.g. naproxen sodium – Anaprox®)
  - 1st line
    - cyclic/continuous estrogen-progestin (OCP)
    - progestin (IM medroxyprogesterone (Depo-Provera®) or oral dienogest (Visanne®))
    - Mirena® IUS
  - 2nd line
    - GnRH-agonist (e.g. leuprolide (Lupron®)): suppresses pituitary
      - side effects: hot flashes, vaginal dryness, reduced libido
      - use >6 mo: include add-back progestin or estrogen to prevent decreased BMD, reduce vasomotor side-effects
    - danazol (Danocrine®): weak androgen
      - side effects: weight gain, fluid retention, acne, hirsutism, voice change
- surgical
  - conservative laparoscopy using laser, electrocautery ± laparotomy
    - ablation/resection of implants, lysis of adhesions, ovarian cystectomy of endometriomas
  - definitive: bilateral salpingo-oophorectomy ± hysterectomy
  - best time to become pregnant is immediately after conservative surgery
  - if patient is not planning to become pregnant post-op, suppress ovulation medically to prevent recurrence

Adenomyosis

- synonym: "endometriosis interna" (uterine wall may be diffusely involved)

Adenomyosis
Extension of areas of endometrial glands and stroma into the myometrium

Epidemiology
- 15% of females >35 yr old; found in 20-40% of hysterectomy specimens
- mean age at presentation: 40-50 yr old (older age group than seen in endometriosis)
- adenomyosis is a common histologic finding in asymptomatic patients

Clinical Features
- often asymptomatic
- heavy menstrual bleeding, secondary dysmenorrhea, pelvic discomfort
- dyspareunia, dyschezia
- uterus symmetrically bulky, usually <14 cm
- Halban sign: tender, softened uterus on premenstrual bimanual exam

Final diagnosis of adenomyosis is based on pathologic findings, but predictably identified on MRI

Investigations
- clinical diagnosis
- U/S or MRI can be helpful
- endometrial sampling to rule out other pathology

Treatment
- medical
  - iron supplements for anemia
  - analgesics, NSAIDs
  - Mirena® IUS
  - CHC, medroxyprogesterone (Depo-Provera®) – limited evidence for efficacy
  - GnRH agonists (e.g. leuprolide (Lupron ®))
  - low dose danazol 100-200 mg PO OD (trial x 4 mo)
- surgical
  - definitive: hysterectomy – treatment of choice in women who have completed childbearing

Fibroids

Leiomyomata/Fibroids
Benign smooth muscle tumour of the uterus (most common gynecological tumour)

Epidemiology
- diagnosed in approximately 40-50% of pre-menopausal women >35 yr
- more common in African Americans, where they are also larger and occur at earlier age
- common indication for major surgery in females
- minimal malignant potential (1:1000)
- typically regress after menopause

Submucosal leiomyomata are most symptomatic (bleeding, infertility)

Pathogenesis
- estrogen stimulates monoclonal smooth muscle proliferation
- progesterone stimulates production of proteins that inhibit apoptosis
- degenerative changes (occur when tumour outgrows blood supply)
  - fibroids can degenerate, become calcified, develop sarcomatous component, or obtain parasitic blood supply

The effect of pregnancy on fibroid size is variable

Clinical Features

- majority asymptomatic (60%), often discovered as incidental finding on pelvic exam or U/S
- abnormal uterine bleeding (30%): dysmenorrhea, heavy menstrual bleeding
- pressure/bulk symptoms (20-50%)
  - pelvic pressure/heaviness
  - increased abdominal girth
  - urinary frequency and urgency
  - constipation, bloating (rare)
  - acute urinary retention (extremely rare, but surgical emergency!)
- acute pelvic pain
  - fibroid degeneration
  - fibroid torsion (if pedunculated subserosal)
- infertility, recurrent pregnancy loss
- pregnancy complications (potential enlargement and increased pain, obstructed labour, difficult C-section)

Investigations

- bimanual exam: uterus asymmetrically enlarged, usually mobile
- CBC: anemia
- U/S: to confirm diagnosis and assess location of fibroids
- sonohysterogram: useful for differentiating endometrial polyps from submucosal fibroids, or for assessing intracavitary growth
- endometrial biopsy to rule out uterine cancer for abnormal uterine bleeding (especially if age >40 yr)
- occasionally MRI is used for pre-operative planning (e.g. before myomectomy)

Treatment

- only if symptomatic (heavy menstrual bleeding, menometrorrhagia, bulk symptoms), rapidly enlarging or intracavitary
- treat anemia if present
- conservative approach (watch and wait) if:
  - symptoms absent or minimal
  - fibroids <6-8 cm or stable in size
  - not submucosal (submucosal fibroids are more likely to be symptomatic)
  - currently pregnant due to increased risk of bleeding (follow-up U/S if symptoms progress)
- medical approach to treat AUB-L
  - antiprostaglandins (ibuprofen, other NSAIDs)
  - tranexamic acid (Cyklokapron®)
  - CHC, IUS or Depo-Provera®
  - GnRH agonist: leuprolide (Lupron®)
    - often used for 3 mo preoperatively to increase Hb and reduce fibroid size
    - reduces bleeding, shrinks fibroids, and corrects anemia
    - can be used long-term to bridge to menopause in combination with add-back progestin or estrogen
  - ulipristal acetate (Fibristal ®): a selective progesterone receptor agonist
    - 5 mg daily for 3 mo
    - reduces bleeding, shrinks fibroids
    - repeat courses only if patient not eligible for surgery; patients must menstruate between courses
    - associated with benign, non-physiological endometrial changes (selective progesterone receptor modulator-associated endometrial changes (PAEC)) which are reversible with discontinuation of therapy
    - note: rare side effect of liver failure. Screen for liver disease prior to prescribing, and monitor liver function before, during, and after treatment courses. Do not prescribe in patients with underlying liver disorder
- interventional radiology approach
  - uterine artery embolization (UAE) occludes both uterine arteries, shrinks fibroids by 50% at 6 mo; improves heavy bleeding in 90% of patients within 1-2 mo; not an option in women considering childbearing
    - higher risk of surgical re-intervention than with surgical approaches
- surgical approach
  - myomectomy (hysteroscopic, transabdominal, or laparoscopic)
  - hysteroscopic resection of fibroid and endometrial ablation for AUB-Lsm
  - hysterectomy (see *Hysterectomy*, GY6)
  - note: avoid operating on fibroids during pregnancy (due to vascularity and potential pregnancy loss); expectant management usually best

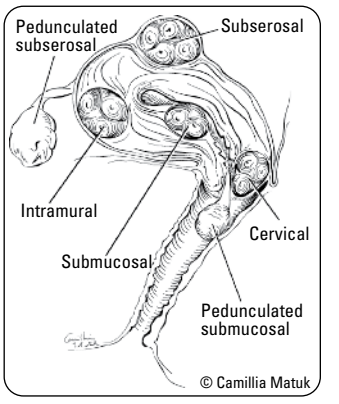


Figure 9. Possible anatomic locations of uterine leiomyomata

Ulipristal Acetate vs. Leuprolide Acetate for Uterine Fibroids
NEJM 2012;366:421-432
Study: Phase III, double-blind RCT of the efficacy and side-effect profile of ulipristal acetate versus those of leuprolide acetate for the treatment of symptomatic uterine fibroids before surgery.
Outcomes: Control of uterine bleeding at week 13 was the primary outcome. Secondary outcomes included bleeding pattern, amenorrhea, changes in fibroid/uterine volume, and global pain score.
Patients: 307 premenopausal women with symptomatic fibroids and excessive uterine bleeding were randomly assigned to oral ulipristal acetate (5 mg or 10 mg) or intramuscular injections of leuprolide acetate.
Results: Control of bleeding at week 13 was not significantly different between the treatment groups. All three treatments reduced uterine volume, although this decrease was significantly greater in the leuprolide group (47% reduction) than in the ulipristal groups (20-22%). 40% of the leuprolide group reported moderate-to-severe hot flashes, but only 11% (5 mg) and 10% (10 mg) of the ulipristal groups did.
Conclusions: Oral ulipristal acetate (5 mg or 10 mg) is noninferior to intramuscular leuprolide acetate for control of uterine bleeding due to fibroids and has a better side-effect profile.

Uterine artery embolization for symptomatic uterine fibroids
Cochrane Database Syst Rev. 2014, 12: CD005073
Purpose: To compare outcomes of uterine artery embolization (UAE) to other medical or surgical therapies for symptomatic uterine fibroids. Primary outcomes were patient satisfaction and live birth rate.
Results: Seven RCTs with 793 women were included. There was no evidence of a difference in the primary outcomes or risk of major complications between the interventions. UAE was associated with a higher risk of minor complications and the need for additional surgical intervention within two years.
Conclusions: No significant differences in patient satisfaction or major complications in UAE compared to surgical intervention. UAE is associated with an increased risk of surgical re-intervention.

Contraception

• see Family Medicine, FM20

Table 7. Classification of Contraceptive Methods

Type	Effectiveness (Perfect Use, Typical Use*)
Physiological	
Withdrawal/coitus interruptus	96%, 77%
Rhythm method/calendar/mucus/symptothermal	76%
Lactational amenorrhea	98% (first 6 mo postpartum)
Chance – no method used	15%
Abstinence of all sexual activity	100%
Barrier Methods	
Condom alone	98%, 82%
Spermicide alone	82%, 72%
Sponge – Parous	80%, 76%
– Nulliparous	91%, 88%
Diaphragm with spermicide	94%, 88%
Female condom	95%, 79%
Cervical cap – Parous	74%, 68%
– Nulliparous	91%, 84%
Hormonal	
OCP	99.7%, 92%
Nuva Ring®	99.7%, 92%
Transdermal (Ortho Evra®)	99.7%, 92%
Depo-Provera®	99.7%, 97%
Progestin-only pill (Micronor®)	90-99%
Mirena® IUS	99.9%
Jaydess® IUS	99.9%
Copper IUD	99.3%
Surgical	
Tubal ligation	99.65%
Vasectomy	99.9%
Emergency Postcoital Contraception (EPC)	
Yuzpe® method	98% (within 24 h), decreases by 30% at 72 h
"Plan B" levonorgestrel only	98% (within 24 h), decreases by 70% at 72 h
Postcoital IUD	99.9%
Ella	98% (within 120 h)

*Effectiveness: percentage of women reporting no pregnancy after 1 yr of use

Counselling the Adolescent about Contraception
More than 90% of adolescent pregnancies are unintended, and ~50% of all pregnancies occur within the first 6 mo of initiating sexual activity; in addition, 85% of sexually active women become pregnant within 1 yr if no contraception is used and even some of the least effective contraceptive methods markedly decrease the risk of pregnancy

New Oral Contraceptive Preparations and the Risk of Venous Thromboembolism vs. Second Generation Drugs
BMJ 2015;350:h2135
Summary: Risks of thromboembolism associated with combined OCPs were higher for drug preparations with newer progesterone types than for second generation drugs (levonorgestrel and noresthisterone) and norgestimate.
Methods: Two nested case-control studies were performed on UK population through two large databases containing total of 1340 practices. Women aged 15-49 years with a first diagnosis of VTE in 2001-13 were matched with five controls by age, practice, and calendar year. OR for VTE incidence and use of combined OCPs were adjusted for smoking status, alcohol consumption, ethnic group, BMI, comorbidities, and other contraceptive drugs.
Results: Current exposure to OCP was associated with adjusted OR of 2.97 (95% CI 2.78-3.17) compared to no exposure in previous year. Risks associated with current exposure to new progesterone drug preparations (desogestrel, gestodene, drospirenone, cyproterone) were significantly higher than those for second generation contraceptives (levonorgestrel, noresthisterone) and norgestimate.

Hormonal Methods

Combined Oral Contraceptive Pills

- progestin: prevents LH surge, suppresses ovulation, thickens cervical mucus, decreases tubal motility, decidualizes endometrium
- estrogen: suppresses FSH and follicular development, causes endometrial proliferation
- most contain low dose ethinyl estradiol (20-35 μg) plus progestin (norethinedrone, norgestrel, levonorgestrel, desogestrel, norgestimate, drospirenone)
- failure rate (0.3% to 8%) depending on compliance
- monophasic or triphasic formulations (varying amount of progestin throughout cycle)

Transdermal (Ortho Evra®)

- continuous release of 6 mg norelgestromin and 0.60 mg ethinyl estradiol into bloodstream
- applied to lower abdomen, back, upper arm, buttocks, NOT breast
- worn for 3 consecutive weeks (changed every wk) with 1 wk off to allow for menstruation
- as effective as OCP in preventing pregnancy (>99% with perfect use)
- may be less effective in women >90 kg
- may not be covered by drug plans

Contraceptive Ring (Nuva Ring®)

- thin flexible plastic ring; releases etonogestrel 120 μg/d and estradiol 15 μg/d
- works for 3 wk then removed for 1 wk to allow for menstruation
- as effective as OCP in preventing pregnancy (98%)
- side effects: vaginal infections/irritation, vaginal discharge
- may have better cycle control; i.e. decreased breakthrough bleeding

Starting Hormonal Contraceptives

- thorough history and physical exam, including blood pressure and breast exam
- can start at any time during cycle but ideal if within 5 d of LMP
- follow-up visit 6 wk after hormonal contraceptives prescribed
- pelvic exam not required as STI screening can be done by urine and pap smear screening does not start until >21 yr

Table 8. Combined Estrogen and Progestin Contraceptive Methods

Advantages	Side Effects	Contraindications
Highly effective Reversible Cycle regulation Decreased dysmenorrhea and heavy menstrual bleeding (less anemia) Decreased benign breast disease and ovarian cyst development Decreased risk of ovarian and endometrial cancer Increased cervical mucus which may lower risk of STIs Decreased PMS symptoms Improved acne Osteoporosis protection (possibly)	**Estrogen-related** Nausea Breast changes (tenderness, enlargement) Fluid retention/bloating/edema Weight gain (rare) Migraine, headaches Thromboembolic events Liver adenoma (rare) Breakthrough bleeding (low estradiol levels) **Progestin-related** Amenorrhea/breakthrough bleeding Headaches Breast tenderness Increased appetite Decreased libido Mood changes HTN Acne/oily skin* Hirsutism* * Androgenic side effects may be minimized by prescribing formulations containing desogestrel, norgestimate, drospirenone, or cyproterone acetate	**Absolute** Known/suspected pregnancy Undiagnosed abnormal vaginal bleeding Prior thromboembolic events, thromboembolic disorders (Factor V Leiden mutation; protein C or S, or antithrombin III deficiency), active thrombophlebitis Cerebrovascular or coronary artery disease Estrogen-dependent tumours (breast, uterus) Impaired liver function associated with acute liver disease Congenital hypertriglyceridemia Smoker age >35 yr Migraines with focal neurological symptoms (excluding aura) Uncontrolled HTN **Relative** Migraines (non-focal with aura <1 h) DM complicated by vascular disease SLE Controlled HTN Hyperlipidemia Sickle cell anemia Gallbladder disease **Drug Interactions/Risks** Rifampin, phenobarbital, phenytoin, griseofulvin, primidone, and St. John's wort can decrease efficacy, requiring use of back-up method No evidence of fetal abnormalities if conceived on OCP No evidence that OCP is harmful to nursing infant but may decrease milk production; not recommended until 6 wk postpartum in breastfeeding and non-breastfeeding moms, ideally ≥3 mo postpartum if BF

Table 9. Selected Examples of OCPs

Type	Active Compounds (estriol and progestin derivative)	Advantages	Disadvantages
Alesse®	20 µg ethinyl estradiol and 0.5 mg levonorgestrel	Low dose (20 µg) OCP Less estrogen side effects	Low-dose pills can often result in breakthrough bleeding If this persists for longer than 3 mo, patient should be switched to an OCP with higher estrogen content
Tri-cyclen®	35 µg ethinyl estradiol and 0.180/0.215/0.250 mg norgestimate Triphasic oral contraceptive (graduated levels of progesterone)	Low androgenic activity can help with acne	Triphasic OCPs not ideal for continuous use >3 wk in a row (unlike monophasic formulation)
Yasmin® and Yaz®	Yasmin®: 30 µg ethinyl estradiol + 3 mg drospirenone (a new progestin) Yaz®: 20 µg ethinyl estradiol + 3 mg drospirenone – 24/4-d pill (4 d pill free interval) Drospirenone has antimineralocorticoid activity and antiandrogenic effects	Decreased perception of cyclic weight gain/bloating Fewer PMS symptoms Improved acne	Hyperkalemia (rare, contraindicated in renal and adrenal insufficiency) Check potassium if patient also on ACEI, ARB, K⁺-sparing diuretic, heparin Continue use of spironolactone

Irregular breakthrough bleeding often occurs in the first few months after starting OCP; usually resolves after three cycles

Progestin only contraceptives must be taken at the same time every day

Missed Combined OCPs

Miss 1 pill in <24 h
- Take 1 pill ASAP, and the next pill at the usual time

Miss ≥1 pill in a row in 1st wk
- Take 1 pill ASAP, and continue taking one pill daily until the end of the pack
- Use back-up contraception for 7 d; EPC may be necessary

Miss <3 pills in 2nd or 3rd wk of cycle
- Take 1 pill ASAP, and continue taking one pill daily until the end of the pack
- Do not take placebo (28-d packs) or do not take a hormone free interval (21-d packs)
- Start the next pack immediately after finishing the previous one
- No need for back-up contraception

Miss ≥3 pills during the 2nd or 3rd wk
- Take 1 pill ASAP, and continue taking one pill daily until the end of the pack
- Do ot take placebo (28-d packs) or do not take a hormone free interval (21-d packs)
- Start the next pack immediately after finishing the previous one
- Use back-up contraception for 7 d; EPC may be necessary

SOGC Committee Opinion on Missed Hormonal Contraceptives: New Recommendations. *JOGC* 2008;30:1050-1062. http://www.sogc.org/guidelines/documents/gui219ECO0811.pdf

PROGESTIN-ONLY METHOD

Table 10. Progestin Only Contraceptive Methods

Indications	Mechanism of Action	Side Effects	Contraindications
Suitable for postpartum women (does not affect breast milk supply) Women with contraindications to combined OCP (e.g. thromboembolic or myocardial disease) Women intolerant of estrogenic side effects of combined OCPs	Progestin prevents LH surge Thickening of cervical mucus Decrease tubal motility Endometrial decidualization Ovulation suppression – oral progestins (not IM) do not consistently suppress compared to combined OCPs	Irregular menstrual bleeding Weight gain Headache Breast tenderness Mood changes Functional ovarian cysts Acne/oily skin Hirsutism	**Absolute** None

SELECTED EXAMPLES OF PROGESTIN-ONLY METHODS

Progestin-Only Pill ("minipill")

- Micronor® 0.35 mg norethindrone
- must be taken daily at same time of day to ensure reliable effect; no pill free interval
- higher failure rate (1.1-13% with typical use, 0.51% with perfect use) than other hormonal methods
- ovulation inhibited only in 60% of women; most have regular cycles (but may cause oligo/amenorrhea)
- highly effective if also post-partum breastfeeding, or if >35 yr
- relies on the progestin effects on the cervical mucous and endometrial lining

Depo-Provera®

- injectable depot medroxyprogesterone acetate
- dose 150 mg IM q12-14wk (convenient dosing)
- initiate ideally within 5 d of beginning of normal menses, immediately postpartum in breastfeeding and non-breastfeeding women. Can consider quick start
- irregular spotting progresses to complete amenorrhea in 70% of women (after 1-2 yr of use)
- highly effective 99%; failure rate 0.3%
- suppresses ovulation very effectively
- side effect: decreased bone density (may be reversible) and weight gain
- disadvantage: restoration of fertility may take up to 9 mo

Missed Progestin-Only Pills >3 h
Use back-up contraceptive method for at least 48 h; continue to take remainder of pills as prescribed

Missed Depo-Provera

- If last injection given 13-14 wk prior: give next injection immediately
- If >14 wk prior, do β-hCG
  - If β-hCG is positive, give EPC and no injection
  - If β-hCG is negative, give next injection right away and:
    - Intercourse occurred in last 5 d: give EPC, use back-up contraception for 7 d ; repeat β-hCG in 3 wk
    - Intercourse occurred >5 d ago but within the last 14 d: use back-up contraception for 7 d; repeat β-hCG in 3 wk
    - Intercourse occurred >14 d ago: use back-up contraception for 7 d
  - No evidence of fetal abnormalities if conceived on DMPA

SOGC Committee Opinion on Missed Hormonal Contraceptives: New Recommendations.
JOGC 2008;30:1050-62. http://www.sogc.org/guidelines/documents/gui219ECO0811.pdf

Intrauterine Device

Table 11. IUS/IUD Contraceptive Methods

Mechanism of Action	Side Effects	Contraindications
Copper-Containing IUD (Nova-T®): mild foreign body reaction in endometrium; toxic to sperm and alters sperm motility **Progesterone-Releasing IUS (MirenaV, Kyleena®, Jaydess®):** decidualization of endometrium and thickening of cervical mucus; minimal effect on ovulation Highly effective (95-99%); failure rate 0-1.2% Contraceptive effects last 5 yr Reversible, private, convenient May be used in women with contraindications to OCPs or wanting long-term contraception	**Both Copper and Progesterone IUD** Breakthrough bleeding Expulsion (5% in the 1st yr, greatest in 1st mo and in nulliparous women) Uterine wall perforation (1/1000) on insertion If pregnancy occurs with an IUD, increased risk of ectopic Increased risk of PID (within first 10 d of insertion only) **Copper IUD:** increased blood loss and duration of menses, dysmenorrhea **Progesterone IUD:** bloating, headache	**Absolute** **Both Copper and Progesterone IUD** Known or suspected pregnancy Undiagnosed genital tract bleeding Acute or chronic PID Lifestyle risk for STIs* **Copper IUD** Known allergy to copper Wilson's disease **Relative** **Both Copper and Progesterone IUD** Valvular heart disease Past history of PID or ectopic pregnancy Presence of prosthesis Abnormalities of uterine cavity, intracavitary fibroids Cervical stenosis Immunosuppressed individuals (e.g. HIV) **Copper IUD** Severe dysmenorrhea or heavy menstrual bleeding

*Cervical swabs for gonorrhea and chlamydia should be done prior to insertion

Continuous or Extended Cycle vs. Cyclic Use of Combined Hormonal Contraceptives for Contraception
Cochrane DB Syst Rev 2014:7
Purpose: Systematic review of RCTs assessing the efficacy and side effects of cyclic administration vs. extended use (longer periods of active pills and/or shorter periods placebo) or continuous use (uninterrupted active pill administration) of combination oral contraceptives (COC).
Results: The initial review published in 2012 identified 12 RCTs that ultimately showed no difference between groups with regards to efficacy (pregnancy rates), safety, and compliance rates. Continuous or extended CHCs were shown to reduce menstrual symptoms (headaches, tiredness, bloating, and menstrual pain). In addition, 11 of 12 studies reported similar or improved bleeding patterns with continuous or extended cycles.
Conclusions: This recently published updated systematic review identified a further 4 RCTs, however, results did not change.

