常見內科疾病的懷孕照護

20190518

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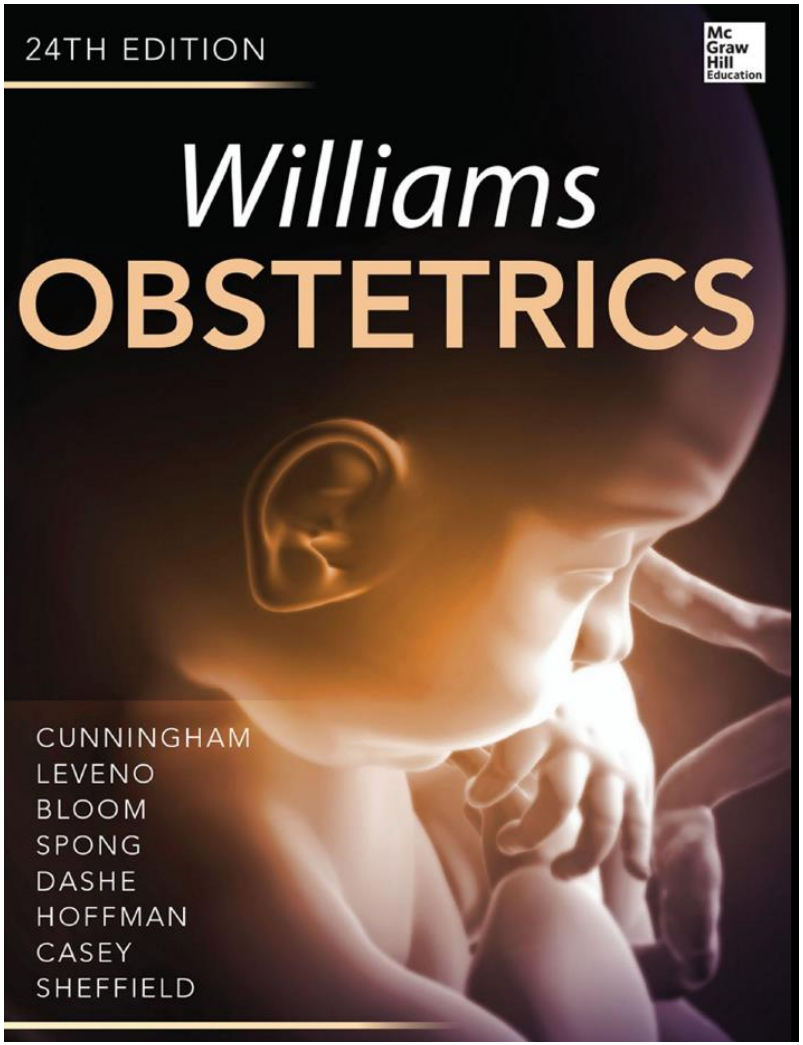
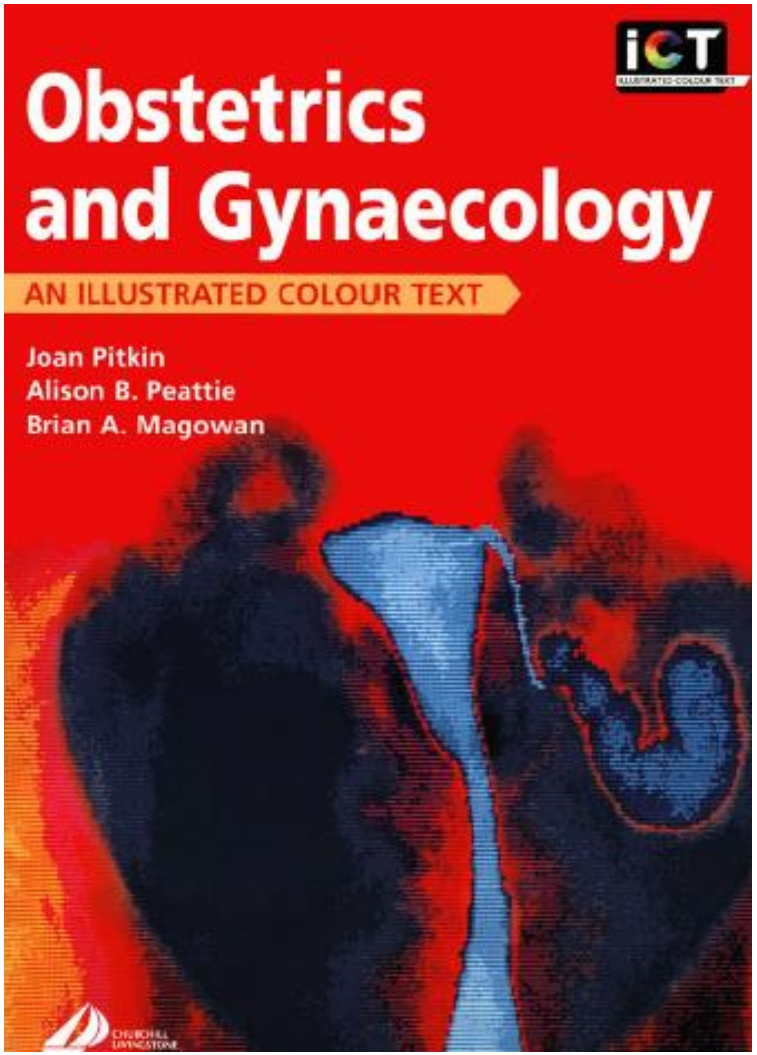




前言

Normal pregnancy – physiological signs and symptoms

Table 1 **Changes in the cardiovascular system**

Change
Increased blood volume 2600 to 3800 ml
Increased red cell mass 1400 to 1650-1800 ml
Decreased haemoglobin (Hb) and haematocrit
Increased resting cardiac output 4.5 to 6 l/min
Raised heart rate 80 to 90 bpm
Increased oxygen consumption by 30-50 ml/min
Decrease in total peripheral resistance (TPR) to parallel rise in cardiac output (CO)
Mid trimester fall in blood pressure due to greater drop in TPR than rise in CO
Increased incidence of heart murmurs due to increased flow across valves

血量增加

血球增加

血色素降低

心臟輸出增加

心跳加快

耗氧量增加

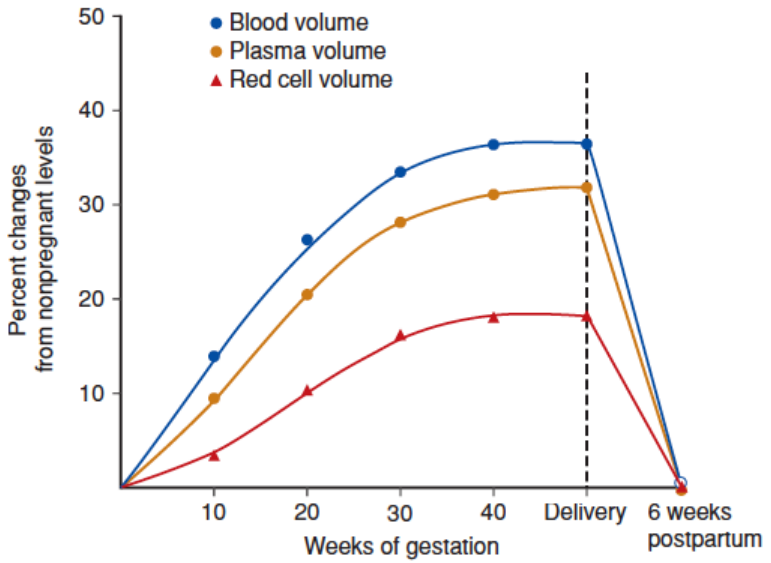
周遭血管阻力減少

血壓降低

心雜音出現

TABLE 4-4. Central Hemodynamic Changes in 10 Normal Nulliparous Women Near Term and Postpartum

	Pregnant[a] (35–38 wk)	Postpartum (11–13 wk)	Change[b]
Mean arterial pressure (mm Hg)	90 ± 6	86 ± 8	NSC
Pulmonary capillary wedge pressure (mm Hg)	8 ± 2	6 ± 2	NSC
Central venous pressure (mm Hg)	4 ± 3	4 ± 3	NSC
Heart rate (beats/min)	83 ± 10	71 ± 10	+17%
Cardiac output (L/min)	6.2 ± 1.0	4.3 ± 0.9	+43%
Systemic vascular resistance (dyn/sec/cm^{-5})	1210 ± 266	1530 ± 520	−21%
Pulmonary vascular resistance (dyn/sec/cm^{-5})	78 ± 22	119 ± 47	−34%
Serum colloid osmotic pressure (mm Hg)	18.0 ± 1.5	20.8 ± 1.0	−14%
COP-PCWP gradient (mm Hg)	10.5 ± 2.7	14.5 ± 2.5	−28%
Left ventricular stroke work index (g/m/m^2)	48 ± 6	41 ± 8	NSC



