COMORBID DISEASES IN PREGNANCY

DIABETES:

EPIDEMIOLOGY:

- 75% of pregnant women with DM have either gestational DM or undiagnosed T2DM, remainder have already diagnosed T2DM (24%) or T1DM (1%)
- Pregnant diabetic patients are at increased risk for spontaneous abortion, especially those with poor glycaemic control, vascular disease or preeclampsia
- Also at ↑d risk of:
    - Pregnancy inducted HT
    - Preterm labour
    - Spontaneous abortion
    - Pyelonephritis
    - DKA

MANAGEMENT OF DIABETES IN PREGNANCY:

- Most gestational diabetics are managed on diet alone
- Almost all patients with pre-existing T1 or T2DM require multiple insulin injections to maintain euglycaemia and avoid complications → need for insulin increases throughout ht ecourse of pregnancy → by late pregnancy, patients often need 1 unit/kg/day
- DKA:
    - Incidence of DKA decreases significantly with early diagnosis and improved counselling
    - Poor patient compliance, maternal emesis and use of tocolytic (β-sympathomimetics) all increase the risk of DKA
    - Ketosis occurs more rapidly and at lower glucose levels → poorly tolerated by the foetus
    - Management is the same
    - Most foetal HR abnormalities subside after correction of maternal hypovolaemia and acidosis
- HYPOGLYCAEMIA:
    - Up to half of diabetics using insulin will experience an episode of severe hypoglycaemia during pregnancy → brief episodes are generally well tolerated by the foetus
    - Treatment is the same, but goal is normoglycaemic control without wide swings

HYPERTHYROIDISM:

- Associated with:
    - ↑d risk of preeclampsia and neonatal morbidity → low birsth weight, congenital malformation
- Placental HCG and oestrogen during pregnancy stimulate TSH and thyroid-binding globulin leading to relative hyperthyroid state
    - Symptosm of hyperthyroidism closely mimic normal pregnancy

    - THYROTOXICOSIS in pregnancy may present as hyperemesis → screening TSH for all women who present with hyperemesis
- Treat with PTU → 50mg tds for 4-6 weeks → aim is to maintain FT3 level at upper range of normal with lowest dose of PTU
    - Beware AGRANULOCYTOSIS (0.3% OF PATIENTS)
- THYROID STORM:
    - Fever, volume depletion or cardiac decompensation → mortality rate of 25%
    - Principles are similar to nonpregnant patients

Table 102-2 Principles of Treatment of Thyroid Storm during Pregnancy

Principle	Comment
Decrease new synthesis of thyroid hormone	PTU, 600–800 milligrams PO once and then 150–200 milligrams PO every 4–6 h.
Block thyroid hormone release	**Do not give iodine until PTU has been administered.**
	Sodium iodide, 1 gram in 500 mL of IV fluid each day.
	Long-term use (>10 d) of sodium iodide results in a high incidence of fetal goiter and hypothyroidism.
	Do not use radioactive iodinebecause the fetus will concentrate iodine 131 after the 10th to 12th week of gestation, resulting in congenital hypothyroidism.
Block peripheral effects	Propranolol, 40 milligrams PO every 6 h.
	Hold if evidence of heart failure is present.
Cool patient	Cooling blankets.
	Acetaminophen, 650 milligrams PO every 4 h.
Supportive care	Left lateral decubitus position.
	Oxygen.
	IV fluids.
	Dexamethasone, 2 milligrams IV every 4 h.[28]

HYPERTENSION IN PREGNANCY:

- Hypertensive disorders are the most common medical complication of pregnancy and can be divided into:
    - CHRONIC HYPERTENSION:
        - Sustained elevation of BP >140/90 before 20 weeks or persistent beyond 12 weeks post-partum
        - Commonly used agents for treatment of chronic HT in pregnancy including methyldopa, labetalol and nifedipine
        - Agents to avoid are listed below

Table 102-3 Antihypertensive Agents to Avoid during Pregnancy

Agents	Comment
Thiazide diuretics	Reduce blood flow to the uterus and placenta
Angiotensin-converting enzyme inhibitors	Teratogenic effects, intrauterine growth retardation, fetal/neonatal renal failure
β-Blockers[29]	Intrauterine growth retardation