Committee Opinion No. 602: Depot Medroxyprogresterone Acetate and Bone Effects
Obstet Gynecol 2014(6):1298-402

- The effect of DMPA on BMD should neither prevent practitioners from prescribing DMPA nor limit its use to 2 consecutive yr.
- BMD loss due to DMPA appears to be substantially or fully reversible.
- Contraceptive implants and intrauterine devices that do not affect BMD should be considered as first-line for adolescents.
- Inform patients about benefits and the potential risks of DMPA, and encourage daily exercise, calcium and vitamin D intake.
- Routine BMD monitoring is not recommended for DMPA users.

Emergency Postcoital Contraception

Table 12. Emergency Contraceptive Methods

Method	Mechanism of Action	Side Effects	Contraindications
HORMONAL			
Yuzpe Method Used within 72 h of unprotected intercourse; limited evidence of benefit up to 5 d Ovral® 2 tablets then repeat in 12 h (ethinyl estradiol 100 µg/ levonorgestrel 500 µg) Can substitute with any OCP as long as same dose of estrogen used 2% overall risk of pregnancy Efficacy decreased with time (e.g. less effective at 72 h than 24 h)	Unknown; theories include: Suppresses ovulation or causes deficient luteal phase Alters endometrium to prevent implantation Affects sperm/ova transport	Nausea (due to estrogen; treat with Gravol®) Irregular spotting	Pre-existing pregnancy (although not teratogenic) Caution in women with contraindications to OCP (although NO absolute contraindications)
"Plan B" Consists of levonorgestrel 750 µg q12h for 2 doses (can also take 2 doses together); taken within 72 h of intercourse. Can be taken up to 5 d Greater efficacy (75-95% if used within 24 h) and better side effect profile than Yuzpe method but efficacy decreases with time; 1st line if >24 h No estrogen thus very few contraindications/side effects (less nausea) Less effective in overweight individuals (>75 kg less effective, >80 kg not recommended)	Same as above	Same as above	Same as above but no caution in women with contraindications to OCP
Ulipristal 30 mg PO within 5 d	Selective Progesterone Receptor Modulator (SPERM) with primarily antiprogestin activity: may delay ovulation by up to 5 d	Headache, hot flashes, constipation, vertigo, endometrial thickening	Same as above but no caution in women with contraindications to OCP
NON-HORMONAL			
Postcoital IUD (Copper) Insert up to 7 d postcoitus Prevents implantation 1% failure rate Can use for short duration in higher risk individuals Mirena® IUS cannot be used as EPC	See Table 11	See Table 11	See Table 11

Follow-up

- 3-4 wk post treatment to confirm efficacy (confirmed by spontaneous menses or pregnancy test)
- contraception counselling

Termination of Pregnancy

There is no association between termination of pregnancy and either future breast cancer or future development of psychiatric disease

Indications

- patient desires an end to pregnancy
- may be for medical reasons (mother or fetus unhealthy) or social reasons, including patient request

Legal Issues

- no current law in Canada concerning abortion therefore considered legal at any gestational age
- CPSO: a physician must refer for abortion services regardless of personal beliefs, but not compelled to perform procedure

Rates

- 13.1 abortions/1000 women aged 15-44 in Canada (2017 CIHI data)
- worldwide: 42 million induced abortions per year; half are unsafe (WHO data)
- maternal mortality almost zero where induced abortion is safe and legal; rises to 100 maternal deaths/100,000 live births in sub-Saharan Africa and other countries where abortion is illegal and unsafe
- in Canada, 91% of induced abortions occur <12 wk GA; very rare after 24 wk (usually only for maternal/fetal reasons)

Methods of induced abortion

- medical
  - gold standard up to 9 wk GA: mifepristone and misprostol : 95-98% effective
  - mifepristone blocks the progesterone receptor (progesterone required in early pregnancy)
  - misoprostol induces uterine contractions
  - can also use misoprostol alone or methotrexate and misoprostol (with lower success rates of 90-95%)
  - side effects: bleeding (self-limited) and pain (while tissue passes) are expected side effects

- surgical
  - <14 wk:
    - manual vacuum aspiration – up to about 8-9 wk with hand held aspiration device
    - suction dilatation + aspiration ± curettage – may involve pre-surgical preparation of cervix with laminaria tents and/or misoprostol
  - 14-24 wk: dilatation and evacuation; pre- surgical preparation of cervix required with laminaria tents
  - pain or discomfort during procedure mitigated by use of appropriate analgesia/sedation/anesthesia (including paracervical blocks)
  - rare complications (1-5%): laceration of cervix, infection/endometritis, retained products of conception, ongoing pregnancy
  - very rare complications: (0.1-2%) : hemorrhage, perforation of uterus, Asherman's syndrome (adhesions within the endometrial cavity causing amenorrhea/infertility), future preterm birth (controversial and likely only with repeated abortion)
- counselling
  - options counselling always provided; always offer possibility of carrying pregnancy with/without adoption
  - offer future contraception and family planning services
  - ensure follow-up

Pregnancy-Related Complications

First and Second Trimester Bleeding

Approach to the Patient with Bleeding in T1/T2

History
- risk factors for ectopic pregnancy (see *Ectopic Pregnancy*, GY20)
- previous spontaneous abortion
- recent trauma
- characteristics of the bleeding (including any tissue passed)
- characteristics of the pain (cramping pain suggests spontaneous abortion)
- history of coagulopathy
- gynecological/obstetric history
- fatigue, dizziness, syncopal episodes due to hypovolemia, fever (may be associated with septic abortion)

Physical
- vitals (including orthostatic changes)
- abdomen (symphysis fundal height, tenderness, presence of contractions)
- perineum (signs of trauma, genital lesions)
- speculum exam (cervical os open or closed, presence of active bleeding/clots/tissue)
- pelvic exam (uterine size, adnexal mass, uterine/adnexal tenderness, cervical motion tenderness)

Investigations
- β-hCG (may be lower than expected for GA in spontaneous abortion, can be used to diagnose viable pregnancy vs. ectopic pregnancy vs. abortion)
- U/S (confirm intrauterine pregnancy and fetal viability)
- CBC
- group and screen

Treatment
- IV resuscitation for hemorrhagic shock
- treat the underlying cause

Bleeding in Pregnancy Definitions
- First trimester bleeding: vaginal bleeding within the first 12 wk
- Second trimester bleeding: 12-20 wk

Differential Diagnosis
- Physiologic bleeding: spotting, due to implantation of placenta – reassure and check serial β-hCGs
- Abortion (threatened, inevitable, incomplete, complete)
- Abnormal pregnancy (ectopic, molar) (see *Hydatidiform Mole*, GY49)
- Trauma (post-coital or after pelvic exam)
- Genital lesion (e.g. cervical polyp, neoplasms)
- Subchorionic hematoma

Every woman of childbearing age presenting to ER with abdominal or pelvic pain should have β-hCG measured

Spontaneous Abortions

- see *Termination of Pregnancy* for therapeutic abortions, GY18

Table 13. Classification of Spontaneous Abortions

Type	History	Clinical	Management (± Rhogam®)
Threatened	Vaginal bleeding ± cramping	Cervix closed and soft	Watch and wait <5% go on to abort
Inevitable	Increasing bleeding and cramps ± rupture of membranes	Cervix closed until products start to expel, then external os opens	a) Watch and wait b) Mifepristone 200 mg PO followed by Misoprostol 800 µg PV 24 h later c) D&C
Incomplete	Extremely heavy bleeding and cramps ± passage of tissue noticed	Cervix open	a) Watch and wait b) Mifepristone 200 mg PO followed by Misoprostol 800 µg PV 24 h later c) D&C
Complete	Bleeding and complete passage of sac and placenta	Cervix closed, bleeding stopped	No D&C – expectant management
Missed	No bleeding (fetal death in utero)	Cervix closed	a) Watch and wait b) Mifepristone 200 mg PO followed by Misoprostol 800 µg PV 24 h later c) D&C
Recurrent	≥3 consecutive spontaneous abortions		Evaluate mechanical, genetic, environmental, and other risk factors
Septic	Contents of uterus infected – infrequent		IV broad spectrum antibiotics and prompt uterine evacuation

Embryonic demise can be diagnosed by ultrasound based on an intrauterine gestational sac, embryonic crown-rump length ≥7 mm, and no cardiac activity

Ectopic Pregnancy

Definition

- embryo implants outside of the endometrial cavity

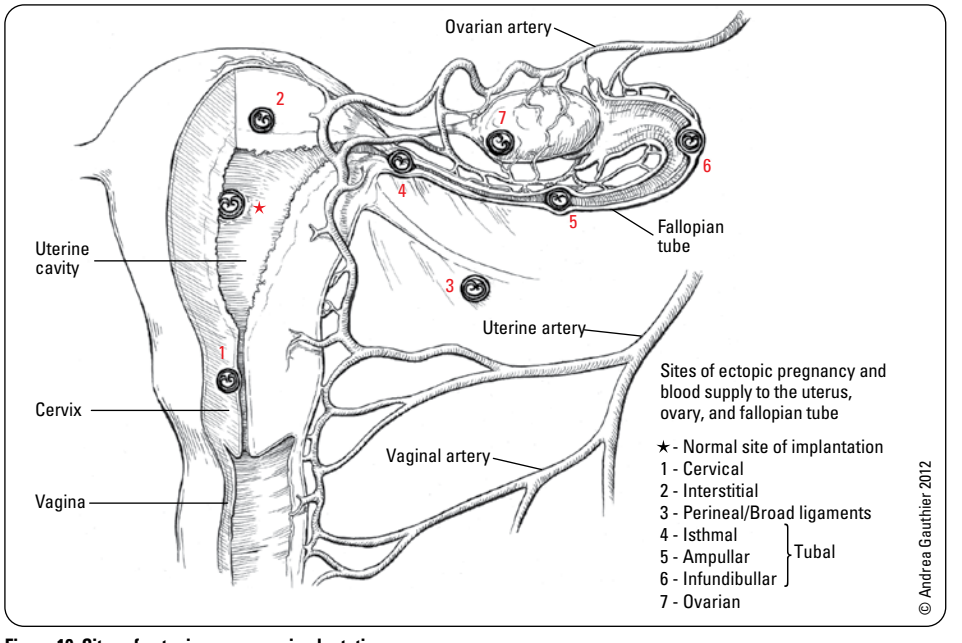


Figure 10. Sites of ectopic pregnancy implantation
ampullary (70%) >> isthmal (12%) > fimbrial (11%) > ovarian (3%) > interstitial (2%) > abdominal (1%)

Epidemiology

- 1/100 pregnancies
- fourth leading cause of maternal mortality, leading cause of maternal death in first trimester
- increase in incidence over the last 3 decades
- three commonest locations for ectopic pregnancy: ampullary (70%), isthmic (12%), fimbrial (11%)

Etiology

- 50% due to damage of fallopian tube cilia following PID
- intrinsic abnormality of the fertilized ovum
- conception late in cycle
- transmigration of fertilized ovum to contralateral tube

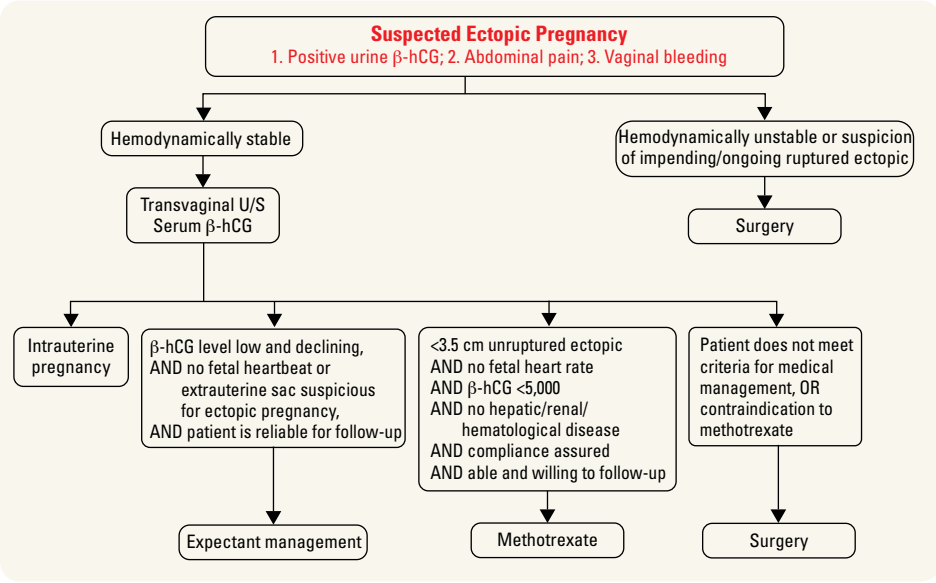


Figure 11. Algorithm for suspected ectopic pregnancy

Risk Factors

- previous ectopic pregnancy
- gynecologic
  - current IUD use – increased risk of ectopic if pregnancy occurs
  - history of PID (especially infection with *C. trachomatis*), salpingitis
  - infertility
- infertility treatment (IVF pregnancies following ovulation induction (7% ectopic rate))
- previous procedures
  - any surgery on fallopian tube (for previous ectopic, tubal ligation, etc.)
  - abdominal surgery for ruptured appendix, etc.
- smoking
- structural
  - uterine leiomyomas
  - adhesions
  - abnormal uterine anatomy (e.g. T-shaped uterus)

Investigations

- serial β-hCG levels; normal doubling time with intrauterine pregnancy is 1.6-2.4 d in early pregnancy
  - rise of <20% of β-hCG (1.6-2.4 d) is 100% predictive of a non-viable pregnancy
  - prolonged doubling time, plateau, or decreasing levels before 8 wk implies nonviable gestation but does not provide information on location of implantation
  - 85% of ectopic pregnancies demonstrate abnormal β-hCG doubling
- ultrasound
  - U/S is only definitive if fetal cardiac activity is detected in the tube or uterus
  - specific finding on transvaginal U/S is a tubal ring
- suspect ectopic in case of empty uterus by TVUS with β-hCG >2000-3000 mIU/ml
- laparoscopy (sometimes used for definitive diagnosis)

Treatment

- goals of treatment: conservative (preserve tube if possible), maintain hemodynamic stability
- surgical = laparoscopy
  - linear salpingostomy an option if tube salvageable, however, patient must be reliable to follow-up with weekly β-hCG
  - salpingectomy if tube damaged or ectopic is ipsilateral recurrence
  - 15% risk of persistent trophoblast if salpingectomy; must monitor β-hCG titres weekly until they reach non-detectable levels
  - consider Rhogam® if Rh negative
  - patient may require laparotomy if unstable, extensive abdominal surgical history, etc.
- medical = methotrexate
  - use 50 mg/m^2 body surface area; given in a single IM dose
  - this is 1/5 to 1/6 chemotherapy dose, therefore minimal side effects (reversible hepatic dysfunction, diarrhea, gastritis, dermatitis)
  - follow β-hCG levels weekly until β-hCG is non-detectable
    - plateaued or rising levels suggest persistent trophoblastic tissue requiring further treatment

Contraindications to Methotrexate Therapy for Ectopic Pregnancy

- Abnormalities in hematologic, hepatic or renal function
- Immunodeficiency
- Active pulmonary disease
- Peptic ulcer disease
- Hypersensitivity to methotrexate
- Heterotopic pregnancy with coexisting viable intrauterine pregnancy
- Breastfeeding
- Unwilling or unable to adhere to methotrexate protocol

DDx of Lower Abdominal Pain

- Urinary tract: UTI, kidney stones
- GI: diverticulitis, appendicitis
- Gyne: endometriosis, PID, fibroid (degenerating, infarcted, torsion), ovarian torsion, ovarian neoplasm, ovarian cyst, pregnancy-related

Any woman presenting with abdominal pain, vaginal bleeding and amenorrhea is an ectopic pregnancy until proven otherwise

More than half of patients with ectopic pregnancy have no risk factors

Presentation of Ectopic Pregnancy Ruptures

- Acute abdomen with increasing pain
- Abdominal distention
- Shock

Management of Abortions

- Always rule out an ectopic
- Always check Rh; if negative, give Rhogam®
- Always ensure patient is hemodynamically stable

  - 82-95% success rate, but up to 25% will require a second dose
    - administer a second dose if β-hCG does not decrease by at least 15% between days 4 and 7
  - tubal patency following methotrexate treatment approaches 80%
- expectant management is an option for patients who are clinically stable, reliable for follow-up, and have β-hCG levels that are low and declining

Prognosis
- 9% of maternal deaths during pregnancy attributed to ectopic pregnancy
- 40-60% of patients will become pregnant again after surgery
- 10-20% will have subsequent ectopic pregnancy

Infertility

Epidemiology
- 10-15% of couples, must investigate both members of the couple

Female Factors

Etiology
- ovulatory dysfunction (15-20%)
  - hypothalamic (hypothalamic amenorrhea)
    - stress, poor nutrition, excessive exercise (even with presence of menstruation), history of eating disorders
  - pituitary (prolactinoma, hypopituitarism)
  - ovarian
    - PCOS
    - primary ovarian insufficiency
    - luteal phase defect (poor follicle production, premature corpus luteum failure, failed uterine lining response to progesterone), poorly understood
  - systemic diseases (thyroid, Cushing's syndrome, renal/hepatic failure), diabetes
  - congenital (Turner's syndrome, gonadal dysgenesis, or gonadotropin deficiency)
- outflow tract abnormality (15-20%)
  - tubal factors (20-30%)
    - PID
    - adhesions (previous surgery, peritonitis, endometriosis)
    - ligation/occlusion (e.g. previous ectopic pregnancy)
  - uterine factors (<5%)
    - congenital anomalies, bicornuate uterus, septate uterus, prenatal DES exposure, intrauterine adhesions (e.g. Asherman's syndrome), fibroids/polyps (particularly intrauterine)
    - infection (endometritis, pelvic tuberculosis)
    - endometrial ablation
  - cervical factors (5%)
    - hostile or acidic cervical mucus, anti-sperm antibodies
    - structural defects (cone biopsies, laser or cryotherapy)
- endometriosis (15-30%)
- multiple factors (30%)
- unknown factors (10-15%)