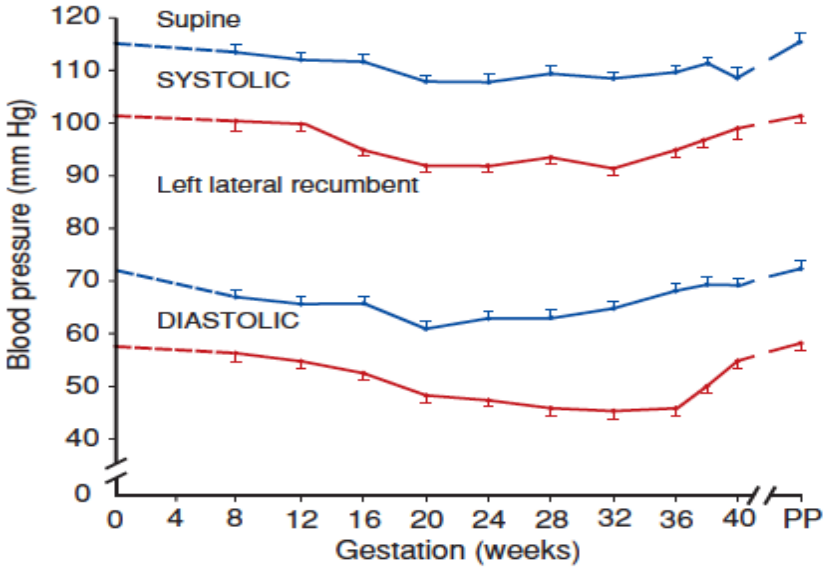


Table 2 **Changes in values**	
Renal blood flow increases	From 1.2 l/min to 1.5 l/min
Glomerular filtration rate rises due to raised blood flow	140 ml/min up to 170 ml/min
Serum urea falls due to increased filtration	4.3 mmol/l down to 3.1 mmol/l
Serum creatinine falls due to greater filtration	73 mmol/l falls to 47 mmol/l