        - **Maternal mortality results from patients with severe HT and CHF or CVA**
        - Antihypertensives for mild to moderate elevations in BP has not been shown to alter the incidence of foetal complications or prevent preeclampsia
    - ACUTE HYPERTENSIVE CRISIS IN PREGNANCY:
        - Treated with labetalol 10mgIV every 5-10 minutes or hydralazine 5-10mg IV every 15 minutes
        - Goal is BP 140-150 and 90-100 diastolic
            - Persistent BP below this may jeopardise placental perfusion
        - CTG monitoring advised
    - PREGNANCY INDUCED HT AND PREECLAMPSIA → SEE PREVIOUS DISCUSSION

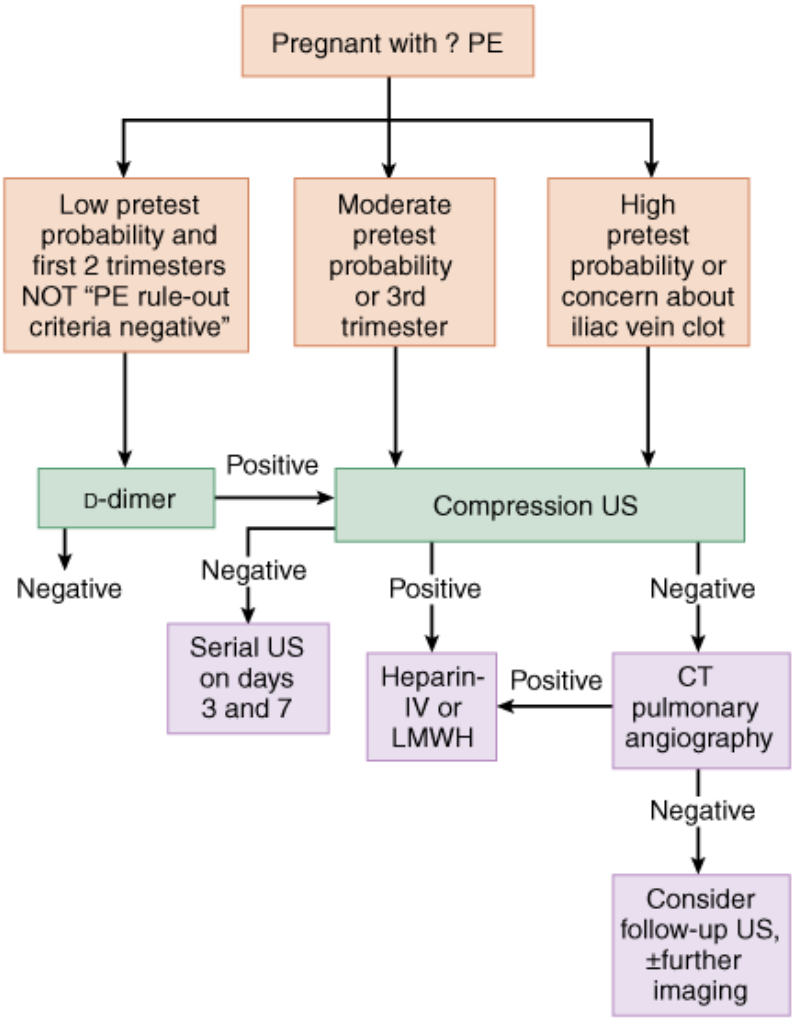
CARDIAC ARRHYTHMIAS:

- Pregnancy can precipitate cardiac arrhythmia and risk is relatively higher during labour and delivery
- TREATMENT:
    - If vagal manoeuvres are not effective for SVT, then the following are safe in pregnancy:
        - Cardioselective β-blockers
        - Adenosine
        - Verapamil
        - Diltiazem
    - Goal of management of AF in pregnancy is rate control or conversion → use cardioselective β-blocker or digoxin
        - Unfractionated or LMWH are safe in pregnancy and should used if indicated
    - Ventricular arrhythmias occur in pregnancy, especially in those with congenital heart disease, cardiomyopathy or valvular heart disease
        - Electrical cardioversion appears safe for the foetus
        - Amiodarone and its metabolite cross the placenta and are associated with foetal neurotoxicity

THROMBOEMBOLISM:

- Pregnant women have a 2-5 fold higher frequency of DVT and PE compared with non-pregnant women of childbearing age
- PE is the most common cause of maternal death in the developed world
- ~85% of all pregnancy related symptomatic events are DVT, 2/3 of all DVT occur antepartum and half of these events occur before the third trimester
- The pregnancy-related changes that increase VTE risk include:
    - Physiologic alterations in coagualtion
    - Reduced venous return
- Additional RF include:
    - Advanced maternal age
    - Increasing parity