Investigations
- ovulatory
  - day 3: FSH, LH, TSH, prolactin ± DHEA, free testosterone (if hirsute) add estradiol for proper FSH interpretation
  - day 21-23: serum progesterone to confirm ovulation
  - initiate basal body temperature monitoring (biphasic pattern)
  - postcoital test: evaluate mucus for clarity, pH, spinnbarkeit/fibrosity (rarely done)
- tubal factors
  - HSG (can be therapeutic – opens fallopian tube)
  - SHG (can be therapeutic; likely less – opens fallopian tube)
  - laparoscopy with dye insufflation (or tubal dye test) rarely done as diagnostic
- peritoneal/uterine factors
  - HSG/SHG, hysteroscopy
- other
  - karyotype

Infertility: inability to conceive or carry to term a pregnancy after one year of regular, unprotected intercourse
Primary infertility: infertility in the context of no prior pregnancies
Secondary infertility: infertility in the context of a prior conception
Generally, 75% of couples achieve pregnancy within 6 mo, 85% within 1 yr, 90% within 2 yr

When Should Investigations Begin?
- <35 yr: after 1 yr of regular unprotected intercourse
- 35-40 yr: after >6 mo
- >40 yr: immediately
- Earlier if
  - History of PID
  - History of infertility in previous relationship
  - Prior pelvic surgery
  - Chemotherapy/radiation in either partner
  - Recurrent pregnancy loss
- Moderate-severe endometriosis

Ethical Considerations in Infertility Treatment
- Infertility demands non-judgmental discussion
- Ethical issues surrounding therapeutic donor insemination in same sex couples, surrogacy, donor gametes, and other advanced reproductive technologies are still evolving and remain controversial
- If the doctor finds that certain treatment options lie outside of their moral boundaries, the infertile couple should be referred to another physician

Treatment
- education: timing intercourse relative to ovulation (from 2 d prior to 2 d following presumed ovulation), every other day
- medical
  - ovulation induction
    - clomiphene citrate (Clomid®): estrogen antagonist causing a perceived decreased estrogen state, resulting in increased pituitary gonadotropins; which increases FSH and LH and induces ovulation (better results if anovulatory)
    - followed by β-hCG for stimulation of ovum release
    - Letrozole: aromatase inhibitor. May be associated with a higher rate of live births in patients with PCOS
  - may add:
    - bromocriptine (dopamine agonist) if elevated prolactin
    - dexamethasone for hyperandrogenism (adult onset congenital adrenal hyperplasia)
    - metformin (for PCOS)
    - luteal phase progesterone supplementation for luteal phase defect (mechanism not completely understood)
    - anticoagulation and ASA (81 mg PO OD) for women with a history of recurrent spontaneous abortions (for antiphospholipid antibody syndrome)
    - thyroid replacement to keep TSH <2.5
- surgical/procedural
  - tubuloplasty
  - lysis of adhesions
  - artificial insemination: intracervical insemination (ICI), intrauterine insemination (IUI), intrauterine tuboperitoneal insemination (IUTPI), intratubal insemination (ITI)
  - sperm washing
  - IVF (fertilization)
  - IFT (intrafallopian transfer)
  - GIFT* (gamete intrafallopian transfer): immediate transfer with sperm after oocyte retrieval
  - ZIFT* (zygote intrafallopian transfer): transfer after 24 h culture of oocyte and sperm
  - TET* (tubal embryo transfer): transfer after >24 h culture
  - ICSI (intracytoplasmic sperm injection)
  - IVM (in vitro maturation)
  - ± oocyte or sperm donors
  - ± pre-genetic screening for single gene defects in karyotype of zygote

*not performed in Canada

Male Factors

- see Urology, U36

Etiology
- varicocele (>40%)
- idiopathic (>20%)
- obstruction (~15%)
- cryptorchidism (~8%)
- immunologic (~3%)

Investigations
- semen analysis and culture
- postcoital (Huhner) test: rarely done

Normal Semen Analysis (WHO lower reference limits)
- Must be obtained after 2-7 d of abstinence
  - Volume 1.5 cc
  - Count 15 million/cc
  - Vitality 58% live
  - Motility 32% progressive, 40% total (progressive + non-progressive)
- Morphology 4.0% normal

Polycystic Ovarian Syndrome

- also called chronic ovarian androgenism

Etiology

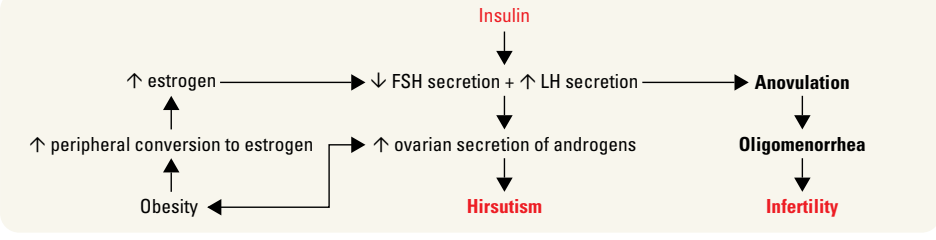


Figure 12. Pathophysiology of polycystic ovarian syndrome

Polycystic Ovarian Syndrome – HAIR-AN
Hirsutism, **H**yper**A**ndrogenism, **I**nfertility, **I**nsulin **R**esistance, **A**canthosis **N**igricans

Diagnosis

- Rotterdam diagnostic criteria: 2 of 3 required
  - oligomenorrhea/irregular menses for 6 mo
  - hyperandrogenism
    - clinical evidence - hirsutism or acne
    - biochemical evidence - raised free testosterone
  - polycystic ovaries on U/S (not appropriate in adolescents)

Clinical Features

- average age 15-35 yr at presentation
- in adolescents, wait at least 1-2 yr to make diagnosis as adolescence resembles PCOS
- abnormal/irregular uterine bleeding, hirsutism, infertility, obesity, virilization
- acanthosis nigricans: browning of skin folds in intertriginous zones (indicative of insulin resistance)
- insulin resistance occurs in both lean and obese patients
- family history of DM

Investigations

- goal: identify hyperandrogenism or chronic anovulation and rule out specific pituitary or adrenal disease as the cause
- laboratory
  - prolactin, 17-hydroxyprogesterone, free testosterone, DHEA-S, TSH, free T4, androstenedione, SHBG
  - LH:FSH >2:1; LH is chronically high with FSH mid-range or low (low sensitivity and specificity)
  - increased DHEA-S, androstenedione and free testosterone (most sensitive), decreased SHBG
- transvaginal or transabdominal U/S: polycystic-appearing ovaries ("string of pearls" – 12 or more small follicles 2-9 mm, or increased ovarian volume)
- tests for insulin resistance or glucose tolerance
  - fasting glucose:insulin ratio <4.5 is consistent with insulin resistance (U.S. units)
  - 75 g OGTT yearly (particularly if obese)
- laparoscopy
  - not required for diagnosis
  - most common to see white, smooth, sclerotic ovaries with a thick capsule; multiple follicular cysts in various stages of atresia; and hyperplastic theca and stroma
- rule out other causes of abnormal bleeding

Treatment

- cycle control
  - lifestyle modification (decrease BMI, increase exercise) to decrease peripheral estrone formation
  - OCP monthly or cyclic Provera® to prevent endometrial hyperplasia due to unopposed estrogen
  - oral hypoglycemic (e.g. metformin) if type 2 diabetic or if trying to become pregnant
  - tranexamic acid (Cyklokapron®) for menorrhagia only
- infertility
  - medical induction of ovulation: letrozole, clomiphene citrate (no longer available in Canada), human menopausal gonadotropins (HMG [Pergonal®]), LHRH, recombinant FSH, and metformin
    - metformin may be used alone or in conjuction with clomiphene citrate for ovulation induction
  - ovarian drilling (perforate the stroma), wedge resection of the ovary
  - bromocriptine (if hyperprolactinemia)
- hirsutism
  - any OCP can be used
    - Diane 35® (cyproterone acetate): antiandrogenic
    - Yasmin® (drospirenone and ethinyl estradiol): spironolactone analogue (inhibits steroid receptors)
  - mechanical removal of hair
  - finasteride (5-α reductase inhibitor)
  - flutamide (androgen reuptake inhibitor)
  - spironolactone: androgen receptor inhibitor

PCOS May be Confused with

- Late onset congenital adrenal hyperplasia (21-hydroxylase deficiency)
- Cushing's syndrome
- Ovarian and adrenal neoplasms
- Hyperprolactinemia
- Hypothyroidism

Clinical Signs of Endocrine Imbalance

- Menstrual disorder/amenorrhea (80%)
- Infertility (74%)
- Hirsutism (69%)
- Obesity (49%)
- Impaired glucose tolerance (35%)
- DM (10%)

Long-Term Health Consequences

- Hyperlipidemia
- Adult-onset DM
- Endometrial hyperplasia
- Infertility
- Obesity
- Sleep apnea

Insulin-Sensitising Drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for Women with Polycystic Ovary Syndrome, Oligo Amenorrhoea and Subfertility

Cochrane Database Syst Rev 2012; (5):CD003053

Purpose: To evaluate efficacy of insulin-sensitising drugs in improving reproductive outcomes of women with PCOS.

Methods: 42 RCTs (n=3992) were included.

Conclusions: Metformin was associated with improved clinical pregnancy rates whether used alone or in combination with clomiphene. However, this did not translate into live birth rates.

Diagnostic Criteria for Polycystic Ovary Syndrome: Pitfalls and Controversies

JOGC 2008;8:671-679

At present, there is no clear-cut definition of biochemical hyperandrogenemia, particularly since there is dependence on poor laboratory standards for measuring androgens in women. Clinical signs of hyperandrogenism are ill-defined in women with PCOS, and diagnosis of both hirsutism and polycystic ovarian morphology remains subjective. There is also the inappropriate tendency to assign ovulatory status solely on basis of menstrual cycle history or poorly timed endocrine measurements. Therefore it is important as clinicians to recognize the multi-factorial and complex nature of PCOS and place this in the context of our present diagnostic limitations.

Gynecological Infections

Physiologic Discharge

- clear, white, flocculent, odourless discharge; pH 3.8-4.2
- smear contains epithelial cells, Lactobacilli
- increases with increased estrogen states: pregnancy, OCP, mid-cycle, PCOS, or premenarchal
- if increased in perimenopausal/postmenopausal woman, consider investigation for other effects of excess estrogen (e.g. endometrial cancer)

Pruritus

- can be caused by physiologic discharge and cervical mucus production
- non-physiologic
  - genital tract infection
  - vulvovaginitis: candidiasis, trichomoniasis, BV, polymicrobial superficial infection
  - chlamydia, gonorrhea
  - pyosalpinx, salpingitis
  - genital tract inflammation (non-infectious)
  - local: chemical irritants, douches, sprays, foreign body, trauma, atrophic vaginitis, desquamative inflammatory vaginitis, focal vulvitis
  - neoplasia: vulvar, vaginal, cervical, endometrial
  - systemic: toxic shock syndrome, Crohn's disease, collagen disease, dermatologic (e.g. lichen sclerosis)
  - IUD, OCP (secondary to progesterone)

Vulvovaginitis

PREPUBERTAL VULVOVAGINITIS

- clinical features: irritation, pruritus, discharge, vulvar erythema, vaginal bleeding (specifically due to Group A Streptococci and Shigella)
- etiology
  - poor hygiene (proximity of anus to vagina)
  - foreign bodies (most commonly tissue paper)
  - irritation by perfumed soaps, chemicals, and tight clothing
  - localized skin disorders: lichen sclerosis, condyloma acuminata
  - trauma: accidental straddle injury, sexual abuse
  - infectious
    - pinworms
    - Candida (if using diapers or chronic antibiotics)
    - Group A streptococcus, *S. aureus* and *Shigella*
    - discovery of STI should raise suspicion of sexual abuse
  - other
    - polyps, tumour (ovarian malignancy)
    - psychosomatic vaginal complaints (specific to vaginal discharge)
    - endocrine abnormalities (specific to vaginal bleeding)
    - blood dyscrasia (specific to vaginal bleeding)
- investigations
  - vaginal swab for culture (specifically state that it is a pre-pubertal specimen)
  - pH, wet-mount, and KOH smear in prepubertal adults only
- treatment
  - enhanced hygiene and local measures (handwashing, white cotton underwear, no nylon tights, no tight fitting clothes, no sleeper pajamas, sitz baths, avoid bubble baths, use mild detergent, eliminate fabric softener, avoid prolonged exposure to wet bathing suits, urination with legs spread apart)
  - A&D® dermatological ointment (vitamin A/D) to protect vulvar skin
  - infectious: treat with antibiotics for organism identified

Table 14. Other Common Causes of Vulvovaginitis in Prepubertal Girls

	Pinworms	Lichen Sclerosis	Foreign Body
Diagnosis	Cellophane tape test	Area of white patches and thinning of skin (figure of 8)	
Treatment	Empirical treatment with mebendazole	Topical steroid creams	Irrigation of vagina with saline, may require local anesthesia or an exam under anesthesia

Vulvovaginitis
Vulvar and vaginal inflammation

Prepubertal and Adolescent Gynecological Infections: Legal Aspects of Confidentiality
- Clinicians who treat adolescents must be aware of federal, state, and provincial laws related to adolescent consent and confidentiality
- Cllinicians must be aware of guidelines governing funding sources for particular services and be familiar with the consent and confidentiality policies of the facility in which they practice

There is no high quality evidence showing a link between vulvovaginal candidiasis and hygienic habits or wearing tight or synthetic clothing

Most common gynecological problem in prepubertal girls is non-specific vulvovaginitis, not yeast

INFECTIOUS VULVOVAGINITIS

Table 15. Infectious Vulvovaginitis

	Candidasis	Bacterial Vaginosis (BV)	Trichomoniasis
Organisms	*Candida albicans* (90%) *Candida glabrata* (<5%) *Candida tropicalis* (<5%)	*Gardnerella vaginalis* *Mycoplasma hominis* Anaerobes: *Prevotella, Mobiluncus, Bacteroides*	*Trichomonas vaginalis* (flagellated protozoan)
Pathophysiology or Transmission	Predisposing factors include: Immunosuppressed host (DM, AIDS, etc.) Recent antibiotic use Increased estrogen levels (e.g. pregnancy, OCP)	Replacement of vaginal *Lactobacillus* with organisms above	Sexual transmission
Discharge	Whitish, "cottage cheese," minimal	Grey, thin, diffuse	Yellow-green, malodourous, diffuse, frothy
Other	20% asymptomatic	50-75% asymptomatic	25% asymptomatic
Signs/Symptoms	Intense pruritus Swollen, inflamed genitals Vulvar burning, dysuria, dyspareunia	Fishy odour, especially after coitus Absence of vulvar/vaginal irritation	Petechiae on vagina and cervix Occasionally irritated, tender vulva Dysuria, frequency
pH	≤4.5	≥4.5	≥4.5
Saline Wetmount	KOH wetmount reveals hyphae and spores	>20% clue cells = squamous epithelial cells dotted with coccobacilli (*Gardnerella*) Paucity of WBC Paucity of *Lactobacilli* Positive whiff test: fishy odour with addition of KOH to slide (due to formation of amines)	Motile flagellated organisms Many WBC Inflammatory cells (PMNs) Can have positive whiff test
Treatment	Clotrimazole, butoconazole, miconazole, terconazole suppositories, and/or creams for 1, 3, or 7 d treatments Treatment in pregnancy is usually topical Fluconazole 150 mg PO in single dose (can be used in pregnancy)	No treatment if non-pregnant and asymptomatic, unless scheduled for pelvic surgery or procedure **Oral** Metronidazole 500 mg PO bid x 7 d **Topical** Metronidazole gel 0.75% x 5 d OD (may be used in pregnancy) Clindamycin 2% 5 g intravaginally at bedtime for 7 d Probiotics (*Lactobacillus* sp.): oral or topical alone or as adjuvant	Treat even if asymptomatic Metronidazole 2 g PO single dose or 500 mg bid x 7 d (alternative) Symptomatic pregnant women should be treated with 2 g metronidazole once
Other	Prophylaxis for recurrent infection includes boric acid, vaginal suppositories, luteal phase fluconazole Routine treatment of partner(s) not recommended (not sexually transmitted)	Associated with recurrent preterm labour, preterm birth, and postpartum endometritis Need to warn patients on metronidazole not to consume alcohol (disulfiram-like action) Routine treatment of partner(s) not recommended (not sexually transmitted)	Warnings accompanying metronidazole use Treat partner(s) (sexually transmitted)

Sexually Transmitted Infections

• see Family Medicine, FM42

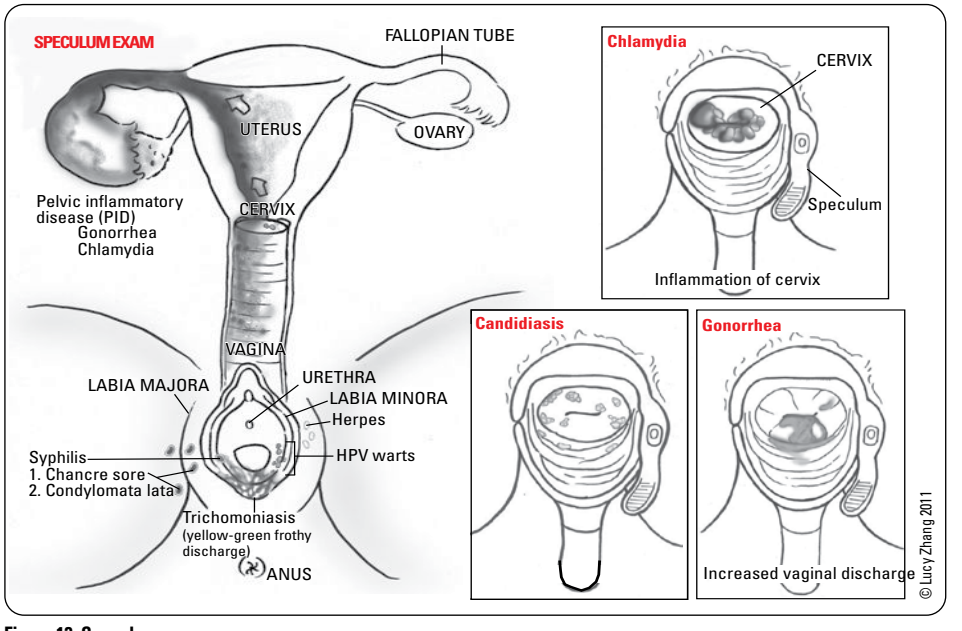


Figure 13. Speculum exam

CDC Notifiable Diseases
- Chancroid
- Chlamydia
- Gonorrhea
- Hepatitis A, B, C
- HIV
- Syphilis

Risk Factors for STIs
- History of previous STI
- Contact with infected person
- Sexually active individual <25 yr
- Multiple partners
- New partner in last 3 mo
- Lack of barrier protection use
- Street involvement (homelessness, drug use)

TRICHOMONIASIS
- see *Infectious Vulvovaginitis*

CHLAMYDIA

Etiology
- Chlamydia trachomatis

Epidemiology
- most common bacterial STI in Canada
- often associated with *N. gonorrhoeae*

Clinical Features
- asymptomatic (80% of women)
- muco-purulent endocervical discharge
- urethral syndrome: dysuria, frequency, pyuria, no bacteria on culture
- pelvic pain
- postcoital bleeding or intermenstrual bleeding (particularly if on OCP and prior history of good cycle control)
- symptomatic sexual partner

Investigations
- cervical culture or nucleic acid amplification test (can present in pharynx, rectum)
- obligate intracellular parasite: tissue culture is the definitive standard
- urine and self vaginal tests now available, which are equally or more effective than cervical culture

STI Testing
- Vaginal swab
  - Tests for bacterial vaginosis, trichomoniasis, candida
- Cervical swab
  - Tests for gonorrhea and chlamydia

Treatment
- doxycycline 100 mg PO bid for 7 d or azithromycin 1 g PO in a single dose. Doxycycline is contra-indictated in the 2nd and 3rd trimesters of pregnancy
- also treat gonorrhea because of high rate of co-infection
- reportable disease, partners should also be referred for treatment
- test of cure for chlamydia required in pregnancy (cure rates lower in pregnant patients) → retest 3-4 wk after initiation of therapy

Screening
- high-risk groups
- during pregnancy
- when initiating OCP if sexually active (independent risk factor)

Test of cure for *C. trachomatis* and *N. gonorrhoeae* is not routinely indicated
Repeat testing if symptomatic, if compliance with treatment is uncertain, or if pregnant