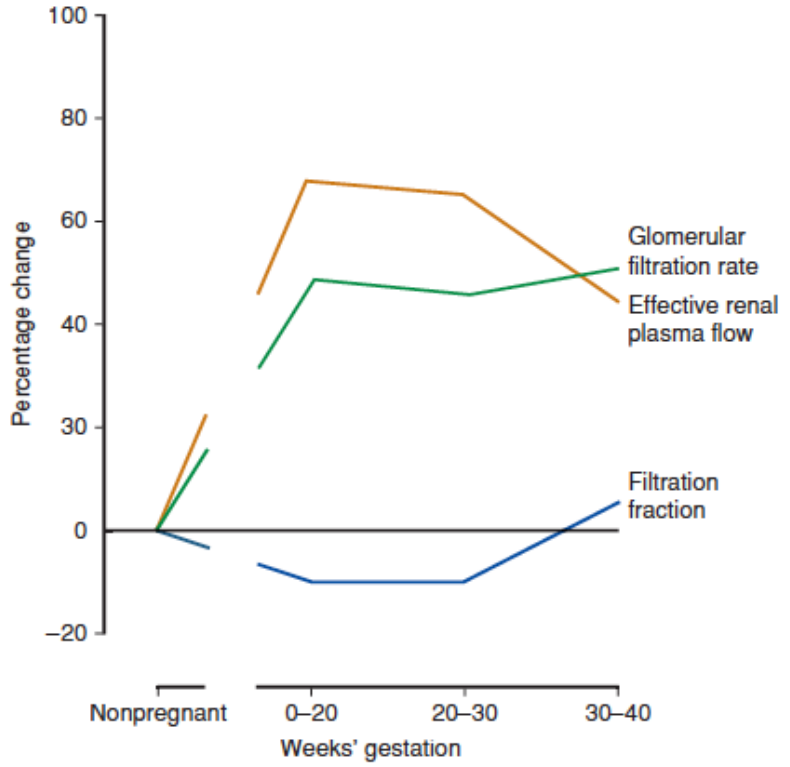
腎臟血流增加

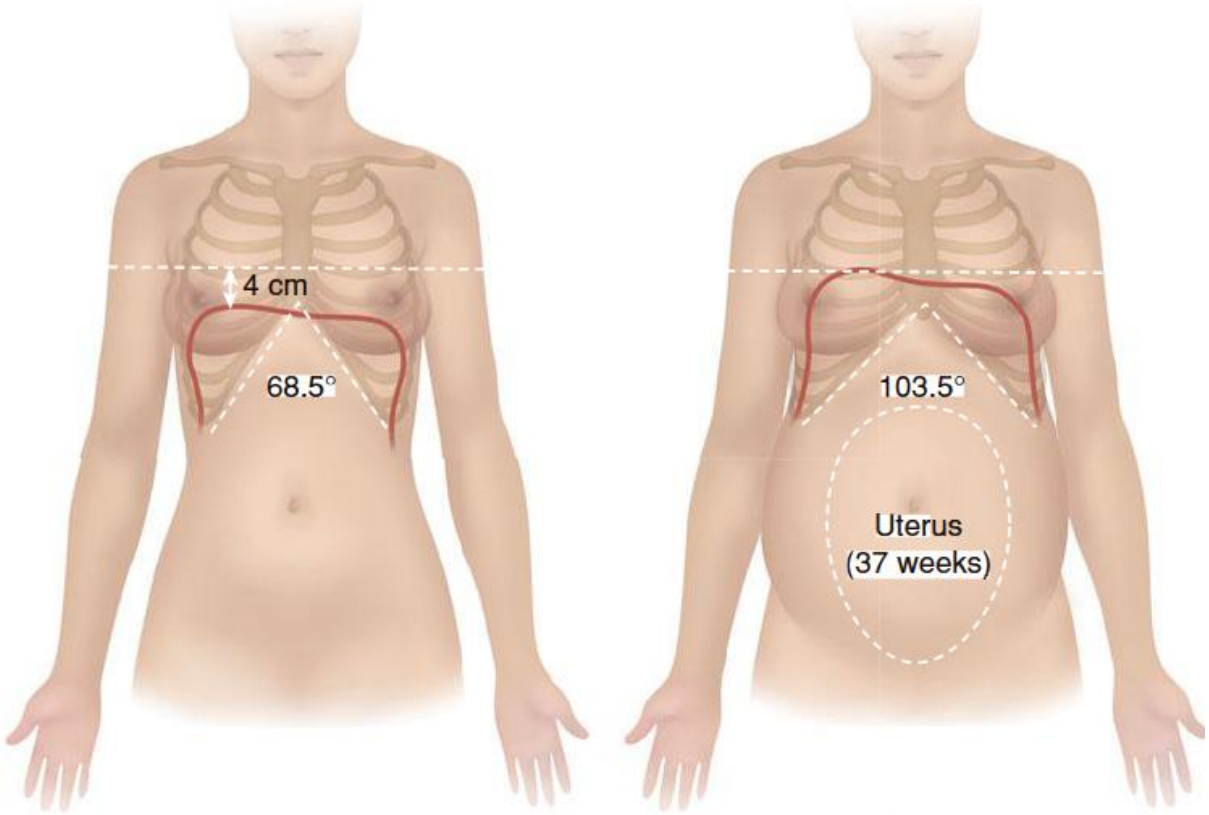
腎絲球過濾率增加

尿素降低

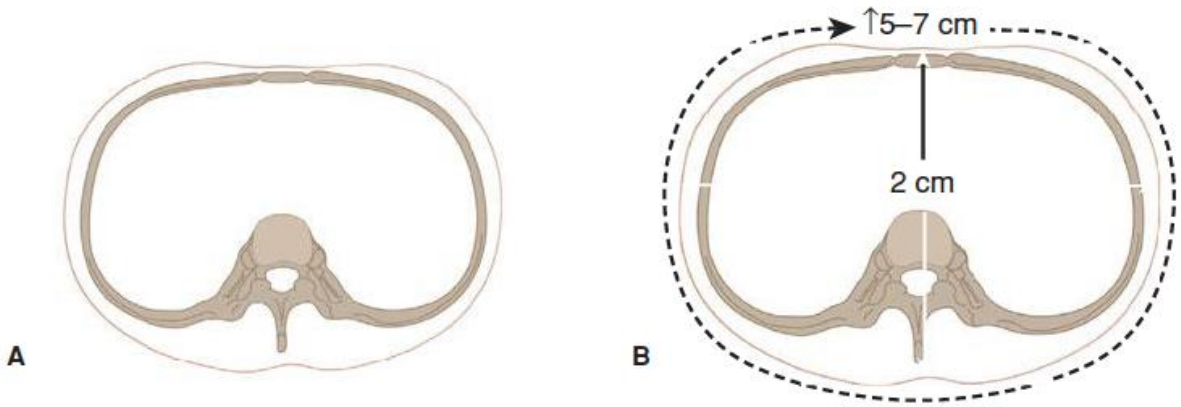
肌酐酸降低

尿糖過濾增加，回收減少





婦女懷孕時的胸廓變化



所有肺容量減少

靜止肺容量降低

換氣肺容量增加

呼吸次數增加

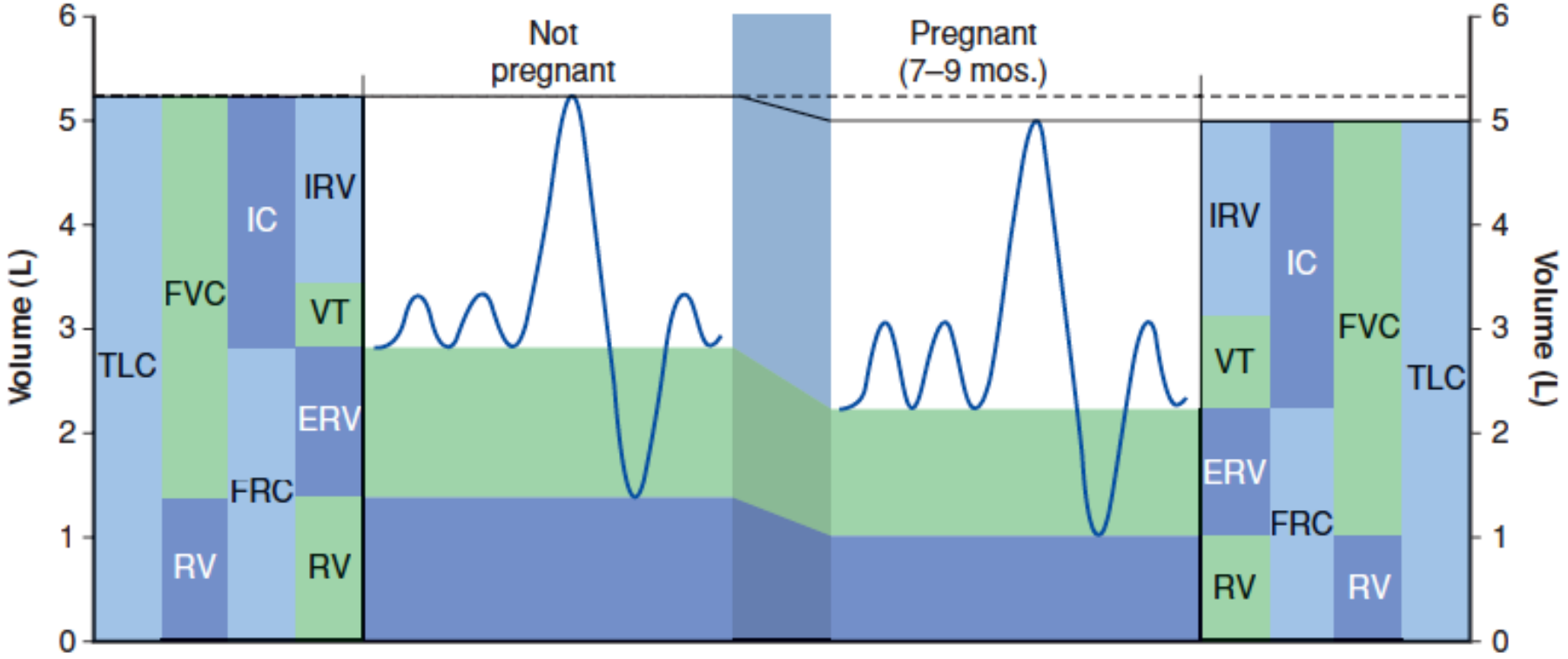


TABLE 4-3. Changes in Measures of Hemostasis During Normal Pregnancy

Parameter	Nonpregnant	Term Pregnant
Activated PTT (sec)	31.6 ± 4.9	31.9 ± 2.9
Fibrinogen (mg/dL)	256 ± 58	473 ± 72[a]
Factor VII (%)	99.3 ± 19.4	181.4 ± 48.0[a]
Factor X (%)	97.7 ± 15.4	144.5 ± 20.1[a]
Plasminogen (%)	105.5 ± 14.1	136.2 ± 19.5[a]
tPA (ng/mL)	5.7 ± 3.6	5.0 ± 1.5
Antithrombin III (%)	98.9 ± 13.2	97.5 ± 33.3
Protein C (%)	77.2 ± 12.0	62.9 ± 20.5[a]
Total protein S (%)	75.6 ± 14.0	49.9 ± 10.2[a]

血液凝固因子會增加

Protein C and protein S 減少

TABLE 4-5. Renal Changes in Normal Pregnancy

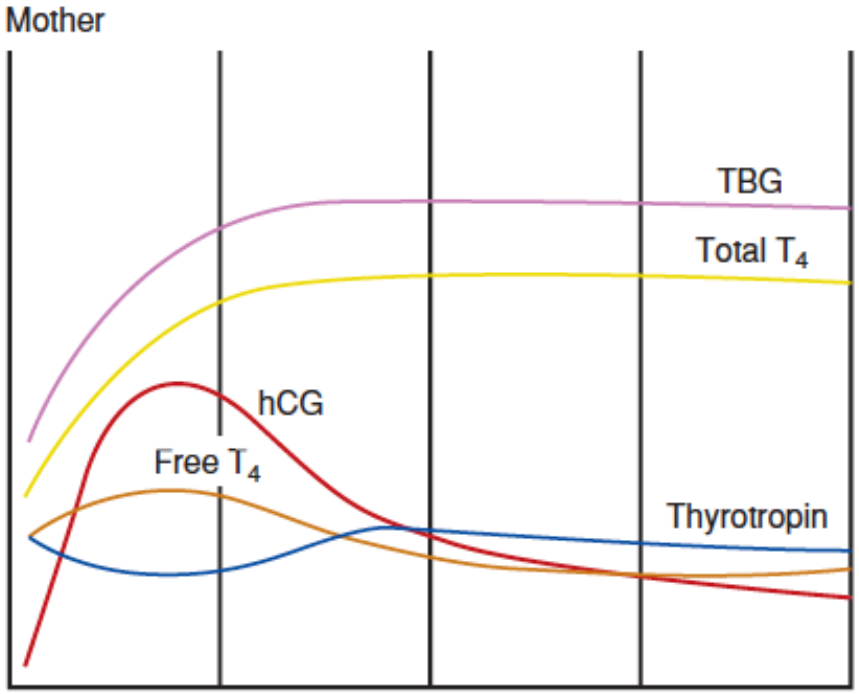
Parameter	Alteration	Clinical Relevance
Kidney size	Approximately 1 cm longer on radiograph	Size returns to normal postpartum
Dilatation	Resembles hydronephrosis on sonogram or IVP (more marked on right)	Can be confused with obstructive uropathy; retained urine leads to collection errors; renal infections are more virulent; may be responsible for "distension syndrome"; elective pyelography should be deferred to at least 12 weeks postpartum
Renal function	Glomerular filtration rate and renal plasma flow increase ~50%	Serum creatinine decreases during normal gestation; > 0.8 mg/dL (> 72 μmol/L) creatinine already borderline; protein, amino acid, and glucose excretion all increase
Maintenance of acid-base	Decreased bicarbonate threshold; progesterone stimulates respiratory center	Serum bicarbonate decreased by 4–5 mEq/L; Pco_2 decreased 10 mm Hg; a Pco_2 of 40 mm Hg already represents CO_2 retention
Plasma osmolality	Osmoregulation altered; osmotic thresholds for AVP release and thirst decrease; hormonal disposal rates increase	Serum osmolality decreases 10 mOsm/L (serum Na ~5 mEq/L) during normal gestation; increased placental metabolism of AVP may cause transient diabetes insipidus during pregnancy

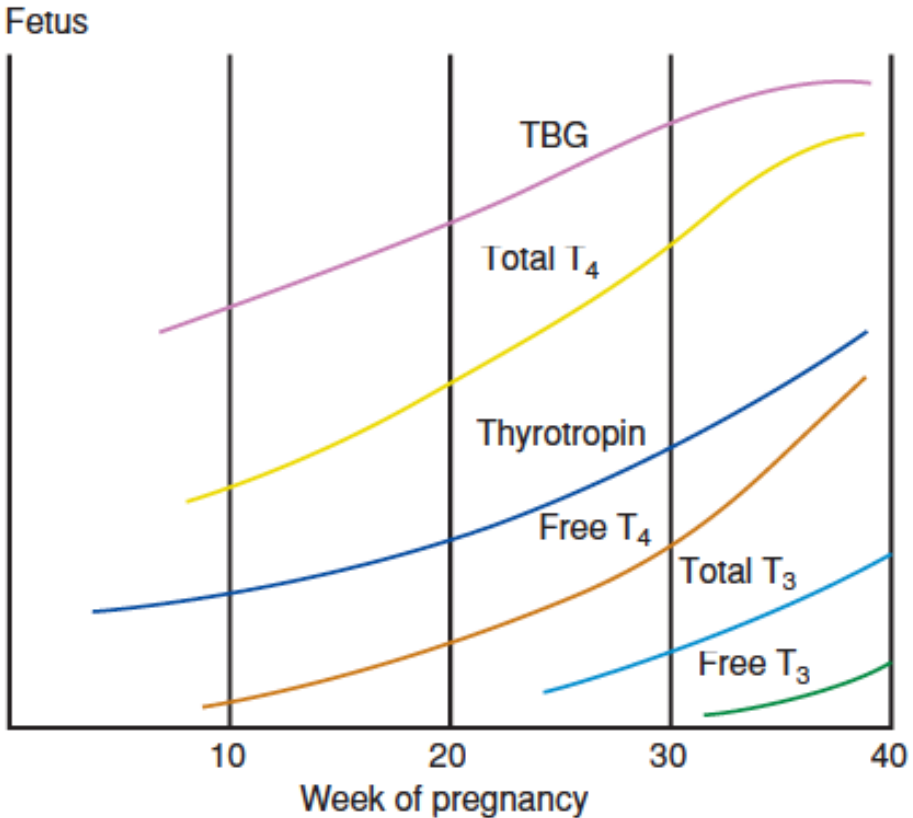
腎臟變大

輕微腎及輸尿管水腫，右邊較明顯

腎功能增加約50%

血中PCO2濃度降低


Mother
TBG
Total T_4
hCG
Free T_4
Thyrotropin


Fetus
TBG
Total T_4
Thyrotropin
Free T_4
Total T_3
Free T_3
10
20
30
40
Week of pregnancy