    - Multiple gestation
    - Operative delivery
    - Bed rest
    - Obesity
    - Prior VTE
    - Antithrombin III defiency or lupus anticoagulant
- CLINICAL FEATURES:
    - Assessment is difficult because many of the typical signs and symptoms are seen in NORMAL PREGNANCY → leg oedema, SOB and tachycardia
    - Clots occur more commonly in the LEFT LEG (~90%) → thought to be due to compression of left iliac vein by right iliac artery
- DIAGNOSIS:
    - For DVT → compression US has sensitivity of 97% and specificity of 94% in symptomatic patients
    - Use of D-dimer is controversial → the level will increase during normal pregnancy
    - Diagnosis of PE in pregnancy is also complicated by concerns about radiation exposure to both developing foetus and the mother



- TREATMENT:
  - IV heparin or LMWH are used to treat both DVT and PE in pregnancy
  - WARFARIN IS NOT USED → crosses the placenta and is associated with embryopathy in first trimester and variety of CNS and ophthalmological abnormalies in $2^{nd}/3^{rd}$ trimester
  - Protamine sulphate can be used safely in pregnancy for rapid reversal of heparinisation
  - There is little experience in use of thrombolytics in pregnancy, but its use may be entertained in life-threatening situations

ASTHMA EXACERBATION:

- Asthma is the most common medical disease in pregnancy
- Clinical course may improve, be unchanged or worsen during pregnancy
- There is a small (but significant ~15-20%) risk of preterm delivery, low birth weight and preeclampsia and the risk increases markedly in poorly controlled asthmatics
- CLINICAL PRESENTATION AND ASSESSMENT:
  - Symptoms identical to non-pregnant population

    - Normal assessment, but add CTG if pregnancy has reached viability
- TREATMENT:
    - Similar to management in the non-pregnant population
    - Standard treatment with bronchodilators and steroids and use ADRENALINE ONLY IN THE MOST CRITICALLY ILL PREGNANT ASTHMATICS, as concerns exist about potential vasocontriction of the uteroplacental circulation
    - Anticipate maternal hyperglycaemia in using steroids

CHRONIC RENAL DISEASE:

- Maternal risks associated with renal disease are linked to the patient's degree of renal compromise
- Those with mild renal insufficiency have good outcomes where those with moderate or severe disease are more prone to further deterioration in renal function and preeclampsia and preterm delivery
- ACE-I and ARB are TERATOGENIC and should be stopped at the first indication of pregnancy
- Patients with lupus nephropathy are at greatly increased risk for disease exacerbation and superimposed preeclampsia

CYSTITIS AND PYELONEPHRITIS:

- Hormonal and mechanical changes of pregnancy INCREASE THE RISK OF URINARY STASIS AND SUBSEQUENT URINARY TRACT INFECTION
- After midpregnancy, mild right hydronephrosis is present in 75%, (33% on left)
- Asymptomatic bacteriuria is present in 2-10% of pregnant women → treatment reduces the incidence of pyelonephritis in pregnant women
    - Acute cystitis and pyelonephritis occurs in ~1-2% of pregnant women
    - Presentation and causative organisms are similar to nonpregnant women
    - UTI need prompt treatment as pyelonephritis can precipitate preterm labor
    - Pregnant women are more prone to complications such as bacteraemia and septic shock
- TREATMENT:
    - Trimethoprim is A FOLATE ANTAGONIST and can lead to neural tube defects if used in the first trimester
    - Sulfonamides can cause kernicterus if used in the third trimester
    - Fluoroquinolones and tetracyclines cannot be used at any stage → toxic effects on the foetus
    - IF SEVERE → TREAT WITH THIRD GENERATION CEPHALOSPORIN OR AMPICILLIN PLUS GENTAMICIN

SICKLE CELL DISEASE:

- These women are at increased risk for miscarriage, preterm labor and other complications due to impaired oxygen supply and sickling infarcts in the placental circulation
- Maternal complications are more common in the third trimester and post-partum period

- Cerebral vein thrombosis, pneumonia, sepsis, pyelonephritis

- SICKLE CELL CRISIS:
  - Presentation of painful crises is similar in pregnant and nonpregnant women
    - Cornerstones of management remain the same → aggressive dehydration, analgesia and treatment of underlying cause
    - Avoid using NSAIDs, especially after 32 weeks, because of OLIGOHYDRAMNIOS and risk of premature closure of the foetal ductus arteriosus
    - Blood transfusions are reserved for sickle cell crises when conservative measure have not improved maternal or foetal status. Indications for transfusion include:
      - Hb < 50
      - Preeclampsia
      - Hypoxaemia
      - Acute chest syndrome
      - New onset neurological event
  - Parvovirus B19 may precipitate an aplastic crisis and is associated with development of hydrops fetalis