Complications
- PID: low-grade salpingitis and adhesions resulting in tubal obstruction
- infertility
- ectopic pregnancy
- chronic pelvic pain
- Fitz-Hugh-Curtis syndrome (liver capsule inflammation)
- reactive arthritis (male predominance, HLA-B27 associated), conjunctivitis, urethritis
- perinatal infection: conjunctivitis, pneumonia

GONORRHEA

Etiology
- Neisseria gonorrhoeae
- symptoms and risk factors same as chlamydia

Investigations
- Gram stain shows Gram-negative intracellular diplococci
- cervical, rectal, and throat culture (if clinically indicated)

Treatment
- single dose of ceftriaxone 250 mg IM plus azithromycin 1 g PO
  - if pregnant: above regimen or 2 g spectinomycin IM plus azithromycin 1 g PO (avoid quinolones)
  - also treat chlamydia, due to high rate of co-infection
- treat partners
  - reportable disease
  - screening as with chlamydia

HUMAN PAPILLOMAVIRUS

Etiology
- most common viral STI in Canada
- >200 subtypes, of which >30 are genital subtypes
- HPV types 6 and 11 are classically associated with anogenital warts/condylomata acuminata
- HPV types 16 and 18 are the most oncogenic (classically associated with cervical HSIL)
- types 16, 18, 31, 33, 35, 36, 45 (and others) associated with increased incidence of cervical and vulvar intraepithelial hyperplasia and carcinoma

Clinical Features
- latent infection
  - no visible lesions, asymptomatic
  - only detected by DNA hybridization tests
- subclinical infection
  - visible lesion found during colposcopy or on Pap test
- clinical infection
  - visible wart-like lesion without magnification (check pharynx too)
  - hyperkeratotic, verrucous or flat, macular lesions
  - vulvar edema

Investigations
- cytology
- koilocytosis: nuclear enlargement and atypia with perinuclear halo
- biopsy of lesions at colposcopy
- detection of HPV DNA subtype using nucleic acid probes (not routinely done but can be done in presence of abnormal Pap test to guide treatment)

Treatment
- patient administered
  - podofilox 0.5% solution or gel bid x 3 d in a row (4 d off) then repeat x 4 wk
  - imiquimod (Aldara®) 5% cream 3x/wk qhs x 16 wk
- provider administered
  - cryotherapy with liquid nitrogen: repeat q1-2wk
  - podophyllin resin in tincture of benzoin: weekly
  - trichloroacetic acid (TCA) (80-90%) or bichloroacetic acid weekly x 4-6 wk; safe in pregnancy
  - surgical removal/laser
  - intralesional interferon

Prevention
- vaccination: Gardasil®9, Gardasil®, Cervarix® (see Table 28, GY45)
- condoms may not fully protect (areas not covered, must be used every time throughout entire sexual act)

HERPES SIMPLEX VIRUS OF VULVA

Etiology
- 90% are HSV-2, 10% are HSV-1

Clinical Features
- may be asymptomatic
- initial symptoms: present 2-21 d after contact
- prodromal symptoms: tingling, burning, pruritus
- multiple, painful, shallow ulcerations with small vesicles appear 7-10 d after initial infection (absent in many infected persons); lesions are infectious
- inguinal lymphadenopathy, malaise, and fever often with first infection
- dysuria and urinary retention if urethral mucosa affected
- recurrent infections: less severe, less frequent, and shorter in duration (usually only HSV-2)

Investigations
- viral culture preferred in patients with ulcer present; however decreased sensitivity as lesions heal
- cytologic smear (Tzanck smear) shows multinucleated giant cells, acidophilic intranuclear inclusion bodies
- HSV DNA PCR
- type specific serologic tests for antibodies to HSV-1 and HSV-2 (not available routinely in Canada)

Genital Warts During Pregnancy
- Condyloma tend to get larger in pregnancy and should be treated early (consider excision)
- C-section only if obstructing birth canal or risk of extensive bleeding
- Do not use imiquimod, podophyllin, or podofilox

Human Rights in Health Equity: Cervical Cancer and HPV Vaccines
Am J Law Med 2009;35:365-87
- While cervical cancer rates have drastically fallen in developed countries due to effective prevention and treatment, socially disadvantaged women within these countries remain disproportionately more likely to develop and die of cervical cancer.
- In most developing countries cervical cancer rates have risen or remained unchanged.
- Must recognize that cervical cancer disparities between race groups, urban and rural residence, and high and low socioeconomic status are attributed to disparate screening and vaccination coverage.
- Programs are implemented without sufficient attention to conditions that render screening less effective or inaccessible to disadvantaged social groups including: lack of information, undervaluing of preventive care, opportunistic delivery in limited health care settings, sexual health stigma, and related [illegible] concerns.

A 9-Valent HPV Vaccine Against Infection and Intraepithelial Neoplasia in Women
NEJM 2015;372:711-23
Purpose: To determine the efficacy and immunogenicity of the qHPV (types 6, 11, 16, 18) vs. 9vHPV (five additional types 31, 33, 45, 52, 58) vaccines.
Method: International randomized, double-blinded phase 2B-3 study of 9vHPV vaccine in 14,215 women between ages of 16-26. Participants were randomized to the 9vHPV vaccine group or the qHPV vaccine group and each received a series of three IM injections (day 1, 2, and 6 mo). Swabs of labial, vulvar, perineal, perianal, endocervical, and ectocervical tissue was obtained and used for HPV DNA testing/Pap smear.
Results: Rate of high-grade cervical, vulvar, or vaginal disease was 14.0 per 1000 person-years in both vaccine groups. The rate of high-grade cervical, vulvar, or vaginal disease related to HPV-31, 33, 45, 52, and 58 was 0.1 per 1000 person-years in the 9vHPV group and 1.6 per 1000 person-years in the qHPV group (95% CI = 80.9-99.8). Antibody responses to HPV-6, 11, 16, and 18 were not significantly different between the two vaccine groups although adverse events related to injection sites were more common in the 9vHPV group.
Conclusions: The 9vHPV vaccine was non-inferior to qHPV vaccine in preventing infection and disease related to HPV-6, 11, 16, and 18 and also covered additional oncogenic types HPV-31, 33, 45, 52, and 58 in a susceptible population.

Treatment
- first episode: acyclovir 200 mg PO five times daily x 7-10 d, or famciclovir 250 mg PO tid x 7-10 d or valacyclovir 1 g PO bid x 7-10 d
- recurrent episode: acyclovir 400 mg PO tid x 5 d, valacylovir 1 g PO OD x 5 d or famciclovir 250 mg PO BID x 5 d
- daily suppressive therapy
  - consider for >6 recurrences per yr or recurrence every 2 mo
  - acyclovir 400 mg PO bid or valacyclovir 500 mg PO OD or valacyclovir 1 g PO OD or famciclovir 250 mg PO bid
- severe disease: IV acyclovir 5-10 mg/kg IV q8h x 2-7 d or until clinical improvement observed followed by oral antiviral therapy to complete 10 d of therapy total
- education regarding transmission: avoid sexual contact from onset of prodrome until lesions have cleared, use barrier contraception

SYPHILIS

Etiology
- Treponema pallidum

Epidemiology of Genital Ulcers

HSV	70-80%
1° Syphilis	5%
Chancroid (*Haemophilus ducreyi*)	<1%

Classifications
- primary syphilis
  - 3-4 wk after exposure
  - painless chancre on vulva, vagina, or cervix
  - painless inguinal lymphadenopathy
  - serological tests usually negative, local infection only
- secondary syphilis (can resolve spontaneously)
  - 2-6 mo after initial infection
  - nonspecific symptoms: malaise, anorexia, headache, diffuse lymphadenopathy
  - generalized maculopapular rash: palms, soles, trunk, limbs
  - condylomata lata: anogenital, broad-based, fleshy, grey lesions
  - serological tests usually positive
- latent syphilis
  - no clinical manifestations; detected by serology only
- tertiary syphilis
  - may involve any organ system
  - neurological: tabes dorsalis, general paresis
  - cardiovascular: aortic aneurysm, dilated aortic root
  - vulvar gumma: nodules that enlarge, ulcerate, and become necrotic (rare)
- congenital syphilis
  - may cause fetal anomalies, stillbirths, or neonatal death

Investigations
- aspiration of ulcer serum or node
- darkfield microscopy (most sensitive and specific diagnostic test for syphilis): look for spirochetes
- non-treponemal screening tests (VDRL, RPR); non-reactive after treatment, can be positive with other conditions
- specific anti-treponemal antibody tests (FTA-ABS, MHA-TP, TP-PA)
  - confirmatory tests; remain reactive for life (even after adequate treatment)

Treatment
- reportable disease, partners should be referred for treatment
- treatment of primary, secondary, latent syphilis of <1 yr duration
  - benzathine penicillin G 2.4 million units IM single dose
- treatment of latent syphilis of >1 yr duration
  - benzathine penicillin G 2.4 million units IM q1wk x 3 wk
- treatment of neurosyphilis
  - IV aqueous penicillin G 3-4 million units IM q4h x 10-14 d
- screening
  - high-risk groups
  - in pregnancy (see Obstetrics, *Infections During Pregnancy*, OB29)

Complications
- if untreated, 1/3 will experience late complications

HIV
- see Infectious Diseases, ID25

Bartholin Gland Abscess

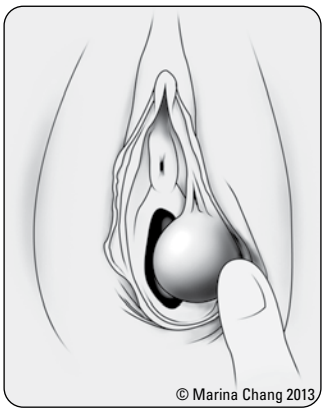


Figure 14. Bartholin gland abscess

Etiology
- often anaerobic and polymicrobial
- *U. urealyticum, N. gonorrhoeae, C. trachomatis, E. coli, P. mirabilis, Streptococcus* spp., *S. aureus* (rare)
- blockage of duct

Clinical Features
- unilateral swelling and pain in inferior lateral opening of vagina
- sitting and walking may become difficult and/or painful

Treatment
- sitz baths, warm compresses
- antibiotics: cephalexin x 1 wk
- incision and drainage using local anesthesia with placement of Word catheter (10 French latex catheter) for 2-3 wk (or as long as stays in situ)
- marsupialization under general anesthetic: more definitive treatment
- rarely treated by removing gland

Pelvic Inflammatory Disease

PID accounts for up to 20% of all gynecological hospital admissions

- up to 20% of all gynecology-related hospital admissions
- inflammation of the upper genital tract (above the cervix) including endometrium, fallopian tubes, ovaries, pelvic peritoneum ± contiguous structures

Etiology
- causative organisms (in order of frequency)
  - *C. trachomatis*
  - *N. gonorrhoeae*
    - gonorrhea and chlamydia often co-exist
  - endogenous flora: anaerobic, aerobic, or both
    - *E. coli, Staphylococcus, Streptococcus, Enterococcus, Bacteroides, Peptostreptococcus, H. influenzae, G. vaginalis*
    - cause of recurrent PID
    - associated with instrumentation
  - *Actinomyces israelii* (Gram-positive, non-acid-fast anaerobe)
    - 1-4% of PID cases associated with IUDs
  - others (TB, Gram-negatives, CMV, *U. urealyticum*, etc.)

Risk Factors
- age <30 yr
- risk factors as for chlamydia and gonorrhea
- vaginal douching
- IUD (within first 10 d after insertion)
- invasive gynecologic procedures (D&C, endometrial biopsy)

Clinical Feature
- up to 2/3 asymptomatic: many subtle or mild symptoms
- common: fever >38.3°C, lower abdominal pain and tenderness, abnormal discharge (cervical or vaginal)
- uncommon: N/V, dysuria, AUB
- chronic disease (often due to chlamydia)
  - constant pelvic pain
  - dyspareunia
  - palpable mass
  - very difficult to treat, may require surgery

PID Diagnosis
Must have
- Lower abdominal pain

Plus one of
- Cervical motion tenderness
- Adnexal tenderness

Plus one or more of
- High risk partner
- Temperature >38°C
- Mucopurulent cervical discharge
- Positive culture for *N. gonorrhoeae, C. trachomatis, E. coli,* or other vaginal flora
- Cul-de-sac fluid, pelvic abscess or inflammatory mass on U/S or bimanual
- Leukocytosis
- Elevated ESR or CRP (not commonly used)

Investigations
- blood work
  - β-hCG (must rule out ectopic pregnancy), CBC, blood cultures if suspect septicemia
- urine R&M
- speculum exam, bimanual exam
  - vaginal swab for Gram stain, C&S
  - cervical cultures for *N. gonorrhoeae, C. trachomatis*
  - endometrial biopsy will give definitive diagnosis (rarely done)
- ultrasound
  - may be normal
  - free fluid in cul-de-sac
  - pelvic or tubo-ovarian abscess
  - hydrosalpinx (dilated fallopian tube)
- laparoscopy (gold standard)
  - for definitive diagnosis: may miss subtle inflammation of tubes or endometritis

Treatment

- must treat with polymicrobial coverage

Table 16. Inpatient and Outpatient Management Options for Pelvic Inflammatory Disease

	Inpatient	Outpatient
Indications	Moderate to severe illness Atypical infection Adnexal mass, tubo-ovarian mass, or pelvic abscess Unable to tolerate oral antibiotics or failed oral therapy Immunocompromised Pregnant Adolescent (first episode) Surgical emergency cannot be excluded (e.g. ovarian torsion) PID is secondary to instrumentation	Typical findings Mild to moderate illness Oral antibiotics tolerated Compliance ensured Follow-up within 48-72 h (to ensure symptoms not worsening)
Antibiotic Regimen	Cefoxitin 2 g IV q6h + doxycycline 100 mg PO/IV q12h or Clindamycin 900 mg IV q8h + gentamycin 2 mg/kg IV/IM loading dose then gentamycin 1.5 mg/kg q8h maintenance dose Continue IV antibiotics for 24 h after symptoms have improved then doxycycline 100 mg PO bid to complete 14 d Percutaneous drainage of abscess under U/S guidance When no response to treatment, laparoscopic drainage If failure, treatment is surgical (salpingectomy, TAH/BSO)	1st line: ceftriaxone 250 mg IM x 1 + doxycycline 100 mg PO bid x 14 d or cefoxitin 2 g IM x 1 + probenecid 1 g PO + doxycycline 100 mg PO bid ± metronidazole 500 mg PO bid x 14 d 2nd line: ofloxacin 400 mg PO bid x14 d or levofloxacin 500 mg PO OD x 14 d ± metronidazole 500 mg PO bid x 14 d Consider removing IUD after a minimum of 24 h of treatment Reportable disease Treat partners Consider re-testing for *C. trachomatis* and *N. gonorrhoeae* 4-6 wk after treatment if documented infection

Complications of Untreated PID

- chronic pelvic pain
- abscess, peritonitis
- adhesion formation
- ectopic pregnancy
- infertility
  - 1 episode of PID: 13% infertility
  - 2 episodes of PID: 36% infertility
- bacteremia
- septic arthritis, endocarditis

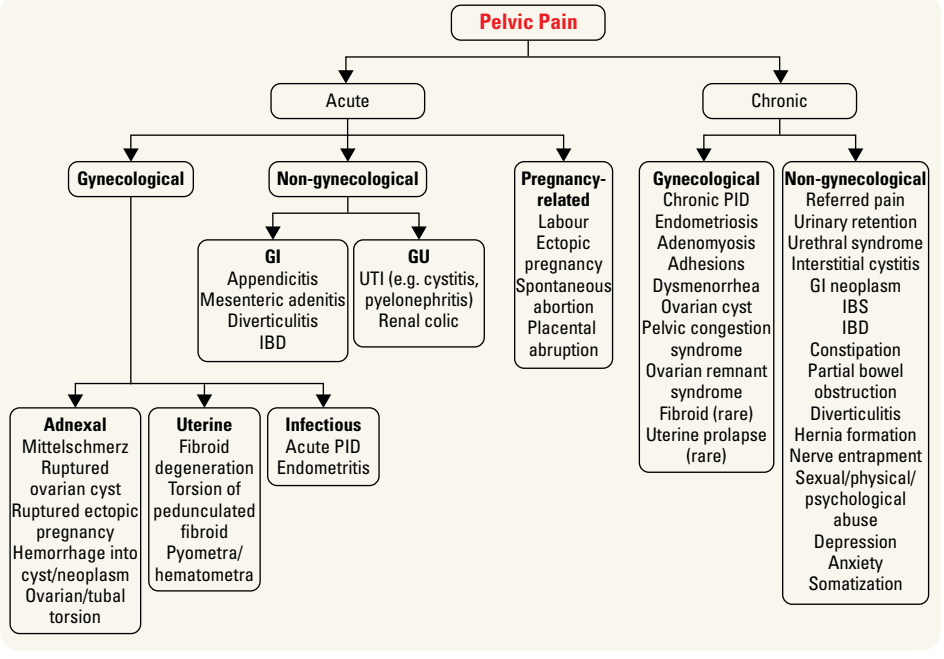


Figure 15. Approach to pelvic pain

Toxic Shock Syndrome

- see Infectious Diseases, ID21

Risk Factors
- tampon use
- diaphragm, cervical cap, or sponge use (prolonged use, i.e. >24 h)
- wound infections
- post-partum infections
- early recognition and treatment of syndrome is imperative as incorrect diagnosis can be fatal

Toxic Shock Syndrome
Multiple organ system failure due to *S. aureus* exotoxin (rare condition)

Clinical Feature
- sudden high fever
- sore throat, headache, diarrhea
- erythroderma
- signs of multisystem organ failure
- refractory hypotension
- exfoliation of palmar and plantar surfaces of the hands and feet 1-2 wk after onset of illness

Treatment
- remove potential sources of infection (foreign objects and wound debris)
- debride necrotic tissues
- adequate hydration
- penicillinase-resistant antibiotics (e.g. cloxacillin)
- steroid use controversial, but, if started within 72 h, may reduce severity of symptoms and duration of fever

Surgical Infections

Post-Operative Infections in Gynecological Surgery
- pelvic cellulitis
  - common post hysterectomy, affects vaginal vault
  - erythema, induration, tenderness, discharge involving vaginal cuff
  - treat if fever and leukocytosis with broad-spectrum antibiotics (i.e. clindamycin and gentamicin)
  - drain if excessive purulence or large mass
  - can result in intra-abdominal and pelvic abscess
- see General Surgery, *Post-Operative Fever*, GS7

Sexual Abuse

- see Family Medicine, FM26, Emergency Medicine, ER27

Sexuality and Sexual Dysfunction

SEXUAL RESPONSE
1. desire: energy that allows an individual to initiate or respond to sexual stimulation
2. arousal: physical and emotional stimulation leading to breast and genital vasodilation and clitoral engorgement
3. orgasm: physical and emotional stimulation is maximized, allowing the individual to relinquish their sense of control
4. resolution: most of the congestion and tension resolves within seconds, complete resolution may take up to 60 min

SEXUAL DYSFUNCTION

Etiology
- psychological or emotional: depression, abuse
- hormonal: menopause
- neurologic dysfunction: spinal cord injury
- vascular insufficiency: DM
- drug side effects: β-blockers
- trauma: episiotomy

Classification
- lack of desire (60-70% of women)
- lack of arousal
- anorgasmia (5-10%)
  - primary anorgasmia: never before achieved orgasm under any circumstances
  - secondary anorgasmia: was able to achieve orgasms before but now unable to

- dyspareunia (3-6%): painful intercourse, superficial or deep
  - vaginismus (15%)
  - vulvodynia
  - vaginal atrophy
  - vulvar vestibulitis: associated with history of frequent yeast infections
  - PID