慢性腎臟病與孕婦

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18 May 2019

如何照護慢性腎臟病的孕婦

病例分享

- 一位32歲，結婚三年婦女
- 因為陰道出血，到門診檢查
- 尿液懷孕檢查，陽性反應
- 超音波檢查，懷孕九週，胎兒心跳(+)
- 病史，19歲開始被診斷為慢性腎絲球炎。
- 在結婚前，曾檢查過腎功能，腎絲球過濾率，約在40mL/min。(CKD 3b)

病例分享

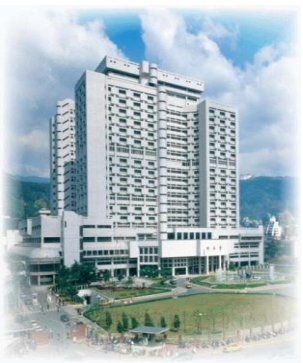
- 血壓約:110/85 mmHg。
- 血中肌肝酸約在2.4 mg/dL，目前無洗腎。
- 白血球數約4000。血色素8.1 g/dL。血小板180K/uL。蛋白尿 300 mg/day。
- 開立micronized progesterone 100 mg 兩顆，陰道使用。

病例分享

- 9~21 周，血壓:110/75~130/85 mmHg。
- 血中肌肝酸約在4~5 mg/dL。
- 白血球數約4000~6000。血色素7~8.1 g/dL。血小板150~190 K/uL。蛋白尿 300 ~700 mg/day。
- 開始EPO 治療。2000 u x 3 times per week

病例分享

- **29周，血壓:160/115 mmHg。**
- **血中肌肝酸 4.3 mg/dL。**
- **白血球數約12000。血色素11.3 g/dL。血小板30 K/uL。蛋白尿 3500 mg/day。**
- **胎兒體重700 gm。**
- **嚴重子癲前症**
- **立即生產**



懷孕時的高血壓疾病

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妊娠高血壓
Gestational hypertension

- **Hypertension firstly noted after 20 weeks of gestation without proteinuria and normalize post partum (transient hypertension of pregnancy)**

  高血壓發生在**20** 周之後，但產後即消失

子癲前症
Preeclampsia

- **Hypertension detected after 20 weeks of gestation in previously normotensive women**
  高血壓發生在**20** 周之後

And 並且需要

- **Proteinuria** 蛋白尿**: urinary protein excretion ≧300 mg in a 24-hour specimen (preferable) or ≧1+ reading on dipstick**

TABLE 40-1. Diagnostic Criteria for Pregnancy-Associated Hypertension

Condition	Criteria Required
Gestational hypertension	BP > 140/90 mmHg after 20 weeks in previously normotensive women
Preeclampsia—Hypertension and:	
Proteinuria	• ≥ 300 mg/24h, or • Protein: creatinine ratio ≥ 0.3 or • Dipstick 1+ persistent[a] ***or***
Thrombocytopenia	• Platelets < 100,000/μL
Renal insufficiency	• Creatinine > 1.1 mg/dL or doubling of baseline[b]
Liver involvement	• Serum transaminase levels[c] twice normal
Cerebral symptoms	• Headache, visual disturbances, convulsions
Pulmonary edema	—

血壓，蛋白尿，血小板，腎功能異常，肝臟功能，腦神經症狀，肺積水

子癲症 Eclampsia

- **Occurrence of seizures in women with preeclampsia, not attributed to other causes**

  沒有其他原因的子癲前症孕婦發生抽搐的情況

TABLE 40-2. Indicators of Severity of Gestational Hypertensive Disorders[a]

Abnormality	Nonsevere[b]	Severe
Diastolic BP	< 110 mm Hg	≥ 110 mm Hg
Systolic BP	< 160 mm Hg	≥ 160 mm Hg
Proteinuria[c]	None to positive	None to positive
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsion (eclampsia)	Absent	Present
Serum creatinine	Normal	Elevated
Thrombocytopenia (< 100,000/μL)	Absent	Present
Serum transaminase elevation	Minimal	Marked
Fetal-growth restriction	Absent	Obvious
Pulmonary edema	Absent	Present

舒張血壓，
收縮血壓，
蛋白尿，
頭痛，
視力影響，
上腹部痛，
尿量減少，
抽蓄，
血小板過低，
腎功能異常，
肝臟功能異常，
胎兒生長遲滯，
肺積水

慢性高血壓

- **Hypertension presented before pregnancy or diagnosed before 20 weeks of gestation**
  高血壓發生在**20** 周之前

- **Hypertension firstly diagnosed during pregnancy and persists post partum**
  產後仍持續高血壓

慢性高血壓併子癲前症
Preeclampsia superimposed on chronic hypertension

- **Newly onset proteinuria in women with hypertension before 20 weeks of gestation**

  高血壓發生在**20** 周之前且有蛋白尿

- **Sudden worsening of high blood pressure and proteinuria, presence of thrombocytopenia (< 100,000 cells/mm^3), or elevated liver enzyme levels in women with hypertension and proteinuria before 20 weeks of gestation** 高

  血壓發生在**20** 周之前，但發生蛋白尿，血壓惡化，血小板過低及肝指數升高

Superimposed Preeclampsia

- 發病率從 **13%** 至 **40%** 不等
- 和高血壓的 **baseline** 嚴重程度直接相關
- 如果懷孕前就有蛋白尿，則風險更高

妊娠加重高血壓 或 合併子癲前症(**Pregnancy-Aggravated Hypertension or Superimposed Preeclampsia)**

- **診斷條件：**
  - **高血壓惡化**
  - **新發生的蛋白尿**
  - **嚴重頭痛和視力障礙等神經系統症狀**
  - **肝腎功能異常**
  - **抽搐**
  - **肺水腫**

懷孕前諮詢

- 高血壓的持續時間
- 血壓控制程度
- 當前治療
- 一般健康狀況，日常活動和飲食習慣
- 需要多種藥物治療或控制不良的女性患有不良妊娠結局的風險較高

懷孕前的進一步評估

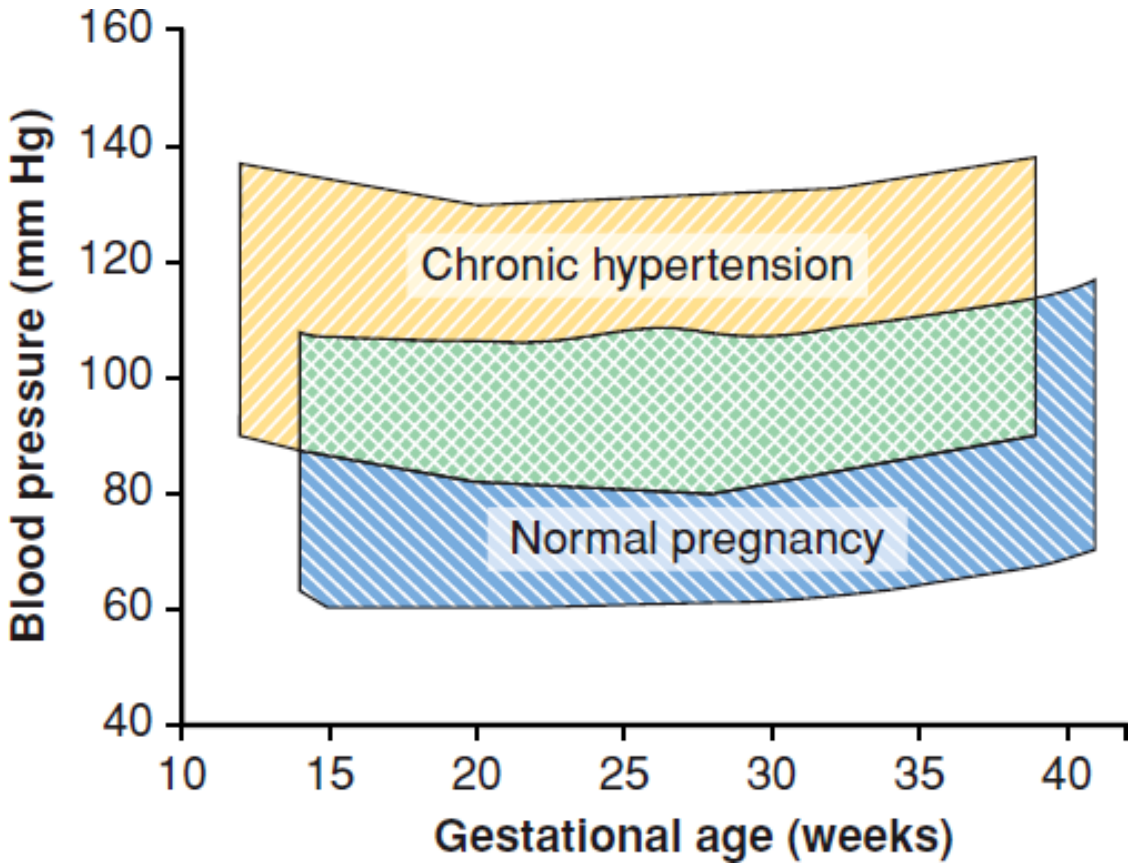
- **疾病持續時間超過5年或合併糖尿病的高血壓婦女**
  - **評估心血管和腎功能**
- 有器官功能障礙證據的婦女或有中風，心肌梗塞，心律失常或心室衰竭等先前不良事件的婦女，在懷孕期間復發或惡化的風險會顯著增加
- 由血清肌酸酐以及尿蛋白測量評估腎功能
- 如果尿意 **spot protein/creatinine ratio > 0.3**，則需要收集**24**小時的小便以進一步量化蛋白尿的總量
- 如果**Creatinine >= 1.4 mg/dl**，則胎兒的死亡率會顯著增加