HEADACHE:

- Headaches can be a presenting symptom of a variety of neurologic or systemic disorders:

Table 102-4 Differential Diagnosis of Headaches in Pregnancy
Life-threatening
Subarachnoid hemorrhage
Intraparenchymal hemorrhage
Central venous thrombosis
Ischemic stroke
Central nervous system tumor or infection
Preeclampsia/eclampsia
Non–life-threatening
Tension headache
Migraine
Sinus headache
Tension headache
Benign intracranial hypertension (pseudotumor cerebri)

- Warning signs of a more sinister cause of headache are outlined below:

Table 102-5 Warning Symptoms and Signs in Patients with Headaches
New-onset headaches in pregnancy
Postpartum headaches
Need to exclude cerebral vein thrombosis
Headaches with different characteristics from previous headaches
Worst headache of life
Focal neurologic deficit
Meningismus
Fever
Altered consciousness
Papilledema or other signs of increased intracranial pressure
Retinal hemorrhages
Increased blood pressure (may herald preeclampsia or eclampsia)

- CT brain can be safely performed with appropriate shielding of the foetus → MRI is superior for evaluation of cerebral infarct, tumour or infection. MR venography is used to diagnose cerebral vein thrombosis

SEIZURE DISORDERS:

- Seizure frequency INCREASES IN PREGNANCY because of increased volume of distribution, increased plasma clearance and poor compliance
- Chronic control of seizures is best managed by the patient's physician
    - Medication doses may need to be increased in pregnancy
    - Valproat, carbamazepine, lamotrigine and phenytoin are all teratogenic
- Acute treatment of seizures is similar to nonpregnant patients
- Foetal bradycardia may persist for 20 minutes after single brief maternal sieuzre → if the seizure is self-limited, administer oxygen and treat conservatively
- Status epilepticus poses a real threat to both mother and foetus (50% foetal mortality and 33% maternal mortality)

HIV INFECTION:

- Pregnancy does not alter the natural course of HIV
- All pregnant HIV-infected patients beyond 14 weeks should be on HAART → use of zidovudine has reduced vertical transmission to <2%
- Prophylaxis for opportuinistic infections is similar → bactrim should be used with caution → folate supplementation if going to take it. Pentamidine is an alternative for PCP prophylaxis
- Treatment of opportunistic infections is similar

SUBSTANCE ABUSE IN PREGNANCY:

- All pregnant women identified as substance abusers should be referred to a high-risk obstetrics clinic and offered counselling
- COCAINE:
    - Associated with increased risk of:
        - PLACENTAL ABRUPTION

        - FOETAL DEATH IN UTERO
        - IUGR
        - Preterm labor
        - PROM
        - Spontaneous abortion
        - Cerebral infarcts in the foetus
    - Maternal complications:
        - AMI
        - Hypertension
        - Aortic dissection
        - Pulmonary oedema
        - Cardiac dysrhythmia
- OPIOIDS:
    - Pregnant women in acute opiate withdrawal are currently treated with clonidine
    - Pregnant women in an opiate avoidance program (methadone) should continue on that program
- ALCOHOL:
    - RF for poor birth outcomes
        - Foetal alcohol syndrome
        - Birth defects
        - Low birth weight
    - Binge drinking is particularly harmful to foetal neurological development

INTIMATE PARTNER VIOLENCE:

- ~4-20% of pregnant women are victims of intimate partner violence
- Violence increases the risk of preterm labour, placental abruption, foetal fractures, uterine rupture, homicide and chorioamnionitis
- Treat according to standard trauma protocols
- Administer anti-D to pregnant women who are Rh-negative and suffer blunt abdominal trauma

MEDICATIONS IN PREGNANCY AND LACTATION:

- THE CLASSIC TERATOGENIC PERIOD IS FORM DAY 31 AFTER FIRST DAY OF LMP TO 71 DAYS
    - During this time, organs are forming and teratogen may cause overt malformation
- There are five categories of drug according to effects on the foetus

Table 102-6 U.S. Food and Drug Administration Categorization of Drug Risk in Pregnancy

Drug Category	Risk during Pregnancy
A	Controlled studies have failed to demonstrate a fetal risk in the first trimester (and there is no evidence of risk in later trimesters), and the possibility of fetal harm is remote.
B	*Either* animal studies have not demonstrated a fetal risk but there are no controlled human studies
	or
	Animal studies have demonstrated an adverse effect that was not confirmed in controlled human studies in women in the first trimester (and there is no evidence of risk in later trimesters).
C	*Either* animal studies have revealed adverse effects on the fetus (teratogenic or embryocidal) and there are no controlled studies in humans
	or
	No human or animal studies are available. Drugs should only be used if the potential benefit justifies the potential fetal risk.
D	Evidence of human fetal risk exists, but the benefits of use in pregnant women may be acceptable despite the risk.
X	Studies in animals or humans have demonstrated fetal risk, or there is evidence of fetal risk based on human experience. The risk of use in pregnancy clearly outweighs any possible benefit. Drugs are contraindicated for use in women who are or may become pregnant.