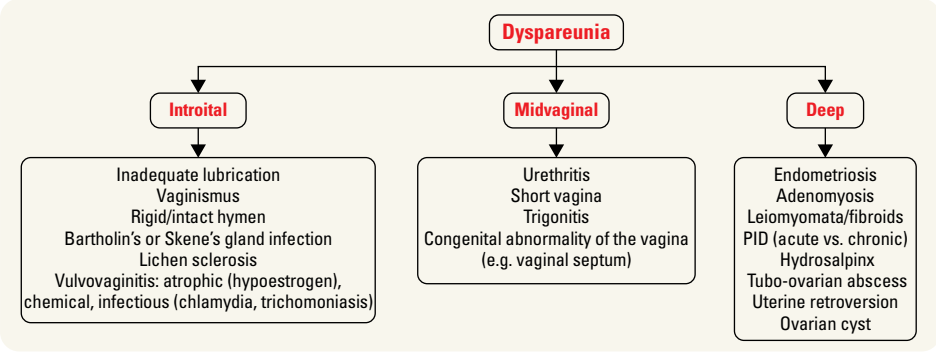


Figure 16. Approach to dyspareunia

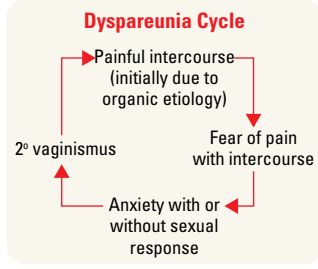


Figure 17. Dyspareunia cycle

Treatment
- lack of desire: assess factors, rule out organic causes, relationship therapy, sensate focus exercises
- anorgasmia: self-exploration/pleasuring, relationship therapy if needed, bridging techniques (different sexual positions, clitoral stimulation during intercourse)
- dyspareunia
  - Kegel and reverse Kegel exercises
  - dilator treatment
  - comfort with self-exam
  - psychotherapy, other behavioural techniques
  - female on top position: allows for control of speed and duration
  - vestibulitis: remove local irritants, change in contraceptive methods, dietary changes (increased citrate, decreased oxalate), and vestibulectomy (rare)
  - vulvodynia: local moisturization, cold compresses, systemic nerve-blocking therapy (amitriptyline, gabapentin) orally or topically, topical anesthetics, estrogen cream
  - pain clinic
  - removal of environmental factors: bubble baths, soaps, perfumes, sanitary pads with plastic lining

Kegel Exercises
Regular contraction and relaxation to strengthen pelvic floor muscles

Reverse Kegel Exercises
1 s contraction then 5 s of relaxation

Menopause

- see Family Medicine, FM40

Definitions
- lack of menses for 1 yr
- types of menopause
  - physiological; average age 51 yr (follicular atresia)
  - primary ovarian insufficiency; before age 40 (autoimmune disorder, infection, Turner's syndrome)
  - iatrogenic (surgical/radiation/chemotherapy)

Menopause
Occurrence of last spontaneous menstrual period, resulting from loss of ovarian function (loss of oocyte response to gonadotropins)

"Being in menopause"
Lack of menses for 1 yr

Perimenopause
Period of time surrounding menopause (2-8 yr preceding + 1 yr after last menses) characterized by fluctuating hormone levels, irregular menstrual cycles, and symptom onset

Clinical Features
- associated with estrogen deficiency
  - vasomotor instability (tends to dissipate with time)
    - hot flushes/flashes, night sweats, sleep disturbances, formication, nausea, palpitations
  - urogenital atrophy involving vagina, urethra, bladder
    - dyspareunia, pruritus, vaginal dryness, bleeding, post-coital bleeding, urinary frequency, urgency, incontinence
    - inspection may reveal: thinning of tissues, erythema, petechiae, bleeding points, dryness on speculum exam
  - skeletal
    - osteoporosis, joint and muscle pain, back pain
  - skin and soft tissue
    - decreased breast size, skin thinning/loss of elasticity
  - psychological
    - increased anxiety, depression, irritability, fatigue, decreased libido, memory loss

- 85% of women experience hot flashes
- 20-30% seek medical attention
- 10% are unable to work

Investigations
- increased levels of FSH (>35 IU/L) on day 3 of cycle (if still cycling) and LH (FSH>LH)
- FSH level not always predictive due to monthly variation; use absence of menses for 1 yr to diagnose
- decreased levels of estradiol (later)

Treatment

Table 17. Treatment of Menopause

Goal is for individual symptom management						
Vasomotor Instability	**Vaginal Atrophy**	**Urogenital Health**	**Osteoporosis**	**Decreased Libido**	**CVD***	**Mood And Memory**
HRT (first line) SSRI venlafaxine gabapentin propranaolol clonidine acupuncture	Local estrogen: cream (Premarin®), vaginal suppository (VagiFem®), ring (Estring®), lubricants (Replens®), oral or transdermal hormone replacement therapy, intravaginal laser	Lifestyle changes (weight loss, bladder re-training), local estrogen replacement, surgery	1000-1500 mg calcium OD, 800-1000 IU vitamin D, weight-bearing exercise, smoking cessation, bisphosphonates (e.g. alendronate), selective estrogen receptor modifiers (SERMs) (e.g.raloxifene [Evista®]), HRT (second-line treatment)	Vaginal lubrications, counselling, androgen-replacement testoterone cream or the oral form (Andriol®)	Manage CVD risk factors	Anti-depressants (first line), HRT (augments effect)

*CVD (cardiovascular disease)

Menopause Pathophysiology

Degenerating theca cells fail to react to endogenous gonadotropins (FSH, LH)
↓
Less estrogen is produced
↓
Decreased negative feedback on hypothalamic-pituitary-adrenal axis
↓
Increased FSH and LH
↓
Stromal cells continue to produce androgens as a result of increased LH stimulation

Figure 18. Menopause pathophysiology

- Osteoporosis is the single most important health hazard associated with menopause
- Cardiovascular disease is the leading cause of death post-menopause

- Increased risk of breast cancer (RR 1.3) is associated with estrogen+progesterone HRT, but not with estrogen-only HRT
- All women taking HRT should have periodic surveillance and counselling regarding its benefits and risks

Hormone Replacement Therapy

- see Family Medicine, FM40
- primary indication is treatment of menopausal symptoms (vasomotor instability)
- keep doses low (e.g. 0.3 mg Premarin®) and duration of treatment short (<5 yr)

HRT Components

- estrogen
- oral or transdermal (e.g. patch, gel)
- transdermal preferred for women overall, especially with hypertriglyceridemia or impaired hepatic function, smokers, and women who suffer from headaches associated with oral HRT
- low-dose (preferred dose: 0.3 mg Premarin®/25 µg Estradot® patch, can increase if necessary)
- progestin
- given in combination with estrogen for women with an intact uterus to prevent development of endometrial hyperplasia/cancer

Table 18. Examples of HRT Regimens

HRT Regimen	Estrogen Dose	Progestin Dose	Notes
Unopposed Estrogen	CEE 0.625 mg PO OD	None	If no intact uterus
Standard-Dose	CEE 0.625 mg PO OD	MPA 2.5 mg PO OD, or micronized progesterone 100 mg PO OD	Withdrawal bleeding may occur in a spotty, unpredictable manner Usually abates after 6-8 mo due to endometrial atrophy Once patient has become amenorrheic on HRT, significant subsequent bleeding episodes require evaluation (endometrial biopsy)
Standard-Dose Cyclic	CEE 0.625 mg PO OD	MPA 5-10 mg PO days 1-14 only, or micronized progesterone 200 mg PO OD days 1-14 only	Bleeding occurs monthly after day 14 of progestin (can continue for years) PMS-like symptoms (breast tenderness, fluid retention, headache, nausea) are more prominent with cyclic HRT
Pulsatile	CEE 0.625 mg PO OD	MPA low-dose	3 d on, 3 d off
Transdermal	Estroderm®-Estradiol 0.05 mg/d or 0.1 mg/d Estalis®-Estradiol 140 µg/d or 250 µg/d	Estroderm®-MPA 2.5 mg PO OD Estalis®-NEA 50 µg/d	Use patch twice weekly Can use oral progestins (Estroderm®) Combined patches available (Estalis®)
Topical	Estrace® 2-4 g/d x 1-2 wk, 1 g/d maintenance Premarin® 0.5-2 g/d for 21 d then off 7 d for vaginal atrophy, 0.5 g/d for 21 d then off 7 d or twice/wk for dyspareunia Estragyn® 2-4 g/d	Crinone® 4% or 8% (45 or 90 mg applicator)	If simultaneously taking oral estrogen tablet, may need to adjust dosing If intact uterus, also take progesterone

CEE = conjugated equine estrogen (e.g. Premarin®); MPA = medroxyprogesterone acetate (e.g. Provera®); NEA = norethindrone acetate
Consider lower dose regimens, PREMPRO® 0.45/1.5 (Premarin® 0.45 mg and Provera® 1.5 mg); Estrace® (topical 17β-estradiol) = 0.1 mg active ingredient/g; Premarin® (topical CEE) = 0.625 mg active ingredient/g; Estragyn® (topical estrone) = 1 mg active ingredient/g

Side Effects of HRT

- abnormal uterine bleeding
- mastodynia: breast tenderness and swelling
- edema, bloating, heartburn, nausea
- mood changes (progesterone)
- can be worse in progesterone phase of combined therapy

Contraindications to HRT

- absolute
  - acute liver disease
  - undiagnosed vaginal bleeding
  - history of breast cancer
  - known or suspected uterine cancer/breast cancer
  - acute vascular thrombosis or history of severe thrombophlebitis or thromboembolic disease
  - cardiovascular disease
- relative
  - pre-existing uncontrolled HTN
  - uterine fibroids and endometriosis
  - familial hyperlipidemias
  - migraine headaches
  - family history of estrogen-dependent cancer
  - chronic thrombophlebitis
  - DM (with vascular disease)
  - gallbladder disease, hypertriglyceridemia, impaired liver function (consider transdermal estrogen)
  - fibrocystic disease of the breasts

Absolute Contraindications to HRT

ABCD
Acute liver disease
Undiagnosed vaginal **B**leeding
Cancer (breast/uterine), **C**ardiovascular disease
DVT (thromboembolic disease)

WOMEN'S HEALTH INITIATIVE (launched in 1991)

- two non-randomized studies investigating health risks and benefits of HRT in healthy postmenopausal women 50-79 yr old
  - continuous combined HRT (CEE 0.625 mg + MPA 2.5 mg OD) in 16,608 women with an intact uterus
  - estrogen-alone (CEE 0.625 mg) in 10,739 women with a previous hysterectomy
- both arms of the trial were stopped early because of evidence of increased risk of breast cancer, stroke, PE, and CHD in the combined HRT arm, and increased risk of stroke with no CHD benefits in the estrogen-alone arm
- the apparent increase in CHD was in disagreement with results of previous observational trial
- results of the WHI study have since been challenged and revision of how CHD was diagnosed led to loss of statistical significance of the results
- benefits and risks reported as number of cases per 10,000 women each year

Table 19. HRT Benefits vs. Risks

Benefits	Risks
Vasomotor Symptoms: less frequent and severe with use of either combined or estrogen alone HRT	**Stroke**: 8 additional cases with combined HRT and 12 additional cases for estrogen alone (WHI)
Osteoporosis: 5 fewer cases of hip fractures and 47 fewer cases of all fractures with combined HRT; 6 fewer cases of hip fractures with estrogen alone	**DVT/PE**: 18 additional cases with combined HRT and 9 additional cases for estrogen-alone (WHI)
Colon Cancer: 6 fewer cases with combined HRT (WHI); one additional case with estrogen alone	**CHD**: 7 additional MIs with combined HRT (WHI); secondary analysis suggests greater absolute risk for women aged >70 yr and for women who start HRT >10 yr post-menopause
	Breast Cancer: 8 additional cases with combined HRT (WHI); risk only increased after >5 yr of combined HRT use; no increased risk for estrogen alone
	Dementia and Mild Cognitive Impairment: 50% greater risk of developing dementia in women taking estrogen alone after age 65; risk is greater for women taking combined HRT; risk of developing dementia was reduced for women taking HRT before age 65

Long-Term Hormone Therapy for Perimenopausal and Postmenopausal Women
Cochrane DB Syst Rev 2012;7:CD004143
Purpose: To determine the effect of long-term HRT on mortality, cardiovascular outcomes, cancer, gallbladder disease, fractures, cognition, and QOL in perimenopausal and postmenopausal women, during HRT use, and after cessation of HRT.
Results: 23 studies with 42,380 women included. 70% of the data from the WHI (1998) and HERS (1998). None of the studies focused on perimenopausal women. Combined continuous HRT: increased risk of coronary event after 1 yr (absolute risk 18/1000, 95% CI 3-7), venous thromboembolism after 1 yr (AR 7/1000, 95% CI 4-11), stroke after 3 yr (AR 18/1000, 95% CI 14-23), breast cancer after 5.6 yr (AR 23/1000, 95% CI 19-29), gallbladder disease after 5.6 yr (AR 27/1000, 95% CI 21-34), and death from lung cancer after 5.6 yr use (AR 9/1000, 95% CI 6-13). Estrogen only HRT: increased risk of venous thromboembolism after 1-2 yr use (AR 5/1000, 95% CI 2-10; after 7 yr AR 21/1000, 95% CI 16-28), stroke after 7 yr (AR 32/1000, 95% CI 25-40), and gallbladder disease after 7 yr use (AR 45/1000, 95% CI 36-57) and did not significantly affect the risk of breast cancer. Women >65 yr of age taking combined HRT had a statistically significant increase in the incidence of dementia after 4 yr use (AR 18/1000, 95% CI 11-30). Women taking HRT had a decreased risk of fractures with combined HRT after 5.6 yr (AR 86/1000, 95% CI 79-84) and 7.1 yr of estrogen only HRT (AR 102/1000, 95% CI 91-112).
Conclusions: HRT is not indicated for primary or secondary prevention of cardiovascular disease or dementia. Although HRT is considered effective for the prevention of postmenopausal osteoporosis, it is generally recommended as an option only for women at significant risk, for whom non-estrogen therapies are unsuitable.

Urogynecology

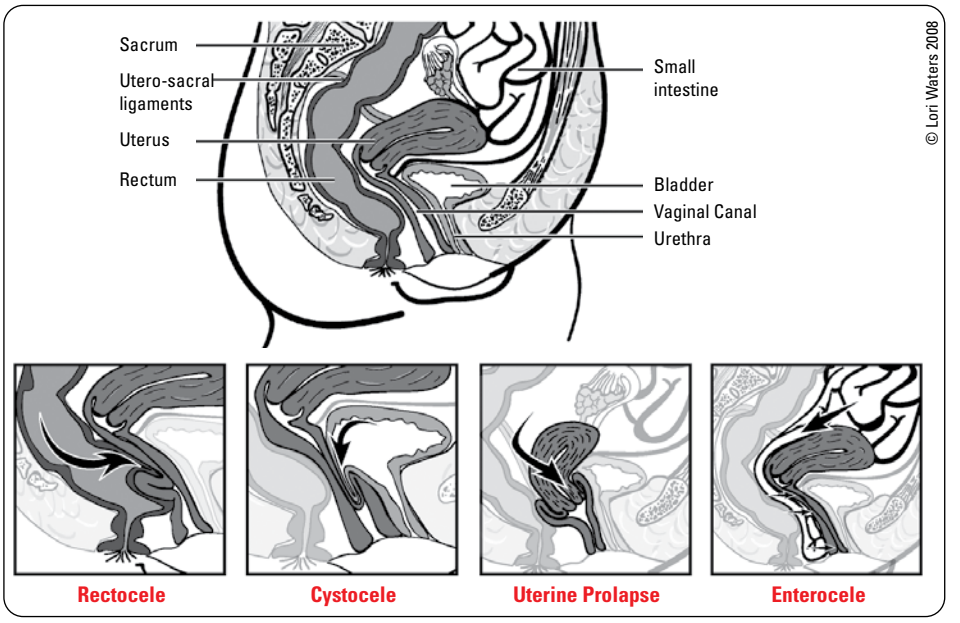


Figure 19. Pelvic anatomy

Prolapse

Etiology

- relaxation, weakness, or defect in the cardinal and uterosacral ligaments which normally maintain the uterus in an anteflexed position and prevent it from descending through the urogenital diaphragm (i.e. levator ani muscles)
- related to:
  - vaginal childbirth
  - aging
  - decreased estrogen (post-menopause)
  - following pelvic surgery
  - increased intra-abdominal pressure (obesity, chronic cough, constipation, ascites, heavy lifting)
  - congenital (rarely)
  - ethnicity (Caucasian women > Asian or African women)
  - collagen disorders

GENERAL CONSERVATIVE TREATMENT

(for pelvic relaxation/prolapse and urinary incontinence)

- Kegel exercises
- local vaginal estrogen therapy
- vaginal pessary (intravaginal suspension disc)

Grading of Pelvic Organ Prolapse

- 0 = no descent during straining
- 1 = distal portion of prolapse >1 cm above level of hymen
- 2 = distal portion of prolapse ≤1 cm above or below level of hymen
- 3 = distal portion of prolapse >1 cm below level of hymen but without complete vaginal eversion
- 4 = complete eversion of total length of lower genital tract
- Procidentia: failure of genital supports and complete protrusion of uterus through the vagina

Pelvic Relaxation/Prolapse

Protrusion of pelvic organs into or out of the vagina

Table 20. Pelvic Prolapse

Type	Clinical Features	Treatment
Cystocele (protrusion of bladder into the anterior vaginal wall)	Frequency, urgency, nocturia Stress incontinence Incomplete bladder emptying ± associated increased incidence of UTIs (may lead to renal impairment)	See above Anterior colporrhaphy ("anterior repair") Consider additional/alternative surgical procedure if documented urinary stress incontinence
Enterocele (prolapse of small bowel in upper posterior vaginal wall)		Similar to hernia repair Contents reduced, neck of peritoneal sac ligated, uterosacral ligaments, and levator ani muscles approximated
Rectocele (protrusion of rectum into posterior vaginal wall)	Straining/digitation to evacuate stool Constipation	See above Also laxatives and stool softeners Posterior colporrhaphy ("posterior repair"), plication of endopelvic fascia and perineal muscles approximated in midline to support rectum and perineum (can result in dyspareunia)
Uterine Prolapse (protrusion of cervix and uterus into vagina)	Groin/back pain (stretching of uterosacral ligaments) Feeling of heaviness/pressure in the pelvis Worse with standing, lifting Worse at the end of the day Relieved by lying down Ulceration/bleeding (particularly if hypoestrogenic) ± urinary incontinence	See above Vaginal hysterectomy ± surgical prevention of vault prolapse Consider additional surgical procedures if urinary incontinence, cystocele, rectocele, and/or enterocele are present
Vault Prolapse (protrusion of apex of vaginal vault into vagina, post-hysterectomy)		See above Sacralcolpopexy (vaginal vault suspension), sacrospinous fixation, or uterosacral ligament suspension

The only **true** hernia of the pelvis is an ENTEROCELE because peritoneum herniates with the small bowel

Urinary Incontinence

• see Urology, U6

STRESS INCONTINENCE

Definition
• involuntary loss of urine with increased intra-abdominal pressure (cough, laugh, sneeze, walk, run)

RISK FACTORS FOR STRESS INCONTINENCE IN WOMEN
• age
• obesity
• parity
• vaginal delivery
• pelvic prolapse
• pelvic surgery
• hypoestrogenic state (post-menopause)
• smoking
• neurological/pulmonary disease

Treatment
• see *Prolapse*, GY36
• surgical
  ▪ tension-free vaginal tape (TVT), tension-free obturator tape (TOT), prosthetic/fascial slings or retropubic bladder suspension (Burch or Marshall-Marchetti-Krantz procedures)

URGE INCONTINENCE

Definition
• urine loss associated with an abrupt, sudden urge to void
• "overactive bladder"
• diagnosed based on symptoms

Urge Incontinence
Urine loss associated with an abrupt, sudden urge to void

Etiology
• idiopathic (90%)
• detrusor muscle overactivity ("detrusor instability")

Associated Symptoms
• frequency, urgency, nocturia, leakage

Rule Out Neurological Causes of Urge Incontinence
• MS
• Herniated disc
• DM

Treatment
• behaviour modification (reduce caffeine/liquid, smoking cessation, regular voiding schedule)
• Kegel exercises
• medications
  ▪ anticholinergics: oxybutinin (Ditropan®), tolterodine (Detrol®), solifenacin (VESIcare®)
  ▪ tricyclic antidepressants: imipramine