需謹慎考慮是否懷孕

- 儘管接受治療，舒張壓仍 **≥110mmHg**
- 需要多種抗高血壓藥
- **Creatinine> 2 mg / dL**
- 過去有中風或心肌梗塞等病史

懷孕對慢性高血壓的影響

- 大多數慢性高血壓婦女在妊娠早期血壓下降，並在第三孕期再次上升



懷孕中可能發生的狀況

Maternal	Perinatal
Superimposed preeclampsia子癇前症	**Stillbirth** 死胎
HELLP syndrome	**Growth restriction** 生長遲滯
Placental abruption 胎盤剝離	**Preterm delivery** 早產
Stroke 中風	**Neonatal death** 嬰兒死亡
Acute kidney injury 急性腎損傷	**Neonatal morbidity** 嬰兒併發症
Heart failure 心臟衰竭	
Hypertensive cardiomyopathy 心肌症	
Myocardial infarction 心肌梗塞	
Maternal death 母體死亡	

產婦發病率和死亡率

- 收縮壓≥160mmHg或舒張壓≥110mmHg會迅速引起腎臟或心肺功能障礙或腦出血
- 胎盤早期剝離是一種常見且嚴重的併發症
- 高血壓性心力衰竭
- 主動脈剝離
- 慢性高血壓會提高產婦死亡的五倍風險

預防

- 從 **12** 週至 **34** 週，低劑量 **Aspirin: 81-150 mg/day**
  - 除慢性高血壓外，**Aspirin** 預防子癲前症高危險群的適應症包括前胎子癲前症，多胞胎妊娠，糖尿病，腎臟病和自身免疫性疾病的病史
- 適當的運動
- 飲食與體重控制
- 定期測量血壓和產檢

預防

TABLE 40-5. Some Methods to Prevent Preeclampsia That Have Been Evaluated in Randomized Trials

Dietary manipulation—low-salt diet, calcium or fish oil supplementation
Exercise—physical activity, stretching
Cardiovascular drugs—diuretics, antihypertensive drugs
Antioxidants—ascorbic acid (vitamin C), α-tocopherol (vitamin E), vitamin D
Antithrombotic drugs—low-dose aspirin, aspirin/dipyridamole, aspirin + heparin, aspirin + ketanserin

Modified from Staff, 2014.

懷孕中的處理

- 個人化健康管理
- 飲食諮詢
- 減少抽菸和飲酒，可卡因或其他物質使用
- 不需要低鈉飲食
- 長期或未經治療的高血壓患者：
  - 四分之一的慢性高血壓孕婦也有同心室肥大
    →心血管和腎臟系統進行評估

抗高血壓藥物

Adrenergic-Receptor Blocking Agents

- 週邊作用：交感神經張力下降和心輸出量減少
- 舉例：**propranolol, metoprolol, and atenolol**
- 最常使用: **Labetalol**（被認為是安全的)

- **Centrally :**使血管張力的普遍降低
- 舉例：**clonidine，α- methyldopa**

- 在妊娠中最常用於治療高血壓的：
  - **Methyldopa & labetalol**

Calcium-Channel Blocking Agents

- 常見藥物：**nifedipine (**Generic Name)
  Brand Names: ***Adalat CC, Afeditab CR, Nifediac CC, Nifedical XL, Procardia, Procardia XL, Adalat***)
- **negative inotropic effects** → 會惡化心室功能障礙和充血性心力衰竭
- 可能會加強硫酸鎂的血管活性作用
- 儘管有關懷孕期間使用的數據有限，但目前認為是慢性高血壓的安全療法

Diuretics

- **Thiazide diuretics**是磺胺類藥物，這是第一個用於成功治療慢性高血壓的藥物
- **mildly diabetogenic**
- 會造成懷孕女性血漿容量的增加, 比一般未服用藥物的懷孕女性少 **(20%:50%)**
- **Thiazide diuretics**在懷孕期間的安全性仍有爭議

Vasodilators

- **Hydralazine**可以放鬆動脈平滑肌，數十年來一直用於治療嚴重的**peripartum hypertension**
- 但通常不單獨使用此藥來治療慢性高血壓，因為它具有較弱的抗高血壓作用和容易引起的心跳過速。
- 它可能是與其他抗高血壓藥長期使用的有效輔助手段，特別是如果存在慢性腎功能不全者。

Angiotensin-Converting Enzyme Inhibitors (ACEI)

- 在**RAAS**（**Renin-Angiotensin-Aldosterone System**，腎素—血管張力素—醛固酮系統）系統中，抑制血管張力素轉化酶作用，使**Angiotensin I**（血管張力素**I**）無法轉換成可以強烈收縮血管的**Angiotensin II**（血管張力素**II**）進而達到降血壓的效果

- **在在第二孕期及第三孕期給予它們會導致嚴重的胎兒畸形。**
  - **include oligohydramnios, hypocalvaria, and renal dysfunction**

- **Angiotensin-receptor blockers** 也是類似的作用
- →推測它們與**ACEI**具有相同的胎兒效應，因此也是禁止使用的

治療建議

- 常使用的單一藥物：
- **β-blocking drug** ：例如**labetalol**
- **Calcium-channel blocking** ：例如**nifedipine.**

治療建議

- 對於過去特殊病史的女性，如中風，心梗，心臟或腎功能不全的證據，治療是強制性的。
- 對於減少器官功能障礙，舒張壓水平控制在**≤90mmHg**的治療可減輕進一步的器官損傷

建議使用硫酸鎂的時機

TABLE 40-15. Selective versus Universal Magnesium Sulfate Prophylaxis: Parkland Hospital Criteria to Define Severity of Gestational Hypertension

In a woman with new-onset proteinuric hypertension, at least one of the following criteria is required:

Systolic BP ≥ 160 or diastolic BP ≥ 110 mm Hg
Proteinuria ≥ 2+ by dipstick in a catheterized urine specimen
Serum creatinine > 1.2 mg/dL
Platelet count < 100,000/μL
Aspartate aminotransferase (AST) elevated two times above upper limit of normal range
Persistent headache or scotomata
Persistent midepigastric or right-upper quadrant pain

硫酸鎂的使用

TABLE 40-11. Magnesium Sulfate Dosage Schedule for Severe Preeclampsia and Eclampsia

Continuous Intravenous (IV) Infusion

Give 4- to 6-g loading dose of magnesium sulfate diluted in 100 mL of IV fluid administered over 15–20 min
Begin 2 g/hr in 100 mL of IV maintenance infusion. Some recommend 1 g/hr
Monitor for magnesium toxicity:
- Assess deep tendon reflexes periodically
- Some measure serum magnesium level at 4–6 hr and adjust infusion to maintain levels between 4 and 7 mEq/L (4.8 to 8.4 mg/dL)
- Measure serum magnesium levels if serum creatinine ≥ 1.0 mg/dL

Magnesium sulfate is discontinued 24 hr after delivery

Intermittent Intramuscular Injections

Give 4 g of magnesium sulfate ($MgSO_4 \cdot 7H_2O$ USP) as a 20% solution intravenously at a rate not to exceed 1 g/min
Follow promptly with 10 g of 50% magnesium sulfate solution, one half (5 g) injected deeply in the upper outer quadrant of each buttock through a 3-inch-long 20-gauge needle. (Addition of 1.0 mL of 2% lidocaine minimizes discomfort.) If convulsions persist after 15 min, give up to 2 g more intravenously as a 20% solution at a rate not to exceed 1 g/min. If the woman is large, up to 4 g may be given slowly
Every 4 hr thereafter, give 5 g of a 50% solution of magnesium sulfate injected deeply in the upper outer quadrant of alternate buttocks, but only after ensuring that:
- The patellar reflex is present,
- Respirations are not depressed, and
- Urine output the previous 4 hr exceeded 100 mL

Magnesium sulfate is discontinued 24 hr after delivery

胎兒評估

- 即使是那些患有輕度高血壓的女性，也比一般女性有更大的子癇前症和胎兒生長遲滯的風險，因此仍建議對胎兒健康進行連續產前及超音波評估。

胎兒評估

胎兒評估

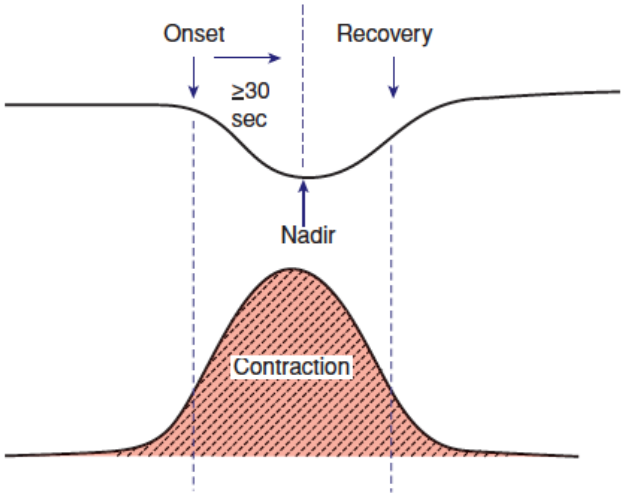


FIGURE 24-14 Features of early fetal heart rate deceleration. Characteristics include a gradual decline in the heart rate with both onset and recovery coincident with the onset and recovery of the contraction. The nadir of the deceleration is 30 seconds or more after the deceleration onset.