Table 102-7 Some Therapeutic Agents Used in Emergency Settings with Known Adverse Effects in Human Pregnancy	
Drug	**Effect**
Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers	Renal failure, oligohydramnios
Aminoglycosides	Ototoxicity
Androgenic steroids	Masculinize female fetus
Anticonvulsants (carbamazepine, hydantoins, valproate)	Dysmorphic syndrome, anomalies
Antithyroid agents	Fetal goiter
Aspirin (high doses)	Bleeding, antepartum and postpartum
Cytotoxic agents (i.e., methotrexate)	Multiple anomalies
Erythromycin estolate	Maternal hepatotoxicity
Fluoroquinolones	Fetal cartilage abnormality
Isotretinoin	Hydrocephalus, deafness, anomalies
Lithium	Congenital heart disease (Ebstein anomaly)
Metronidazole	Fetal midline facial defects (first trimester)
NSAIDs (prolonged use after 32 wk)	Oligohydramnios, constriction of fetal ductus arteriosus
Streptomycin	Fetal cranial nerve VIII damage
Sulfonamides	Fetal hemolysis, neonatal kernicterus (near term)
Tetracyclines	Fetal teeth and bone abnormalities
Trimethoprim, methotrexate	Folate antagonist (first trimester)
Thalidomide	Phocomelia
Warfarin	Embryopathy—nasal hypoplasia, optic atrophy

Table 102-8 Some Medications Contraindicated during Breastfeeding
Amphetamines
Aspirin (high doses)
Bromocriptine (Parlodel)
Cytotoxic agents
Ergotamines
Lithium
Nitrofurantoin (for <1 mo old, and for those with glucose-6-phosphate dehydrogenase deficiency)
Radiopharmaceuticals

FOETAL RADIATION EFFECTS:

- When deciding whether or not to order an imaging study during pregnancy, the risks of exposure and subsequent adverse effects must be weighed against risk of incorrect maternal diagnosis
- The major factor determing the degree of risk to the foetus is the quantity of ionising radiation exposure during imaging

- Data suggest that foetal exposure to low-dose radiation (<5 rads, 5omGy) does NOT INCRESAE THE RISK OF FOETAL OR INFANT DEATH, MENTAL DEFECT OR GROWTH RETARDATION
- Risk of exposure varies with gestational age → 2^{nd}-8^{th} week postconception is period of organogenesis. Neurologic develop occurs in next 7 weeks. Significant x-ray exposure between weeks 8-15 may result in small head size and decreased neurodevelopment
- Cumulative doses from multiple procedures are summative and the environmental radiation dose over 9 months is 0.1rad
- VQ scanning results in more radiation exposure compared to CTPA → hydration and frequent voiding reduces foetal exposure to the radionuclide particles during excretion

Table 102-9 Radiation Exposure to the Uterus/Fetus

Procedure	Dosage in Rads
Chest radiography (two view) with shielding of the maternal abdomen	<0.0001
Cervical spine (two view)	<0.0001
IV pyelogram	0.686–1.398
Abdominal series (two view)	0.2
Thoracic spine series (two view)	0.009
Lumbosacral spine series (three view)	0.168–0.359
Anteroposterior pelvis	0.04
Mammography—diagnostic for suspected breast cancers	0.007–0.02
Cerebral angiography	0.01
Upper GI series	0.056
Barium enema	1.9–3.9
Head CT	<0.05
Chest CT (10-mm slices, 10 slices), for standard or pulmonary embolism protocol	0.02–0.1
CT aortogram (chest through abdomen)	3.4
Abdominal/pelvis CT	2.6–3.5
CT, kidney-ureter-bladder protocol (reduced radiation dose)	1
Lumbar spine CT	3.5
Pelvimetry CT	0.25
Ventilation–perfusion scan (total)	0.215
Lung perfusion scan with technetium	0.175
Lung ventilation scan with xenon	0.04