Gynecological Oncology

Pelvic Mass

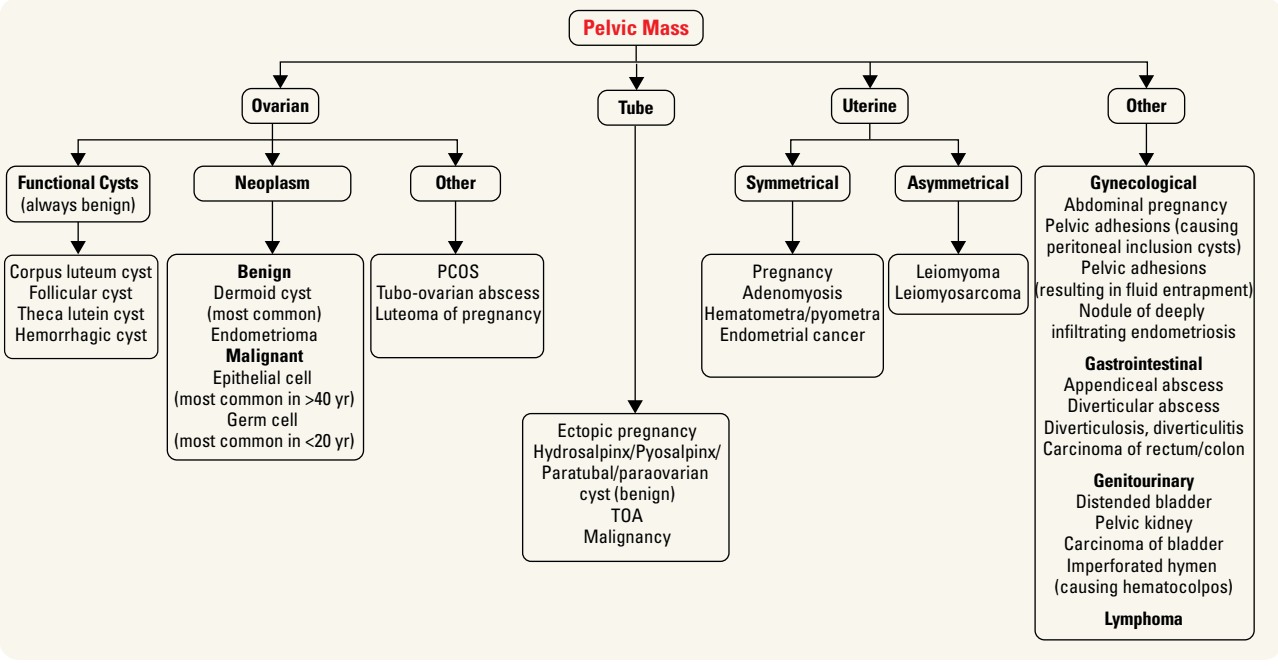


Figure 20. Differential diagnosis of pelvic mass

Uterus

ENDOMETRIAL CARCINOMA

Epidemiology

- most common gynecological malignancy in North America (40%); 4th most common cancer in women
- 2-3% of women develop endometrial carcinoma during lifetime
- mean age is 60 yr
- majority are diagnosed in early stage due to detection of symptoms
- 85-90% 5 yr survival for stage I disease
- 70-80% 5 yr survival for all stages

Table 21. Features of Type I and Type II Endometrial Cancer

	Type I	Type II
Description (Both types related to estrogen, but Type II to a lesser degree)	Characterized as estrogen-related (i.e. excess/unopposed estrogen): Endometrioid Includes well-differentiated endometrioid adenocarcinoma	Characterized as non-estrogen related: Non-endometrioid Includes serous, clear cell, grade 4 endometrioid and undifferentiated carcinomas, as well as carcinosarcoma More aggressive histologic subtypes; prognosis typically worse than type I, with a poorer 5 yr survival
Risk Factors (Increasing age and family history are risk factors for both types)	PCOS Diabetes mellitus Unbalanced HRT (balanced HRT is protective) Nulliparity Late menopause (>55 yr), early menarche Estrogen-producing ovarian tumours (e.g. granulosa cell tumours) HNPCC (hereditary non-polyposis colorectal cancer)/Lynch II syndrome Tamoxifen	Parous women Increasing age of menarche and number of children not significantly associated with reduced risk in clear-cell endometrial carcinoma Has been associated with p53 mutations
Clinical Features	~80% of cases Postmenopausal bleeding in majority Abnormal uterine bleeding in majority of affected pre-menopausal women (menorrhagia, intermenstrual bleeding)	~15% of cases Post-menstrual bleeding Abnormal uterine bleeding

Incidence of Malignant Gynecological Lesions in North America
endometrium > ovary > cervix > vulva > vagina > fallopian tube

Risk Factors for Endometrial Cancer

COLD NUT
Cancer (ovarian, breast, colon)
Obesity
Late menopause
Diabetes mellitus
Nulliparity
Unopposed estrogen: PCOS, anovulation, HRT
Tamoxifen: chronic use

Postmenopausal bleeding = endometrial cancer until proven otherwise (95% present with vaginal bleeding)

An endometrial thickness of 5 mm or more is considered abnormal in a postmenopausal woman with vaginal bleeding

Screening
- no known benefit for mass screening
- annual endometrial sampling starting at age 30-35 only for women at high risk (HNPCC [Hereditary Non-Polyposis Colorectal Cancer]/ Lynch II syndrome)
- routine pelvic ultrasound should not be used as screening test (high false positives)

Investigations
- endometrial sampling
  - office endometrial biopsy
  - D&C ± hysteroscopy
- ± pelvic ultrasound (in women where adequate endometrial sampling not feasible without invasive methods)
  - not acceptable as alternative to pelvic exam or endometrial sampling to rule out cancer

Table 22. FIGO Staging of Endometrial Cancer (2009)

Stage	Description	Stage	Description
I	Confined to corpus uteri including endocervical glandular involvement	**IIIC**	Metastasis to pelvic ± para-aortic LNs
IA	No or less than half myometrial invasion	**IIIC1**	Positive pelvic LN
IB	Invades through ≥½ of myometrium	**IIIC2**	Positive para-aortic LN ± positive pelvic LNs
II	Tumour invades cervical stroma, but does not extend beyond uterus*	IV	Invasion of bladder ± bowel mucosa ± distant metastases (note: omental disease is stage IV)
III	Tumour involving serosa, adnexa, vagina, or parametrium	**IVA**	Invasion of bladder ± bowel mucosa
IIIA	Invasion of serosa ± adnexae	**IVB**	Distant mets, including intra-abdominal and intraperitoneal mets ± inguinal LNs
IIIB	Vaginal ± parametrial involvement		

FIGO: International Federation of Gynecology and Obstetrics *Note: endocervical glandular involvement is now considered as Stage I (previously Stage II)

Treatment
- surgical: hysterectomy/bilateral salpingo-oophorectomy (BSO) and pelvic washings ± pelvic and para-aortic node dissection ± omentectomy
  - goals: diagnosis, staging, treatment, defining optimal adjuvant treatment
  - laparoscopic approach associated with improved quality of life (optimal for most patients)
- adjuvant radiotherapy (for improved local control in patients at risk for local recurrence) and adjuvant chemotherapy (in patients at risk for distant recurrence or with metastatic disease): based on presence of poor prognostic factors in definitive pathology
- chemotherapy: often used for recurrent disease (if high grade or aggressive histology)
- hormonal therapy: progestins can be used for recurrent disease (especially if low-grade)

Prognostic Factors
Most important is FIGO stage
Other Prognostic Factors:
- Age
- Grade
- Histologic subtype
- Depth of myometrial invasion
- Presence of lymphovascular space involvement (LVSI)

Complications of Therapy

Surgical Complications
- Surgical site infection
- Lymphedema

Radiation Complications
- Radiation fibrosis
- Cystitis
- Proctois

Uterine Sarcoma – Symptoms
BAD-P
Bleeding
Abdominal distention
Foul-smelling vaginal **D**ischarge
Pelvic pressure

A rapidly enlarging uterus, especially in a postmenopausal woman, should prompt consideration of leiomyosarcoma. Nevertheless, all postmenopausal patients with an enlarging uterus should have an endometrial biopsy

UTERINE SARCOMA
- rare; 3-9% of all uterine malignancies
- arise from stromal components (endometrial stroma, mesenchymal or myometrial tissues)
- behave more aggressively and are associated with worse prognosis than endometrial carcinoma; 5 yr survival is 35%
- vaginal bleeding is most common presenting symptom

Table 23. Summary of Uterine Sarcoma Subtypes and Features

Type	Epidemiology	Features	Diagnosis	Treatment
PURE TYPE				
1. Leiomyosarcoma	Most common type of uterine sarcoma Average age of presentation is 55 yr, but may present in pre-menopausal women Often coexists with benign leiomyomata (fibroids)	Histologic distinction from leiomyoma 1. Increased mitotic count (>10 mitoses/10 high-power fields) 2. Tumour necrosis 3. Cellular atypia Rapidly enlarging fibroids in a pre-menopausal woman Enlarging fibroids in a postmenopausal woman	Often post-operatively after uterus removed for presumed fibroids Stage using FIGO 2009 staging for leiomyosarcomas and ECC	Hysterectomy/BSO usually No routine pelvic lymphadenectomy Chemotherapy is used in cases of metastatic disease Radiation therapy does not improve local control or survival Poor outcomes overall, even for early-stage disease
2. Endometrial Stromal Sarcoma (ESS)	Usually presents in perimenopausal or postmenopausal women with abnormal uterine bleeding	Abnormal uterine bleeding Good prognosis	Diagnosed by histology of endometrial biopsy or D&C Stage using FIGO 2009 staging for leiomyosarcomas and ECC	Hysterectomy & BSO (remove ovaries as ovarian hormones may stimulate growth) No routine pelvic lymphadenectomy Adjuvant therapy based on stage and histologic features (hormones and/or radiation) Hormonal therapy (progestins) may be used for metastatic disease
3. Undifferentiated Sarcoma	Rare; less common than leiomyosarcoma, endometrial stromal sarcoma	Severe nuclear pleomorphism, high mitotic activity, tumour cell necrosis, and lack smooth muscle or endometrial stromal differentiation Poor prognosis	Often found incidentally post-operatively for abnormal bleeding	Treatment primarily surgical Radiation and/or chemotherapy for advanced diseased or unresectable disease
MIXED TYPE				
4. Adenosarcoma	The rarest of the uterine sarcoma Mixed tumour of low malignancy potential	Present with abnormal vaginal bleeding Polypoid mass in uterine cavity	Mixture of benign epithelium with malignant low-grade sarcoma Often found incidentally at time of hysterectomy for PMB Stage using FIGO 2009 staging for adenosarcoma	Treatment is surgical with hysterectomy and BSO

Table 24. FIGO Staging of Uterine Sarcoma (2009)

Stage	Description	Stage	Description
I	**Tumour limited to uterus**	**III**	
IA	<5 cm	IIIA	Tumour invades abdominal tissues, one site
IB	>5 cm	IIIB	Metastasis to pelvic and/or para-aortic lymph nodes
		IIIC	Tumour invades bladder and/or rectum
II	**Tumour extends beyond uterus**	**IV**	
IIA	To the pelvis, adnexal involvement	IVA	Tumour invades bladder and/or rectum
IIB	To extra-uterine pelvic tissue	IVB	Distant metastasis

Ovary

BENIGN OVARIAN TUMOURS

- see Table 25
- many are asymptomatic
- usually enlarge slowly, if at all
- may rupture or undergo torsion, causing pain
  - pain associated with torsion of an adnexal mass usually originates in the iliac fossa and radiates to the flank
- peritoneal irritation may result from an infarcted tumour (rare)

MALIGNANT OVARIAN TUMOURS

- see Table 25

Epidemiology

- lifetime risk 1.4%
- in women >50 yr, more than 50% of ovarian tumours are malignant
- causes more deaths in North America than all other gynecologic malignancies combined
- 4th leading cause of cancer death in women
- 85% epithelial; 15% non-epithelial
- 10-15% of epithelial ovarian cancers are related to hereditary predisposition

Risk Factors (for epithelial ovarian cancers)

- early menarche and/or late menopause
- personal history of breast, colon, endometrial cancer
- family history of breast, colon, endometrial, ovarian cancer
- Lynch syndrome and BRCA mutations
- use of fertility drugs

Protective Factors (for epithelial ovarian cancers)

- OCP: likely due to ovulation suppression (significant reduction in risk even after 1 yr of use)
- pregnancy/breastfeeding

Prophylactic Measures

- salpingectomy (prophylactic)
- BSO (prophylactic hysterectomy or tubal ligation performed for this reason in high-risk women [i.e. BRCA mutation carriers])

Screening

- no effective method of mass screening
- routine CA-125 level measurements or U/S not recommended
  - high false positive rates
- controversial in high-risk groups: transvaginal U/S and CA-125, starting age 30 (no consensus on interval)
  - familial ovarian cancer (>1 first degree relative affected, BRCA-1 mutation)
  - other cancers (e.g. endometrial, breast, colon)
  - BRCA-1 or BRCA-2 mutation: recommendation is prophylactic bilateral oophorectomy after age 35 or when childbearing is completed

Clinical Features

- most women with epithelial ovarian cancer present with advanced stage disease as patients often asymptomatic until disseminated (symptoms with early-stage disease are vague and non-specific)
- when present, symptoms may include:
  - abdominal symptoms (nausea, bloating, pain, dyspepsia, anorexia, early satiety)
  - symptoms of mass effect
    - increased abdominal girth (from ascites or tumour itself)
    - urinary urgency and frequency
    - constipation

Ovaries are like GEMS
Germ-cell
Epithelial
Metastatic
Sex cord stromal

Most (70%) epithelial ovarian cancers present at stage III disease

Ovarian Tumour Markers
- Epithelial cell: CA-125
- Stromal
- Granulosa cell: inhibin
- Sertoli-Leydig: androgens
- Germ cell
- Dysgerminoma: LDH
- Yolk sac: AFP
- Choriocarcinoma: β-hCG
- Immature teratoma: none
- Embryonal cell: AFP + β-hCG

Diagnosis of ovarian tumours requires surgical pathology

Any adnexal mass in postmenopausal women should be considered malignant until proven otherwise

Omental Cake: a term for ascites plus a fixed upper abdominal and pelvic mass; almost always signifies ovarian cancer

Malignant Ovarian Tumour Prognosis
5 Year Survival

Stage I	75-95%
Stage II	60-75%
Stage III	23-41%
Stage IV	11%

Screening for Ovarian Cancer Updated Evidence Report and Systematic Review for the US Preventive Services Task Force
JAMA 2018; 319(6):595-606
Objective: To systematically review evidence on benefits and harms of ovarian cancer screening among average-risk, asymptomatic women.
Methods: Systematic review of RCTs of ovarian cancer screening in average-risk women that reported mortality or quality-of-life outcomes. Interventions included transvaginal ultrasound and/or CA-125 testing. Comparators were usual care or no screening.
Results: Four trials (N = 293 587) were included. No trial found a significant difference in ovarian cancer mortality with screening. In 2 trials, screening led to surgery for suspected ovarian cancer in 1% of women without cancer and in 3% for transvaginal ultrasound with or without CA-125 screening, with major complications occurring in 3% to 15% of surgeries. Evidence of psychological harms was found in cases of repeat follow-up scans and tests.
Conclusions: Ovarian cancer mortality did not significantly differ between screened women and those with no screening or in usual care.

Low Malignant Potential (also called "Borderline") Tumours

- a subcategory of epithelial ovarian cancer (~15% of all epithelial ovarian tumours)
- pregnancy, OCP, and breastfeeding are protective factors
- tumour cells with histologically malignant characteristics arise from the ovarian surface, but do not invade ovarian stroma
- able to metastasize, but not commonly
- treated primarily with surgery (BSO/omental biopsy ± hysterectomy)
  - chemotherapy has limited benefit: can be treated with hormonal manipulation (letrozole)
- generally slow growing, excellent prognosis
  - 5 yr survival >99%
  - recurrences tend to occur late, may be associated with low-grade serous carcinoma

Table 25. Ovarian Tumours

Type	Description	Presentation	Ultrasound/Cytology	Treatment
FUNCTIONAL TUMOURS (all benign)				
Follicular Cyst	Follicle fails to rupture during ovulation	Usually asymptomatic May rupture, bleed, tort, infarct causing pain ± signs of peritoneal irritation	4-8 cm mass, unilocular, lined with granulosa cells	Symptomatic or suspicious masses warrant surgical exploration Otherwise if <6 cm, wait 6 wk then re-examine as cyst usually regresses with next cycle OCP (ovarian suppression): will prevent development of new cysts Treatment usually laparoscopic (cystectomy vs. oophorectomy, based on fertility choice)
Corpus Luteum Cyst	Corpus luteum fails to regress after 14 d, becoming cystic or hemorrhagic	More likely to cause pain than follicular cyst May delay onset of next period	Larger (10-15 cm) and firmer than follicular cysts	Same as for follicular cysts
Theca-Lutein Cyst	Due to atretic follicles stimulated by abnormal β-hCG levels	Associated with molar pregnancy, ovulation induction with clomiphene		Conservative Cyst will regress as β-hCG levels fall
Endometrioma	See *Endometriosis*, GY11			
Polycystic Ovaries	See *Polycystic Ovarian Syndrome*, GY23			
BENIGN GERM-CELL TUMOURS				
Benign Cystic Teratoma (dermoid)	Single most common ovarian germ cell neoplasm Elements of all 3 cell lines; contains dermal appendages (sweat and sebaceous glands, hair follicles, teeth)	May rupture, twist, infarct 20% bilateral 20% occur outside of reproductive yr	Smooth-walled, mobile, unilocular Ultrasound may show calcification which is pathognomonic	Treatment usually laparoscopic cystectomy; may recur
MALIGNANT GERM-CELL TUMOURS				
General Information	Rapidly growing, 2-3% of all ovarian cancers	Usually children and young women (<30 yr)		Surgical resection (often conservative unilateral salpingo-oophorectomy ± nodes) ± chemotherapy
Dysgerminoma	Produces LDH	10% bilateral		When diagnosed at stage IA, no adjuvant treatment is indicated If diagnosed at advanced stage, very responsive to chemotherapy, therefore complete resection is not necessary for cure
Immature Teratoma	No tumour marker identified	Almost always unilateral		When diagnosed at stage IA Grade 1, no adjuvant treatment is indicated When diagnosed at Grade 2-3, either adjuvant chemotherapy or surgical staging If diagnosed at advanced stage, very responsive to chemotherapy, therefore complete resection is not necessary for cure
Yolk Sac Tumour	Produces AFP	Abdominal pain and pelvic mass		When diagnosed at stage IA Grade 1, no adjuvant treatment is indicated If diagnosed at advanced stage, very responsive to chemotherapy, therefore complete resection is not necessary for cure
Ovarian Choriocarcinoma	Produces hCG	Precocious puberty and irregular vaginal bleeding		When diagnosed at stage IA Grade 1, no adjuvant treatment is indicated If diagnosed at advanced stage, very responsive to chemotherapy, therefore complete resection is not necessary for cure
EPITHELIAL OVARIAN TUMOURS (malignant or borderline)				
General Information	Derived from mesothelial cells lining peritoneal cavity Classified based on histologic type 80-85% of all ovarian neoplasms (includes malignant)		Varies depending on subtype	**Borderline** Cystectomy vs. unilateral salpingo-oophorectomy **Malignant** 1. Early stage (stage I): Hysterectomy/BSO/staging (omentectomy, peritoneal biopsies, washings, pelvic and para-aortic lymphadenectomy) 2. Advanced stage: Upfront cytoreductive (debulking) followed by adjuvant chemotherapy consisting of IV carboplatic/paclitaxel vs. intraperitoneal chemotherapy (stage III) neoadjuvant chemotherapy with IV carboplatin/paclitaxel, followed by delayed debulking with further adjuvant IV chemotherapy
Serous	Most common ovarian tumour 50% of all ovarian cancers 75% of epithelial tumours 70% benign	20-30% bilateral	Lining similar to fallopian tube epithelium Often multilocular Histologically contain Psamomma bodies (calcified concentric concretions)	

Table 25. Ovarian Tumours (continued)

Type	Description	Presentation	Ultrasound/Cytology	Treatment
EPITHELIAL OVARIAN TUMOURS (malignant or borderline)				
Mucinous	20% of epithelial tumours	Rarely complicated by Pseudomyxoma peritoneii: implants seed abdominal cavity and produce large quantities of mucin	Resembles endocervical epithelium Often multilocular May reach enormous size	Poor response to chemotherapy If mucinous, remove appendix as well to rule out possible source of primary disease
SEX CORD STROMAL OVARIAN TUMOURS				
General Information				Surgical resection of tumour Chemotherapy may be used for unresectable metastatic disease
Fibroma/Thecoma (benign)	From mature fibroblasts in ovarian stroma	Non-functioning Occasionally associated with Meig's syndrome (benign ovarian tumour and ascites and pleural effusion)	Firm, smooth rounded tumour with interlacing fibrocytes	
Granulosa-Theca Cell Tumours (benign or malignant)	Can be associated with endometrial cancer Inhibin is tumour marker	Estrogen-producing: feminizing effects (precocious puberty, menorrhagia, postmenopausal bleeding)	Histologic hallmark of cancer is small groups of cells known as Call-Exner bodies	
Sertoli-Leydig Cell Tumour (benign or malignant)	Can measure elevated androgens as tumour markers	Androgen-producing: virilizing effects (hirsutism, deep voice, recession of front hairline)		
METASTATIC OVARIAN TUMOURS				
From GI Tract, Breast, Endometrium, Lymphoma	4-8% of ovarian malignancies Krukenberg tumour – metastatic ovarian tumour (usually GI tract, commonly stomach or colon, breast) with "signet-ring" cells			