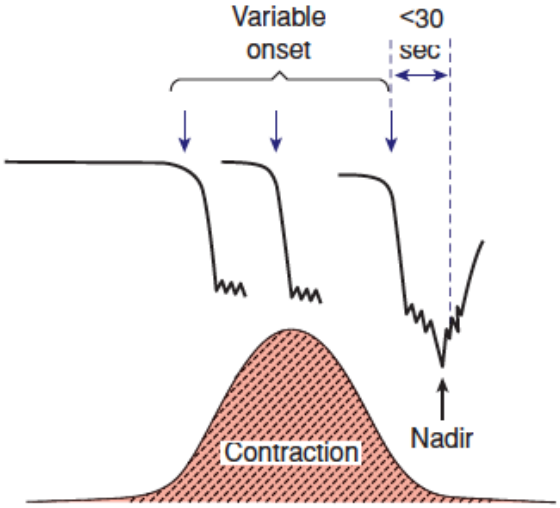


FIGURE 24-18 Features of variable fetal heart rate decelerations. Characteristics include an abrupt decline in the heart rate, and onset that commonly varies with successive contractions. The decelerations measure ≥ 15 bpm for ≥ 15 seconds and have an onset-to-nadir phase of < 30 seconds. Total duration is < 2 minutes.

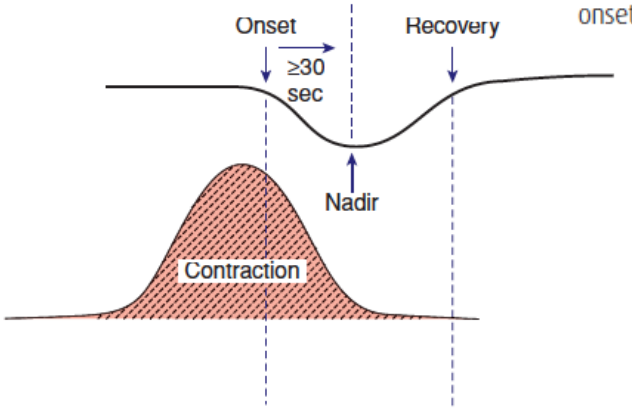


FIGURE 24-16 Features of late fetal heart rate deceleration. Characteristics include gradual decline in the heart rate with the contraction nadir, and recovery occurring after the end of the contraction. The nadir of the deceleration occurs 30 seconds or more after the onset of the deceleration.

胎兒評估

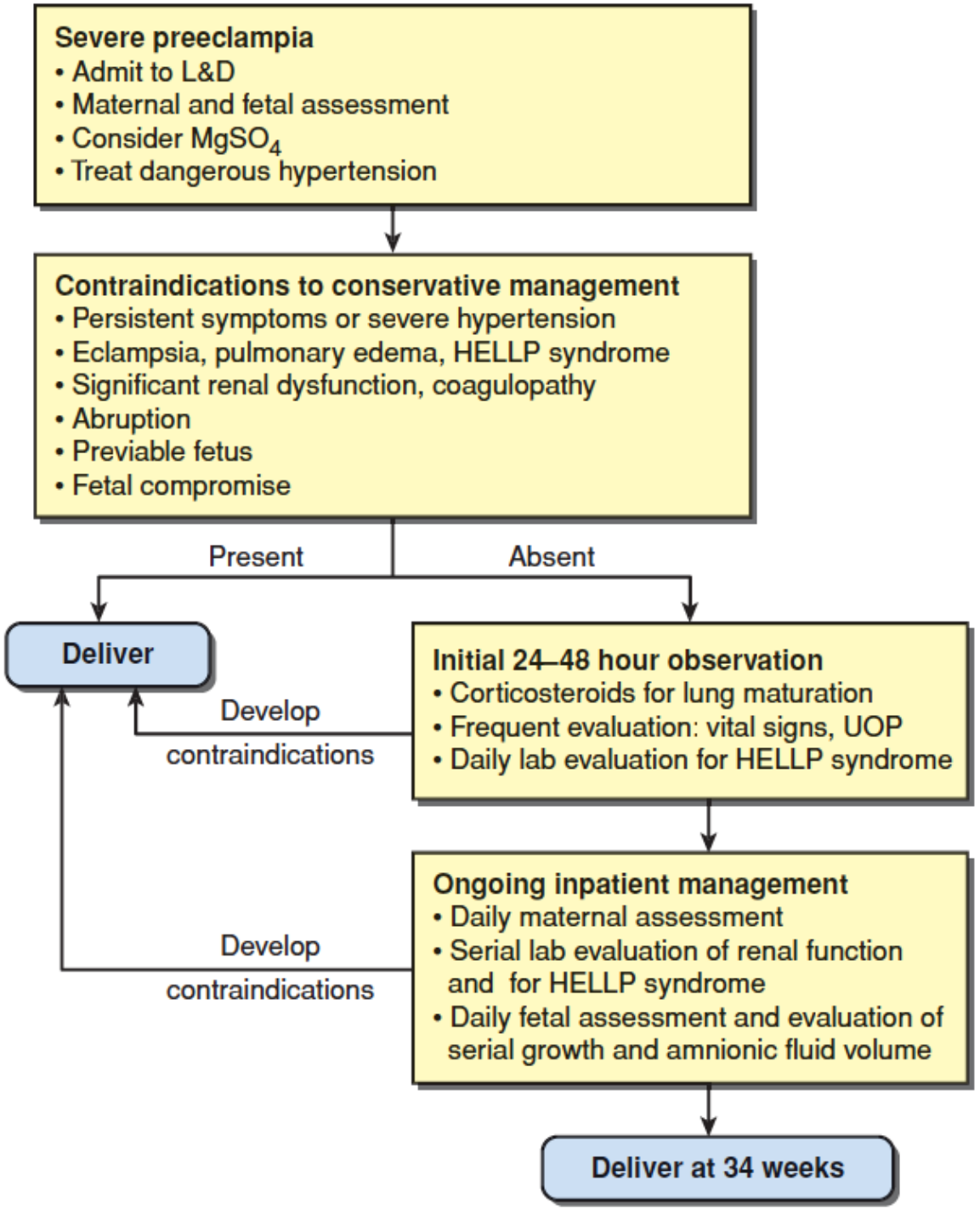
TABLE 17-2. Components and Scores for the Biophysical Profile

Component	Score 2	Score 0
Nonstress test[a]	≥ 2 accelerations of ≥ 15 beats/min for ≥ 15 sec within 20–40 min	0 or 1 acceleration within 20–40 min
Fetal breathing	≥ 1 episode of rhythmic breathing lasting ≥ 30 sec within 30 min	< 30 sec of breathing within 30 min
Fetal movement	≥ 3 discrete body or limb movements within 30 min	< 3 discrete movements
Fetal tone	≥ 1 episode of extremity extension and subsequent return to flexion	0 extension/flexion events
Amnionic fluid volume[b]	A pocket of amnionic fluid that measures at least 2 cm in two planes perpendicular to each other (2 × 2 cm pocket)	Largest single vertical pocket ≤ 2 cm

胎兒評估

TABLE 17-3. Interpretation of Biophysical Profile Score

Biophysical Profile Score	Interpretation	Recommended Management
10	Normal, nonasphyxiated fetus	No fetal indication for intervention; repeat test weekly except in diabetic patients and postterm pregnancy (twice weekly)
8/10 (Normal AFV) 8/8 (NST not done)	Normal, nonasphyxiated fetus	No fetal indication for intervention; repeat testing per protocol
8/10 (Decreased AFV)	Chronic fetal asphyxia suspected	Deliver
6	Possible fetal asphyxia	If amnionic fluid volume abnormal, deliver If normal fluid at > 36 weeks with favorable cervix, deliver If repeat test ≤ 6, deliver If repeat test > 6, observe and repeat per protocol
4	Probable fetal asphyxia	Repeat testing same day; if biophysical profile score ≤ 6, deliver
0 to 2	Almost certain fetal asphyxia	Deliver


Severe preeclampia
• Admit to L&D
• Maternal and fetal assessment
• Consider $MgSO_4$
• Treat dangerous hypertension
Contraindications to conservative management
• Persistent symptoms or severe hypertension
• Eclampsia, pulmonary edema, HELLP syndrome
• Significant renal dysfunction, coagulopathy
• Abruption
• Previable fetus
• Fetal compromise
Present
Absent
Deliver
Develop contraindications
Initial 24–48 hour observation
• Corticosteroids for lung maturation
• Frequent evaluation: vital signs, UOP
• Daily lab evaluation for HELLP syndrome
Develop contraindications
Ongoing inpatient management
• Daily maternal assessment
• Serial lab evaluation of renal function and for HELLP syndrome
• Daily fetal assessment and evaluation of serial growth and amnionic fluid volume
Deliver at 34 weeks

Severe preeclampia

- Admit to L&D
- Maternal and fetal assessment
- Consider $MgSO_4$
- Treat dangerous hypertension

Contraindications to conservative management

- Persistent symptoms or severe hypertension
- Eclampsia, pulmonary edema, HELLP syndrome
- Significant renal dysfunction, coagulopathy
- Abruption
- Previable fetus
- Fetal compromise

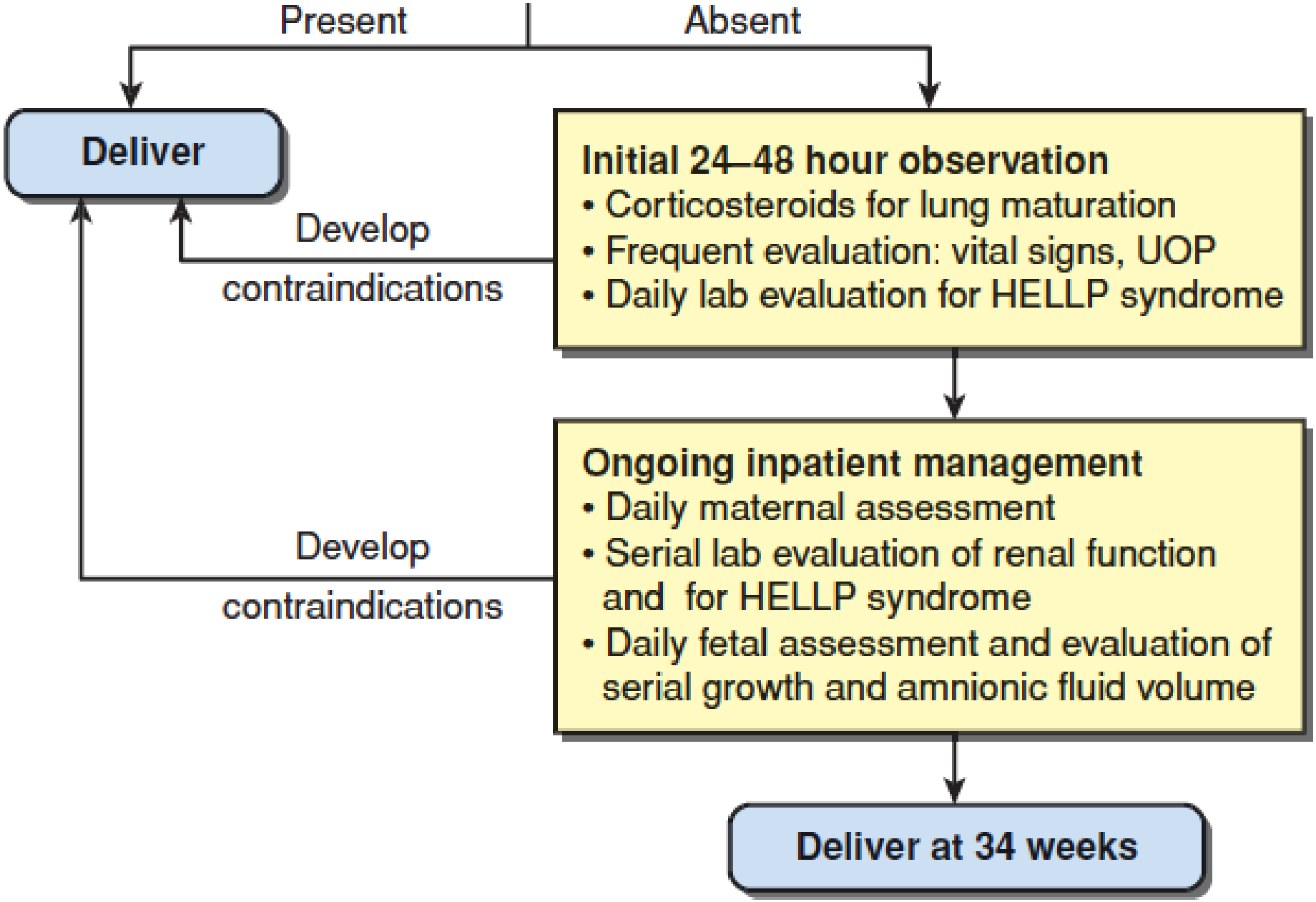

Present
Absent
Deliver
Initial 24–48 hour observation
• Corticosteroids for lung maturation
• Frequent evaluation: vital signs, UOP
• Daily lab evaluation for HELLP syndrome
Develop
contraindications
Ongoing inpatient management
• Daily maternal assessment
• Serial lab evaluation of renal function and for HELLP syndrome
• Daily fetal assessment and evaluation of serial growth and amnionic fluid volume
Develop
contraindications
Deliver at 34 weeks

TABLE 40-10. Indications for Delivery in Women < 34 Weeks' Gestation Managed Expectantly

Corticosteroid Therapy for Lung Maturation[a] and Delivery after Maternal Stabilization:
Uncontrolled severe hypertension
Eclampsia
Pulmonary edema
Placental abruption
Disseminated intravascular coagulation
Nonreassuring fetal status
Fetal demise

TABLE 40-10. Indications for Delivery in Women < 34 Weeks' Gestation Managed Expectantly

Corticosteroid Therapy for Lung Maturation—Delay Delivery 48 hr If Possible:

- Preterm ruptured membranes or labor
- Thrombocytopenia < 100,000/μL
- Hepatic transaminase levels twice upper limit of normal
- Fetal-growth restriction
- Oligohydramnios
- Reversed end-diastolic Doppler flow in umbilical artery
- Worsening renal dysfunction

生產

- 對於沒有合併子癲前症的慢性高血壓懷孕婦女：
  - 超過39周生產會增加嚴重型子癲前症的機率
  - 小於37周生產會增加新生兒的併發症
  - 可以考慮催生，且大多能經陰道生產

產後照護

- **對於持續性嚴重高血壓，要考慮其他可能病因，例如嗜鉻細胞瘤（pheochromocytoma）或庫欣病（Cushing disease）等病因**

產後照護

- 生產後可能的併發症：腦水腫或肺水腫，心力衰竭，腎功能不全或腦出血
  - 特別是生產後的前48小時，突發的血壓升高 < spikes >
  - 中度或重度的突發性高血壓可能加劇舒張功能障礙，引起收縮功能障礙，並導致肺水腫
  - 及時控制高血壓以及合併使用 lasix 的利尿通常可以迅速消除肺水腫

產後照護

- 分娩後，隨著孕婦周邊血管阻力的增加，左心室的負荷也會增加。
- 子癲前症造成的內皮破壞釋出interstitial fluid 會加劇上述狀況

- 產前的抗高血壓治療可以在產褥期重新開始
- 有些女性可使用靜脈注射會口服的**lasix**來增加產後的排尿
- 可監測每日體重
- 有研究顯示在嚴重型子癲前症的女性，產後使用**NSAIDs**會升高血壓
- 患有慢性高血壓的女性患有終身心血管併發症的風險很高，特別是合併有糖尿病，肥胖和代謝症候群。

懷孕時的心血管疾病

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TABLE 49-2. Clinical Indicators of Heart Disease During Pregnancy

Symptoms

- Progressive dyspnea or orthopnea
- Nocturnal cough
- Hemoptysis
- Syncope
- Chest pain

Clinical Findings

- Cyanosis
- Clubbing of fingers
- Persistent neck vein distention
- Systolic murmur grade 3/6 or greater
- Diastolic murmur
- Cardiomegaly
- Persistent arrhythmia
- Persistent split second sound
- Criteria for pulmonary hypertension

TABLE 49-3. World Health Organization (WHO) Risk Classification of Cardiovascular Disease and Pregnancy

Risk Category	Associated Conditions
WHO 1—Risk no higher than general population	Uncomplicated, small, or mild: Pulmonary stenosis Ventricular septal defect Patent ductus arteriosus Mitral valve prolapse with no more than trivial mitral regurgitation Successfully repaired simple lesions: Ostium secundum atrial septal defect Ventricular septal defect Patent ductus arteriosus Total anomalous pulmonary venous drainage Isolated ventricular extrasystoles and atrial ectopic beats

TABLE 49-3. World Health Organization (WHO) Risk Classification of Cardiovascular Disease and Pregnancy