Investigation of Suspicious Ovarian Mass

- women with suspected ovarian cancer based on history, physical, or investigations should be referred to a gynecologic oncologist
  - bimanual examination
    - solid, irregular, or fixed pelvic mass is suggestive of ovarian cancer
  - RMI (Risk of Malignancy Index) is best tool available to assess likelihood of ovarian malignancy and need for pre-operative gynecologic oncology referral (see sidebar)
- physical exam findings largely dependent on stage of disease
- blood work: CA-125 for baseline, CBC, liver function tests, electrolytes, creatinine
- radiology
  - transvaginal ultrasound best to visualize ovaries
  - CT abdomen and pelvis to look for metastatic disease
  - bone scan or PET scan not indicated
- try to rule out other primary source if suspected, based on:
  - occult blood per rectum: endoscopy ± barium enema
  - gastric symptoms: gastroscopy ± upper GI series
  - abnormal vaginal bleeding: endometrial biopsy to rule out concurrent endometrial cancer; abnormal cervix: need to biopsy cervix (not Pap smear); breast lesion identified or risk factors present: mammogram

A Risk of Malignancy Incorporating CA-125, Ultrasound, and Menopausal Status for the Accurate Pre-Operative Diagnosis of Ovarian Cancer
BJOG 1990;97:922-29
RMI = U x M x CA-125
Ultrasound Findings (1 pt for each)
- Multilocular cyst
- Evidence of solid areas
- Evidence of metastases
- Presence of ascites
- Bilateral lesions

U = 1 (for U/S scores of 0 or 1)
U = 4 (for U/S scores of 2-5)
Menopausal Status
- Postmenopausal: M = 4
- Premenopausal: M = 1

Absolute Value of CA-125 Serum Level
- For RMI>200: gynecologic oncology referral is recommended

Table 26. FIGO Staging for Primary Carcinoma of the Ovary (Surgical Staging) (2014)

Stage	Description
I	**Growth limited to the ovaries**
IA	1 ovary, no ascites, no tumour on external surface, capsule intact, negative washings
IB	2 ovaries, no ascites, no tumour on external surface, capsule intact
IC	1 or 2 ovaries with any of the following: surgical spill (IC1), capsule ruptured (IC2), tumour on ovarian surface (IC2), or malignant cells in ascites (IC3)
II	**Growth involving one or both ovaries with pelvic extension or primary peritoneal cancer**
IIA	Extension ± implants to uterus/tubes
IIB	Extension to other pelvic structures
III	**Tumour involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal nodes**
IIIA	Positive retroperitoneal LNs and/or microscopic metastasis beyond pelvis
IIIA1	Positive retroperitoneal LNs
IIIA2	Microscopic, extrapelvic peritoneal involvement ± positive retroperitoneal LNs
IIIB	Macroscopic peritoneal metastasis beyond pelvis ≤2 cm, ± positive retroperitoneal LNs. Includes extension to capsule of liver/spleen
IIIC	Same as above but peritoneal metastasis >2 cm
IV	**Distant metastasis beyond peritoneal cavity**
IVA	Pleural effusion with positive cytology
IVB	Hepatic and/or splenic parenchymal metastasis or metastasis to extra-abdominal organs (inguinal LNs and LNs outside of abdominal cavity included)

FIGO = International Federation of Gynecology and Obstetrics

Fallopian Tube

- least common site for carcinoma of female reproductive system (0.3%)
- usually serous epithelial carcinoma
- new evidence shows that some serous ovarian cancers originate in the fallopian tube
- more common in fifth and sixth decade

Clinical Features
- classic triad present in minority of cases, but very specific
  - watery discharge (most specific): "hydrops tubae profluens"
  - vaginal bleeding or discharge in 50% of patients
  - crampy lower abdominal/pelvic pain
  - most patients present with a pelvic mass (see *Ovarian Tumours*, GY41 for guidelines regarding diagnosis/investigation)

Treatment
- as for malignant epithelial ovarian tumours

Effectiveness, Safety, and Cost-Effectiveness of Primary Cytoreductive Surgery
Cochrane Database Syst *Rev* 2011;(8):CD007565
Summary: During primary surgery for stage III or IV epithelial ovarian cancer, all attempts should be made to achieve complete cytoreduction. When this is not achievable, optimal (<1cm) residual disease should be the goal.
Methods: Identified 11 retrospective studies consisting of 4735 women using comprehensive search strategy.
Results:
1. When suboptimal (margins >1cm) was compared with optimal (<1cm) cytoreduction, the survival estimates were reduced but remained statistically in favour of the lower volume disease group
2. No significant difference in overall survival between suboptimal and optimal cytoreduction
3. Borderline difference in progression-free survival when residual disease >2 cm and <2 cm were compared (p=0.05)

Cervix

BENIGN CERVICAL LESIONS
- Nabothian cyst/inclusion cyst: no treatment required
- endocervical polyps: treatment is polypectomy (office procedure)

MALIGNANT CERVICAL LESIONS

Epidemiology
- majority are SCC (95%); adenocarcinomas increasing (5%); rare subtypes include small cell, adenosquamous
- 8000 deaths annually in North America
- annual Pap test reduces a woman's chance of dying from cervical cancer from 0.4% to 0.05%
- average age at presentation: 52 yr old

Etiology
- at birth, vagina is lined with squamous epithelium; columnar epithelium lines only the endocervix and the central area of the ectocervix (original squamocolumnar junction)
- during puberty, estrogen stimulates eversion of a single columnar layer (ectopy), thus exposing it to the acidic pH of the vagina, leading to metaplasia (change of exposed epithelium from columnar to squamous)
  - a new squamocolumnar junction forms as a result
- the transformation zone (TZ) is the area located between the original and the current squamocolumnar junction
- the majority of dysplasias and cancers arise in the TZ of the cervix
- must have active metaplasia in presence of inducing agent (HPV) to get dysplasia
- dysplasia progresses to carcinoma in situ (CIS), which further progresses to invasion
- slow process (~10 yr on average)
- growth is by local extension
- metastasis occurs late

Risk Factors
- HPV infection
  - see *Sexually Transmitted Infections*, GY26
  - high risk of neoplasia associated with types 16, 18
  - low risk of neoplasia associated with types 6, 11
  - >99% of cervical cancers contain one of the high risk HPV types
- high-risk behaviours (risk factors for HPV infection)
  - multiple partners
  - other STIs (HSV, trichomonas)
  - early age at first intercourse
  - high-risk male partner
- smoking
- poor screening uptake is the most important risk factor for cervical cancer in Canada
- at-risk groups include:
  - immigrant Canadians
  - First Nations Canadians
  - geographically-isolated Canadians
  - sex-trade workers
  - low socioeconomic status Canadians

Cervical Cancer Screening Guidelines (Pap Test)
- see Family Medicine, FM5

Causes of Elevated CA-125
- Age influences reliability of test as a tumour marker
- 50% sensitivity in early-stage ovarian cancer (poor), therefore not good for screening

Malignant
- Gyne: ovary, uterus
- Non-Gyne: pancreas, stomach, colon, rectum

Non-Malignant
- Gyne: benign ovarian neoplasm, endometriosis, pregnancy, fibroids, PID
- Non-Gyne: cirrhosis, pancreatitis, renal failure

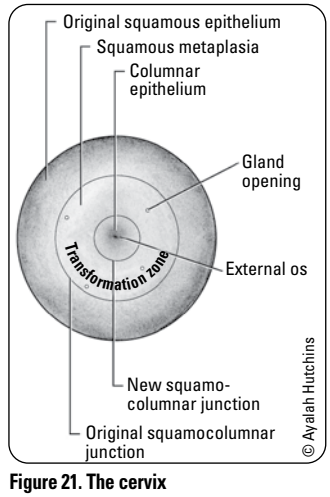


Figure 21. The cervix

Cervical cancer is most prevalent in developing countries and, therefore, is the only gynecologic cancer that uses clinical staging; this facilitates consistent international staging with countries that do not have technologies, such as CT and MRI

Clinical Features

- SCC: exophytic, fungating tumour
- adenocarcinoma: endophytic, with barrel-shaped cervix
- early
  - asymptomatic
  - discharge: initially watery, becoming brown or red
  - postcoital bleeding
- late
  - 80-90% present with bleeding: either postcoital, postmenopausal or irregular bleeding
  - pelvic or back pain (extension of tumour to pelvic walls)
  - bladder/bowel symptoms
- signs
  - friable, raised, reddened, or ulcerated area visible on cervix

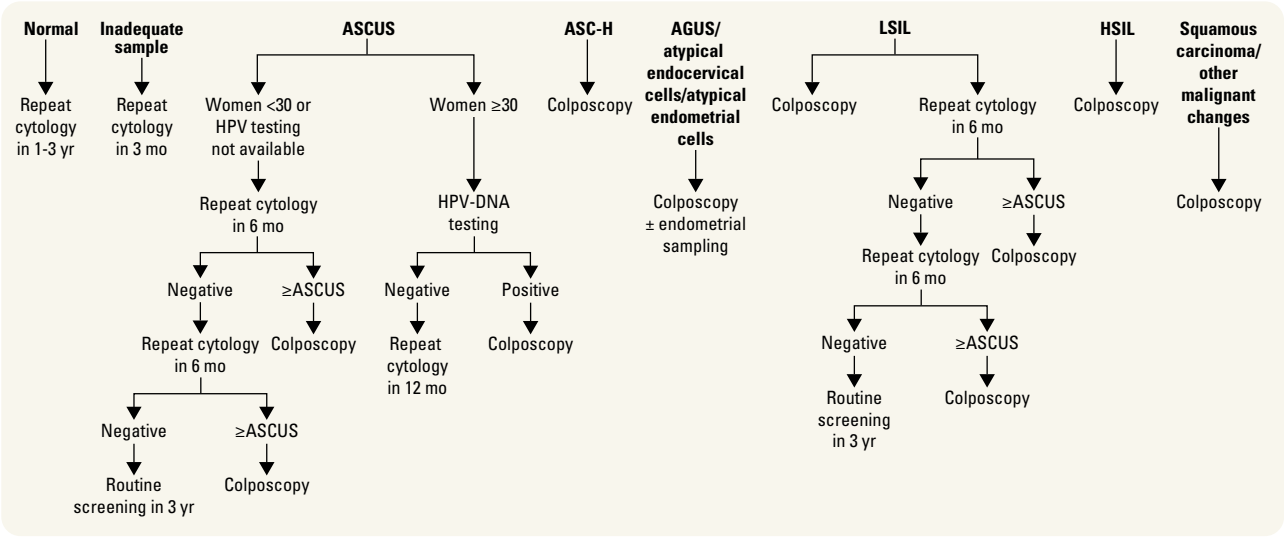


Figure 22. Decision making chart for Pap test (not applicable for adolescents)
Adapted from: Ontario Cervical Screening Practice Guidelines. May 2012. Cervical screening guidelines unique to each province

Diagnosis

- colposcopy is a clinical procedure that facilitates identification and biopsy of suspicious cells
- in colposcopy:
  - apply acetic acid and identify acetowhite lesions, punctation, mosaicism, and abnormal blood vessels to guide cervical biopsy
  - endocervical curettage (ECC) if entire lesion is not visible or no lesion visible
  - diagnostic excision (LEEP) if:
    - unsatisfactory colposcopy (poor visualization/access to transformation zone)
    - discrepancy between cytology, colposcopy, and histological findings
    - positive findings/glandular abnormalities in endocervical curettage
    - suspicious for adenocarcinoma in situ (consider cold-knife conization)
    - recurrence of lesion post-ablation or excision
    - inability to rule out invasive disease, i.e. large lesions (lesions extending into endocervical canal, extending widely on cervix, or onto vaginal epithelium)
- consider cold-knife conization (in OR) if glandular abnormality suspected based on cytology or colposcopic findings due to concern for margin interpretation
- tests permitted for FIGO clinical staging include: physical exam (including examination under anesthesia), cervical biopsy (including cone biopsy), proctoscopy/cystoscopy, intravenous pyelogram, ultrasound liver/kidneys, CXR, LFTs
- MRI and/or CT and/or PET scan often done to facilitate planning of radiation therapy, results do not influence clinical stage

The Bethesda Classification System is based on cytological results of a Pap test that permits the examination of cells but not tissue structure. Cervical intraepithelial neoplasia (CIN) or cervical carcinoma is a histological diagnosis, requiring a tissue sample via biopsy of suspicious lesions seen during colposcopy

With development of hypertension early in pregnancy (i.e. <20 wk), think gestational trophoblastic disease

CA-125 is indicated for monitoring response to treatment

Table 27. FIGO Staging Classification of Cervical Cancer (Clinical Staging) (2018)

Stage	Description
I	**Confined to cervix**
IA	Microinvasive (diagnosed only by microscopy)
IA1	Stromal invasion not >3 mm deep, not >7 mm wide
IA2	3-5 mm deep; not >7 mm wide
IB	Clinically visible lesion confined to cervix, or microscopic lesion >IA
IB1	Clinically visible lesion ≤4 mm in greatest dimension
IB2	Clinically visible lesion >4 mm in greatest dimension
II	**Beyond uterus but not to the pelvic wall or lower 1/3 of vagina**
IIA	No obvious parametrial involvement
IIA1	Clinically visible lesion ≤4 mm in greatest dimension
IIA2	Clinically visible lesion >4 mm in greatest dimension
IIB	Obvious parametrial involvement
III	**Extends to pelvic wall, and/or involves lower 1/3 of vagina and/or causes hydronephrosis or non-functioning kidney**
IIIA	Involves lower 1/3 vagina but no extension into pelvic side wall
IIIB	Extension into pelvic side wall and/or hydronephrosis or non-functioning kidney
IV	**Carcinoma has extended beyond true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum**
IVA	Spread of the growth to adjacent organs (bladder or rectum)
IVB	Distant metastases

Treatment: Prevention and Management

Prevention: HPV Vaccine

- two vaccines currently approved (Gardasil®, Cervarix®)

Table 28. Comparison of Two Vaccines against Human Papillomavirus (HPV)

	Gardasil®*	Cervarix®
Viral Strains Covered	6, 11, 16, 18	16, 18
Route of Administration	IM	IM
Schedule of Dosing	0, 2, 6 mo	0, 1, 6 mo
Side Effects	Local: redness, pain, swelling General: headache, low grade fever, GI upset	Local: redness, pain, swelling General: headache, low grade fever, GI upset
Approved Age	Females age 9-45, males age 9-26	Females age 10-25
Contraindications	Pregnant women and women who are nursing (limited data)	

*Gardasil-9 also covers types 31, 33, 45, 52, and 58; also used to prevent genital wards

- should be administered before onset of sexual activity (i.e. before exposure to virus) for optimal benefit of vaccination
- may be given at the same time as hepatitis B or other vaccines using a different injection site
- not for treatment of active infections
- most women will not be infected with all four types of the virus at the same time, therefore vaccine is still indicated for sexually active females or those with a history of previous HPV infection or HPV-related disease
- conception should be avoided until 30 d after last dose of vaccination

Causes of Elevated CA-125

- Age influences reliability of test as a tumour marker
- 50% sensitivity in early stage ovarian cancer (poor) – therefore not good for screening

Malignant

- Gyne: ovary, uterus
- Non-Gyne: pancreas, stomach, colon, rectum

Non-Malignant

- Gyne: benign ovarian neoplasm, endometriosis, pregnancy, fibroids, PID
- Non-Gyne: cirrhosis, pancreatitis, renal failure

Cervical Cancer Prognosis 5 yr Survival

Stage 0	99%
Stage I	75%
Stage II	55%
Stage III	30%
Stage IV	7%
Overall	50-60%

Efficacy of Human Papillomavirus (HPV)-16/18 AS04-Adjuvanted Vaccine Against Cervical Infection and Precancer Caused by Oncogenic HPV Types (PATRICIA): Final Analysis of a Double-Blind, Randomized Study in Young Women

Lancet 2009;374:301-14

Study: Phase III double-blind, controlled RCT.

Patients: 18,644 women aged 15-25.

Selected Outcomes: Development of HPV-16/18 associated CIN II+ was the primary outcome. Secondary to this were persistence of infections with HPV-16, HPV-18, or other oncogenic HPV types.

Selected Results: Efficacy against development of HPV-16/18 associated CIN II+ was 98.1% ($p<0.0001$). High levels of cross-protection were observed for persistent infection with HPV-31 and HPV-45 and HPV-31 or HPV-45 associated CIN II+.

Conclusions: The HPV-16/18 AS04-adjuvanted vaccine protected against HPV-16/18 associated CIN II+ lesions and lesions associated with HPV-31, HPV-33, and HPV-45.

Table 29. Management of Abnormal Cervical Histology and Cervical Cancer

	Management
CIN I	Preferred option for biopsy-proven CIN I is observation Repeat assessment and cytology in 12 mo Management according to cytology results If after HSIL or AGC: Cytology and histology should be reviewed If discrepancy remains, excisional biopsy may be considered
CIN II and CIN III	Women ≥25 yr CIN II or III should be treated Excisional procedures preferred for CIN III Those with positive margins should have follow-up with colposcopy and directed biopsies and/or endocervical curettage Women <25 yr Same treatment for CN II and CN III: observe with colposcopy at 6-mo intervals for up to 24 mo before treatment considered During pregnancy CIN II or III suspected or diagnosed during pregnancy: repeat colposcopy and treatment delayed until 8-12 wk after delivery
Stage IA1 (no LVSI)	LEEP if future fertility desired (and lesion ≤2 cm) Simple hysterectomy if future fertility is not desired
Stage IA2, IB1	Typically treated with radical hysterectomy and pelvic lymphadenectomy (sentinel nodes under study) If high chance of adjuvant radiation then consider primary chemoradiation as more morbidity occurs from double-modality treatment (surgery and radiation) Equal cure rates may be obtained with primary radiation therapy; advantage of surgery: may accurately stage and grade and more targeted adjuvant therapy Advantage is that ovaries can be spared if pre-menopausal For fertility preservation (if tumour <2 cm), may have radical trachelectomy (removal of cervix and parametria) and nodes instead of radical hysterectomy for early-stage disease Chemoradiation therapy if adverse high-risk prognostic factors on radical surgical specimen, such as: positive pelvic lymph nodes, positive parametria, and/or positive margins or adverse cervical factors (2 or more): deep stromal invasion, size >4 cm, LVSI
Stages IB2 (>4 cm), II, III, IV	Primary chemoradiation therapy CT assess extent of disease: evaluate pelvic and para-aortic nodes For positive nodes on PET: primary chemoradiation with extended field RT Hysterectomy generally not suggested following primary treatment with curative intent

Abnormal Pap Tests in Pregnancy

- incidence: 1/2200
- Pap test at all initial prenatal visits
  - if abnormal Pap or suspicious lesion, refer to colposcopy
  - if diagnostic conization required, should be deferred until second trimester (T2) to minimize risk of pregnancy loss
  - if invasive cancer ruled out, management of dysplasia deferred until completion of pregnancy (may deliver vaginally)
  - if invasive cancer present, management depends on prognostic factors, degree of fetal maturity, and patient wishes
    - general recommendations in T1: consider pregnancy termination, management with either radical surgery (hysterectomy vs. trachelectomy if desires future fertility), or concurrent chemoradiation therapy
    - recommendations in T2/T3: delay of therapy until viable fetus and C-sectionfor delivery with concurrent radical surgery or subsequent concurrent chemoradiation therapy

Vulva

BENIGN VULVAR LESIONS

Non-Neoplastic Disorders of Vulvar Epithelium

- biopsy is necessary to make diagnosis and/or rule out malignancy:

1) Hyperplastic dystrophy (squamous cell hyperplasia)
   - surface thickened and hyperkeratotic
   - pruritus most common symptom
   - typically postmenopausal women
   - treatment: 1% fluorinated corticosteroid ointment bid for 6 wk
2) Lichen sclerosis
   - subepithelial fat becomes diminished; labia become thin, atrophic, with membrane-like epithelium and labial fusion
   - pruritus, dyspareunia, burning
   - 'figure of 8' distribution
   - most common in postmenopausal women but can occur at any age
   - treatment: ultrapotent topical steroid 0.05% clobetasol x 2-4 wk then taper down, can consider long-term suppression twice a week
3) Mixed dystrophy (lichen sclerosis with epithelial hyperplasia)
   - hyperkeratotic areas with areas of thin, shiny epithelium
   - treatment: fluorinated corticosteroid ointment

Tumours
- papillary hidradenoma, nevus, fibroma, hemangioma

MALIGNANT VULVAR LESIONS

Epidemiology
- 5% of genital tract malignancies
- 90% SCC; remainder melanomas, basal cell carcinoma, Paget's disease, Bartholin's gland carcinoma
  - Type I disease: HPV-related (50-70%)
    - more likely in younger women
    - 90% of vulvar intraepithelial neoplasia (VIN) contain HPV DNA (usually types 16, 18)
  - Type II disease: not HPV-related, associated with current or previous vulvar dystrophy
    - usually postmenopausal women

Risk Factors
- HPV infection
- VIN: precancerous change which presents as multicentric white or pigmented plaques on vulva (may only be visible at colposcopy)
  - progression to cancer rarely occurs with appropriate management
  - treatment: local excision (i.e. superficial vulvectomy ± split thickness skin grafting to cover defects if required) vs. ablative therapy (i.e. laser, cauterization) vs. local immunotherapy (imiquimod)
- history of cervical cancer
- cigarette smoking
- immunodeficiency

Clinical Features
- many patients asymptomatic at diagnosis (many also deny or minimize symptoms)
- most lesions occur on the labia majora, followed by the labia minora (less commonly on the clitoris or perineum)
- localized pruritus or lesion most common
- less common: raised red, white or pigmented plaque, ulcer, bleeding, discharge, pain, dysuria
- patterns of spread
  - local
  - groin lymph nodes (usually inguinal, then spreading to pelvic nodes)
  - hematogenous

Investigations
- ± vulvar biopsy
- always biopsy any suspicious lesion
  - do not remove entire lesion (allows for site identification through sentinel LN injection if malignant)

Any suspicious lesion of the vulva should be biopsied

Prognosis
- depends on stage: particularly nodal involvement (single most important predictor followed by tumour size)
- lesions >4 cm associated with poorer prognosis
- overall 5 yr survival rate: 79%

Treatment
- T1 lesions (tumour confined to vulva; no extension to adjacent perineal structures): radical local excision
- T2 lesions (tumour of any size with extension to adjacent perineal structures): modified radical vulvectomy
- T3 lesions (extension to any of: proximal 2/3 of urethra, proximal 2/3 of the vagina, bladder mucosa, rectal mucosa, or fixed to pelvic bone): chemoradiation followed by selective resection of residual primary
- node positive disease: adjuvant chemoradiation or radiation therapy

Vagina

BENIGN VAGINAL LESIONS

- inclusion cysts
  - cysts form at site of abnormal healing of laceration (e.g. episiotomy)
  - no treatment required
- endometriosis
  - dark lesions that tend to bleed at time of menses
  - treatment: excision
- Gartner's duct cysts
  - remnants of Wolffian duct, seen along side of cervix
  - treatment: conservative unless symptomatic
- urethral diverticulum
  - can lead to recurrent urethral infection, dyspareunia
  - treatment: surgical correction if symptomatic

MALIGNANT VAGINAL LESIONS

Epidemiology

- primary carcinomas of the vagina represent 2-3% of malignant neoplasms of the female genital tract
- 80-90% are SCC
- more than 50% diagnosed between 70-90 yr old

Risk Factors

- associated with HPV infection (analogous to cervical cancer)
- increased incidence in patients with prior history of cervical and vulvar cancer

Investigations

- cytology
  - significant false negative rate for existing malignancy (i.e. if gross lesion present, biopsy)
- colposcopy
- Schiller test (normal squamous epithelium takes up Lugol's iodine)
- biopsy, partial vaginectomy (wide local excision for diagnosis)
- rule out disease on cervix, vulva, or anus (most vaginal cancers are metastatic from one of these sites)
- staging

Clinical Features

Table 30. Clinical Features of Malignant Vaginal Lesions

Type	Clinical Features
Vaginal Intra-Epithelial Neoplasia (VAIN)	Grades: analogous to cervical dysplasia
Squamous Cell Carcinoma (SCC)	Most common site is upper 1/3 of posterior wall of vagina Asymptomatic Painless discharge and bleeding Vaginal discharge (often foul-smelling) Vaginal bleeding especially during/post-coitus Urinary and/or rectal symptom 2° to compression
Adenocarcinoma	Most are metastatic, usually from cervix, endometrium, ovary, or colon Most primaries are clear-cell adenocarcinomas 2 types: non-DES and DES syndrome

Treatment

- Stage I
  - radiation therapy: for tumours >2 cm diameter or tumour involvement of the mid- to low-grade vagina
  - surgical excision: radical hysterectomy, upper vaginectomy, and bilateral pelvic lymphadenectomy
- Stage II-IV: chemoradiation

Gestational Trophoblastic Disease/Neoplasia

- refers to a spectrum of proliferative abnormalities of the trophoblast

Epidemiology
- 1/1000 pregnancies
- marked geographic variation (as high as 1/125 in Taiwan)
- 80% benign, 15% locally invasive, 5% metastatic
- cure rate >95%

HYDATIDIFORM MOLE (Benign GTD)

Complete Mole
- most common type of hydatidiform mole
- diffuse trophoblastic hyperplasia, hydropic swelling of chorionic villi, no fetal tissues or membranes present
- 46XX or 46XY, chromosomes completely of paternal origin (90%)
- 2 sperm fertilize empty egg or 1 sperm with reduplication
- 15-20% risk of progression to malignant sequelae
- risk factors
  - geographic (South East Asia most common)
  - others (maternal age >40 yr, β-carotene deficiency, vitamin A deficiency not proven)
- clinical features often present during apparent pregnancy with abnormal symptoms/findings
  - vaginal bleeding (97%)
  - hyperemesis gravidarum (26%)
  - excessive uterine size for LMP (51%)
  - hyperthyroidism (7%)
  - theca-lutein cysts >6 cm (50%)
  - β-hCG >100,000 IU/L
  - preeclampsia (27%)
  - no fetal heartbeat detected

With development of hypertension early in pregnancy (i.e. <20 wk), think gestational trophoblastic disease

Partial (or Incomplete) Mole
- focal trophoblastic hyperplasia and hydropic villi are associated with fetus or fetal parts
- often triploid (XXY, XYY, XXX) with chromosome complement from both parents
  - usually related to single ovum fertilized by two sperm
- low risk of progression to malignant sequelae (<4%)
- associated with fetus, which may be growth-restricted, and/or have multiple congenital malformations
- clinical features
  - typically present similar to threatened/spontaneous/missed abortion
  - pathological diagnosis often made after D&C

Investigations
- quantitative β-hCG levels (tumour marker) abnormally high for gestational age
- U/S findings
  - if complete: no fetus (classic "snow storm" due to swelling of villi)
  - if partial: molar degeneration of placenta ± fetal anomalies, multiple echogenic regions corresponding to hydropic villi, and focal intrauterine hemorrhage
- CXR (may show metastatic lesions)
- features of molar pregnancies at high risk of developing persistent GTN post-evacuation
  - local uterine invasion as high as 31%
  - β-hCG >100,000 IU/L
  - excessive uterine size
  - prominent theca-lutein cysts

Treatment
- suction D&C with sharp curettage and oxytocin
- Rhogam® if Rh negative
- prophylactic chemotherapy of no proven benefit
- chemotherapy for GTN if develops after evacuation

Follow-up
- contraception required to avoid pregnancy during entire follow-up period
- serial β-hCGs (as tumour marker) every week until negative x 3 (usually takes several wk), then monthly for 6-12 mo prior to trying to conceive again
- increase or plateau of β-hCG indicates GTN: patient needs chemotherapy

GTN (MALIGNANT GTD)

Invasive Mole or Persistent GTN
- diagnosis made by rising or plateau in β-hCG, development of metastases following treatment of documented molar pregnancy
- histology: molar tissue from D&C
- metastases are rare (4%)

Choriocarcinoma
- often present with symptoms from metastases
- highly anaplastic, highly vascular
- no chorionic villi, elements of syncytiotrophoblast and cytotrophoblast
- may follow molar pregnancy, abortion, ectopic, or normal pregnancy

Placental-Site Trophoblastic Tumour
- rare aggressive form of GTN
- abnormal growth of intermediate trophoblastic cells
- low β-hCG, production of human placental lactogen (hPL), relatively insensitive to chemotherapy

CLASSIFICATION of GTN
- non-metastatic
  - ~15% of patients after molar evacuation
  - may present with abnormal bleeding
  - all have rising or plateau of β-hCG
  - negative metastases on staging investigations
- metastatic
  - 4% of patients after treatment of complete molar pregnancy
  - metastasis more common with choriocarcinoma, which tends toward early vascular invasion and widespread dissemination
  - if signs or symptoms suggest hematogenous spread, do not biopsy (they bleed)
    - lungs (80%): cough, hemoptysis, CXR lesion(s)
    - vagina (30%): vaginal bleeding, "blue lesions" on speculum exam
    - pelvis (20%): rectal bleeding (if invades bowel), U/S lesion(s)
    - liver (10%): elevated LFTs, U/S or CT findings
    - brain (10%): headaches, dizziness, seizure (symptoms of space-occupying lesion), CT/MRI findings
  - highly vascular tumour, which is more likely to bleed and result in anemia
  - all have rising or plateau of β-hCG
  - classification of metastatic GTN
    - divided into good prognosis and bad prognosis
    - features of bad prognosis
      - long duration (>4 mo from antecedent pregnancy)
      - high pre-treatment β-hCG titre: >100,000 IU/24 h urine or >40,000 IU/L of blood
      - brain or liver metastases
      - prior chemotherapy
      - metastatic disease following term pregnancy
    - good prognosis characterized by the absence of each of these features

Lungs are the primary site for malignant GTN metastases; when pelvic exam and chest x-ray are negative, metastases are uncommon

Investigations (for Staging)
- blood work: CBC, electrolytes, creatinine, β-hCG, TSH, LFTs
- imaging: CXR, U/S pelvis only
- if CXR shows lung metastasis then CT abdo/pelvis, MRI brain
- if suspect brain metastasis but CT brain negative, consider lumbar puncture for CSF β-hCG
- ratio of plasma β-hCG:CSF β-hCG <60 indicates metastases

Table 31. FIGO Staging and Management of Malignant GTN

Stage	Findings	Management
I	Disease confined to uterine corpus	Single agent chemotherapy for low risk disease (WHO score ≤6) 1st line: pulsed actinomycin D (Act-D) IV q2wk Alternatives: MTX-based regimen 20% of patients need to switch to alternate single-agent regimen due to failure of β-hCG to return to normal Combination chemotherapy (EMA-CO: etoposide, MTX, ACT-D, cyclophosphamide, vincristine) if high risk (WHO score ≥7) or if resistant to single-agent chemotherapy Can consider hysterectomy if fertility not desired or placental-site trophoblastic tumour
II	Metastatic disease to genital structures	As above
III	Metastatic disease to lungs with or without genital tract involvement	As above
IV	Distant metastatic sites including brain, liver, kidney, GI tract	Usually high risk (EMA-CO) with surgical resection of sites of disease Persistence/resistance to chemotherapy Consider radiation for brain mets

Table 32. WHO Prognostic Score for GTD (2011)

	Score			
Prognostic Factor	**0**	**1**	**2**	**4**
Maternal Age	>40	40		
Antecedent Pregnancy	Mole	Abortion	Term	
Interval (End of Antecedent Pregnancy to Chemotherapy in Months)	<4	4-6	7-13	>13
HCG IU/1	<103	103-104	104-105	>105
Number of Metastases	0	1-4	5-8	>8
Site of Metastases	Lung	Spleen, kidney	GI tract	Brain, liver
Largest Tumour Mass		3-5 cm	>5 cm	
Prior Chemotherapy			Single drug	Two drug

Follow-up (for GTN)

- contraception for all stages to avoid pregnancy during entire follow-up period
- stage I, II, III
  - weekly β-hCG until 3 consecutive normal results
  - then monthly x 12 mo
- stage IV
  - weekly β-hCG until 3 consecutive normal results
  - then monthly x 24 mo

GTN Diagnosis

- β-hCG plateau: <10% drop in β-hCG over four values in 3 wk (e.g. days 1, 7, 14, and 21) OR
- β-hCG rise >20% in any two values over two wk or longer (e.g. measure at days 1, 7, 14) OR
- β-hCG persistently elevated >6 mo OR
- metastases on work-up

Common Medications

Table 33. Common Medications

Drug Name (Brand Name)	Action	Dosing Schedule	Indications	Side Effects (S/E), Contraindications (C/I), Drug Interactions (D/I)
acyclovir (Zovirax®)	Antiviral; inhibits DNA synthesis and viral replication	**First Episode**: 400 mg PO tid x 7-10 d **Recurrence**: 400 mg PO tid x 5 d	Genital herpes	**S/E**: headache, GI upset **D/I**: zidovudine, probenecid
bromocriptine (Parlodel®)	Dopaminomimetic, agonist at D2R and antagonist at D1R; acts directly on anterior pituitary cells to inhibit synthesis and release of prolactin	**Initial**: 1.25-2.5 mg PO qhs with food Then: increase by 2.5 mg every 2-7 d as needed until optimal therapeutic response **Usual Range**: 1.5-15 mg OD For IVF: **Initial**: 1.25 mg/d PO between days 4-6 of follicular phase **Then**: 2.5 mg/d until 3 d after onset menstruation	Galactorrhea + amenorrhea 2° to hyperprolactinemia Prolactin-dependent menstrual disorders and infertility Prolactin-secreting adenomas (microadenomas, prior to surgery of macroadenomas) IVF	**S/E**: N/V, headache, postural hypotension, somnolence **C/I**: uncontrolled HTN, pregnancy-induced HTN, CAD, breastfeeding **D/I**: domperidone, macrolides, octreotide
clomiphene citrate (Clomid®)	Increases output of pituitary gonadotropins to induce ovulation	50 mg OD x 5 d Try 100 mg or 160 mg OD If ineffective 3 courses: adequate trial	Patients with persistent ovulatory dysfunction (e.g. amenorrhea, PCOS) who desire pregnancy	**S/E**: Common: hot flashes, abdominal discomfort, exaggerated cyclic ovarian enlargement, accentuation of Mittelschmerz Rare: ovarian hyperstimulation syndrome, multiple pregnancy, visual blurring, birth defects **C/I**: pregnancy, liver disease, hormone-dependent tumours, ovarian cyst, undiagnosed vaginal bleeding
clotrimazole (Canesten®)	Antifungal; disrupt fungal cell membrane	**Tablet**: 100 mg/d intravaginally x 7 d or 200 mg/d x 3 d or 500 mg x 1 dose **Cream** (1 or 2%): 1 applicator intravaginally qhs x 3-7 d **Topical**: apply bid x 7 d	Vulvovaginal candidiasis	**S/E**: vulvar/vaginal burning
danazol (Cyclomen® [CAN]) (Danocrine® [US])	Synthetic steroid: inhibits pituitary gonadotropin output and ovarian steroid synthesis Has mild androgenic properties	200-800 mg in 2-3 divided doses Use for 3-6 mo Biannual hepatic U/S required if >6 mo use	Endometriosis 1° menorrhagia/DUB	**S/E**: weight gain, acne, mild hirsutism, hepatic dysfunction **C/I**: pregnancy, undiagnosed vaginal bleeding, breastfeeding, severely impaired renal/hepatic/cardiac function, porphyria, genital neoplasia, thromboembolic disease **D/I**: warfarin, carbamazepine, cyclosporine, tacrolimus, anti-hypertensives

Table 33. Common Medications (continued)

Drug Name (Brand Name)	Action	Dosing Schedule	Indications	Side Effects (S/E), Contraindications (C/I), Drug Interactions (D/I)
doxycycline	Tetracycline derivative; inhibit protein synthesis	100 mg PO bid x ≥7 d	Chlamydia, gonococcal infection, syphilis	**S/E**: GI upset, hepatotoxicity **C/I**: pregnancy, severe hepatic dysfunction **D/I**: warfarin, digoxin
fluconazole (Diflucan®)	Antifungal; disrupt fungal cell membrane	150 mg PO x 1 dose	Vulvovaginal candidiasis unresponsive to clotrimazole	**S/E**: headache, rash, N/V, abdominal pain, diarrhea **D/I**: terfenadine, cisapride, astemizole, hydrochlorothiazide, phenytoin, warfarin, rifampin
leuprolide (Lupron®)	Synthetic GnRH analog; induces reversible hypoestrogenic state	3.75 mg IM q1mo or 11.25 mg IM q3mo Usually ≤6 mo, check bone density if >6 mo Retreatment with Lupron® alone not recommended because of effects on bone density	Endometriosis Leiomyomata DUB Precocious puberty	**S/E**: hot flashes, sweats, headache, vaginitis, reduction in bone density, acne, GI upset **C/I**: pregnancy, undiagnosed vaginal bleeding, breastfeeding
menotropin (Pergonal®)	Human gonadotropin with FSH and LH effects; induce ovulation and stimulate ovarian follicle development	75-150 U of FSH and LH IM OD x 7-12 d, then 10,000 U HCG 1 d after last dose	Infertility	**S/E**: bloating, irritation at injection site, abdominal/pelvic pain, headache, N/V, multiple pregnancy **C/I**: primary ovarian failure, intracranial lesion (e.g. pituitary tumour), uncontrolled thyroid/adrenal dysfunction, ovarian cyst (not PCOS), pregnancy, undiagnosed uterine bleeding
metronidazole (Flagyl®)	Bactericidal; forms toxic metabolites which damage bacterial DNA	2 g PO x 1 dose or 500 mg PO bid x 7 d	Bacterial vaginosis, trichomonas vaginitis	**S/E**: headache, dizziness, N/V, diarrhea, disulfiram-like reaction (flushing, tachycardia, N/V) **C/I**: pregnancy (1st trimester) **D/I**: cisapride, warfarin, cimetidine, lithium, alcohol, amiodarone, milk thistle, carbamazepine
oxybutinin (Ditropan®)	Anticholinergic; relaxes bladder smooth muscle, inhibits involuntary detrusor contraction	5 or 10 mg/d PO May increase doses by 5 mg weekly to a max of 30 mg/d	Overactive bladder (urge incontinence)	**S/E**: dry mouth/eyes, constipation, palpitations, urinary retention, dizziness, headache **C/I**: glaucoma, GI ileus, severe colitis, obstructive uropathy, use with caution if impaired hepatic/renal function
tolterodine (Detrol®)	Anticholinergic	1-2 mg PO bid	Overactive bladder (urge incontinence)	**S/E**: anaphylaxis, psychosis, tachycardia, dry mouth/eyes, headache, constipation, urinary retention, chest pain, abdominal pain **C/I**: glaucoma, gastric/urinary retention, use with caution if impaired hepatic/renal function
tranexamic acid (Cyklokapron®)	Anti-fibrinolytic; reversibly inhibits plasminogen activation	1-1.5 g tid-qid for first 4 d of cycle Max 4 g/d Ophthalmic check if used for several wk	Menorrhagia	**S/E**: N/V, diarrhea, dizziness, rare cases of thrombosis, abdominal pain, MSK pain **C/I**: thromboembolic disease, acquired disturbances of colour vision, subarachnoid hemorrhage, age <15 yr
ulipristal acetate (Fibristal®)	Selective progesterone receptor modulator (SPRM)	5 mg PO OD for max 3 mo; first tablet taken anytime during first 7 d of menstruation	Leiomyoma (pre-operative)	**S/E**: headache, hot flushes, constipation, vertigo, endometrial thickening **C/I**: pregnancy, undiagnosed vaginal bleeding, any gynecological cancer
urofollitropin (Metrodin®)	FSH	75 U/d SC x 7-12 d	Ovulation induction in PCOS	**S/E**: ovarian enlargement or cysts, edema and pain at injection site, arterial thromboembolism, fever, abdominal pain, headache, multiple pregnancy **C/I**: primary ovarian failure, intracranial lesion (e.g. pituitary tumour), uncontrolled thyroid/adrenal dysfunction, ovarian cyst (not PCOS), pregnancy, abnormal uterine bleeding
combined oral contraceptive pill (OCP)	Ovulatory suppression by inhibiting LH and FSH Decidualization of endometrium Thickening of cervical mucus to prevent sperm penetration		Contraception Disorders of menstruation	See Table 8-12
intrauterine device (IUD) **copper IUD (Nova-T®)** **progesterone-releasing IUD (Mirena®, Jaydess®)**	**Copper IUD**: mild foreign body reaction in endometrium, which is toxic to sperm and alters sperm motility **Progesterone-releasing IUD**: decidualization of endometrium and thickening of cervical mucus, may suppress ovulation	Contraceptive effects last 3 yr (Jaydess®); up to 5 yr (Copper IUD, Mirena®)	Same as above	See Table 8-12

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