Risk Category	Associated Conditions
WHO 2—Small increase in risk of maternal mortality and morbidity	If otherwise uncomplicated: Unoperated atrial septal defect Repaired Fallot tetralogy Most arrhythmias
WHO 2 or 3—depends on individual case	Mild left ventricular impairment Hypertrophic cardiomyopathy Native or tissue valvular heart disease not considered WHO 4 Marfan syndrome without aortic dilation Heart transplantation
WHO 3—Significantly increased risk of maternal mortality or expert cardiac and obstetrical care required	Mechanical valve Systemic right ventricle—congenitally corrected transposition, simple transposition post-Mustard or -Senning repair Post-Fontan operation Cyanotic heart disease Other complex congenital heart disease

TABLE 49-3. World Health Organization (WHO) Risk Classification of Cardiovascular Disease and Pregnancy

Risk Category	Associated Conditions
WHO 4—Very high risk of maternal mortality or severe morbidity; pregnancy contraindicated and termination discussed	Pulmonary arterial hypertension Severe systemic ventricular dysfunction (NYHA III-IV or LVEF < 30%) Previous peripartum cardiomyopathy with any residual impairment of left ventricular function Severe left heart obstruction Marfan syndrome with aorta dilated > 40 mm

TABLE 49-6. American College of Chest Physicians Guidelines for Anticoagulation of Pregnant Women with Mechanical Prosthetic Valves

Any one of the following anticoagulant regimens is recommended:
Adjusted-dose LMWH twice daily throughout pregnancy. The doses should be adjusted to achieve the manufacturer's peak anti-Xa level 4 hours after subcutaneous injection
Adjusted-dose UFH administered every 12 hours throughout pregnancy. The doses should be adjusted to keep the midinterval aPTT at least twice control or attain an anti-Xa level of 0.35 to 0.70 U/mL
LMWH or UFH as above until 13 weeks' gestation, then warfarin substitution until close to delivery when LMWH or UFH is resumed
In women judged to be at very high risk of thromboembolism and in whom concerns exist about the efficacy and safety of LMWH or UFH as dosed above—some examples include older-generation prosthesis in the mitral position or history of thromboembolism—warfarin treatment is suggested throughout pregnancy with replacement by UFH or LMWH (as above) close to delivery. In addition, low-dose aspirin—75 to 100 mg daily—should be orally administered

aPTT = activated partial thromboplastin time; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin.

TABLE 49-7. Major Cardiac Valve Disorders

Type	Cause	Pathophysiology	Pregnancy
Mitral stenosis	Rheumatic valvulitis	LA dilation and passive pulmonary hypertension Atrial fibrillation	Heart failure from fluid overload, tachycardia
Mitral insufficiency	Rheumatic valvulitis Mitral-valve prolapse LV dilatation	LV dilatation and eccentric hypertrophy	Ventricular function improves with afterload decrease
Aortic stenosis	Congenital bicuspid valve	LV concentric hypertrophy, decreased cardiac output	Moderate stenosis is tolerated; severe is life-threatening with decreased preload, e.g., obstetrical hemorrhage or regional analgesia
Aortic insufficiency	Rheumatic valvulitis Connective-tissue disease Congenital	LV hypertrophy and dilatation	Ventricular function improves with afterload decrease
Pulmonary stenosis	Rheumatic valvulitis Congenital	Severe stenosis associated with RA and RV enlargement	Mild stenosis usually well tolerated; severe stenosis associated with right heart failure and atrial arrhythmias

LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

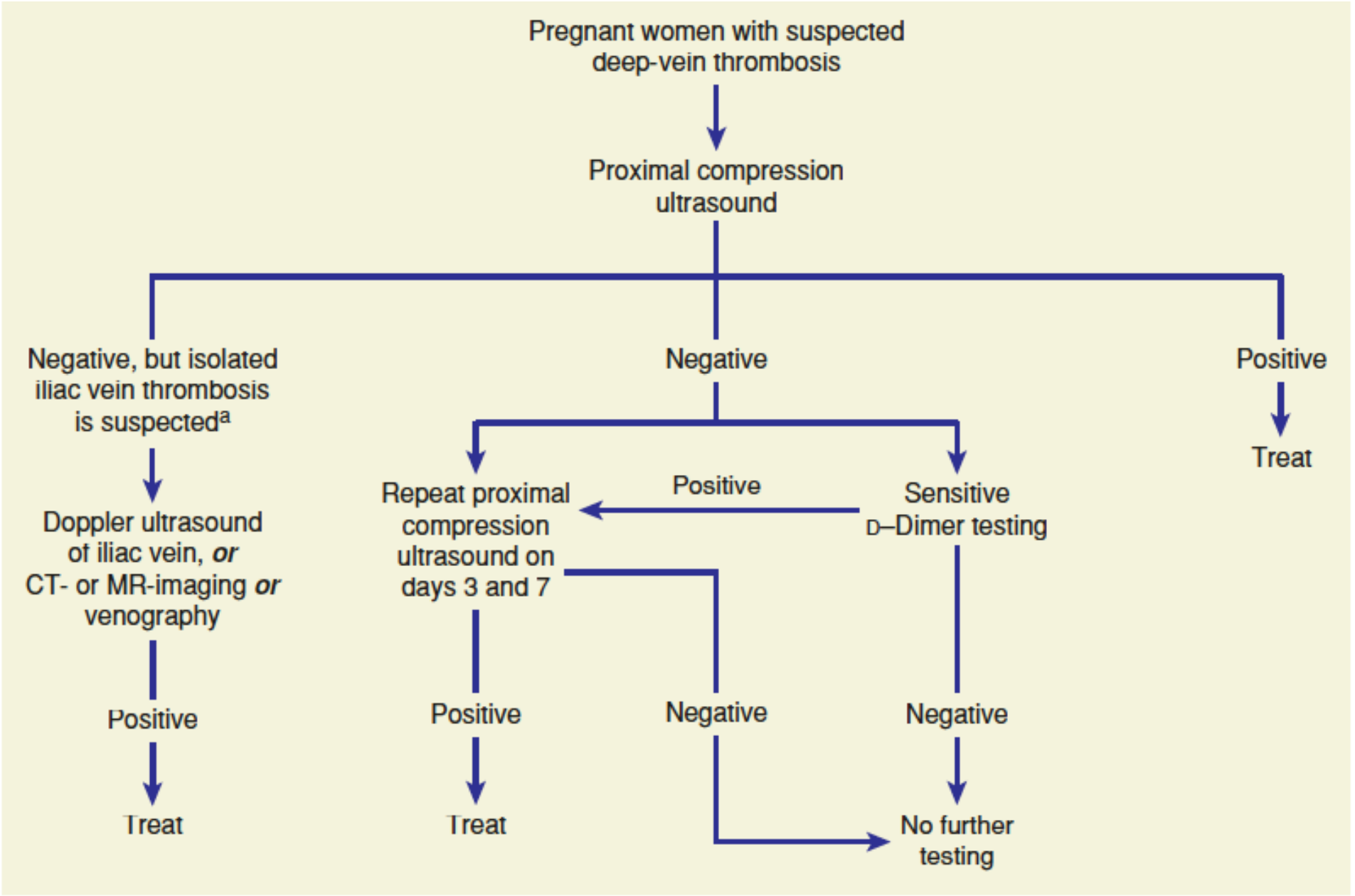
Pregnant women with suspected deep-vein thrombosis
Proximal compression ultrasound
Negative, but isolated iliac vein thrombosis is suspected[a]
Doppler ultrasound of iliac vein, or CT- or MR-imaging or venography
Positive
Treat
Negative
Repeat proximal compression ultrasound on days 3 and 7
Positive
Positive
Treat
Negative
No further testing
Sensitive D–Dimer testing
Positive
Negative
Positive
Treat

TABLE 52-5. Anticoagulation Regimen Definitions

Anticoagulation Regimen	Definition
Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily Tinzaparin, 4,500 units SC once daily
Therapeutic LMWH†	Enoxaparin, 1 mg/kg every 12 hours Dalteparin, 200 units/kg once daily Tinzaparin, 175 units/kg once daily Dalteparin, 100 units/kg every 12 hours May target an anti-Xa level in the therapeutic range of 0.6–1.0 units/mL for twice daily regimen; slightly higher doses may be needed for a once-daily regimen.
Minidose prophylactic UFH	UFH, 5,000 units SC every 12 hours
Prophylactic UFH	UFH, 5,000–10,000 units SC every 12 hours UFH, 5,000–7,500 units SC every 12 hours in first trimester UFH 7,500–10,000 units SC every 12 hours in the second trimester UFH, 10,000 units SC every 12 hours in the third trimester, unless the aPTT is elevated
Therapeutic UFH†	UFH, 10,000 units or more SC every 12 hours in doses adjusted to target aPTT in the therapeutic range (1.5–2.5) 6 hours after injection
Postpartum anticoagulation	Prophylactic LMWH/UFH for 4–6 weeks or vitamin K antagonists for 4–6 weeks with a target INR of 2.0–3.0, with initial UFH or LMWH therapy overlap until the INR is 2.0 or more for 2 days
Surveillance	Clinical vigilance and appropriate objective investigation of women with symptoms suspicious of deep vein thrombosis or pulmonary embolism

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; LMWH, low molecular weight heparin; SC, subcutaneously; UFH, unfractionated heparin.
*Although at extremes of body weight, modification of dose may be required.
†Also referred to as weight adjusted, full treatment dose.

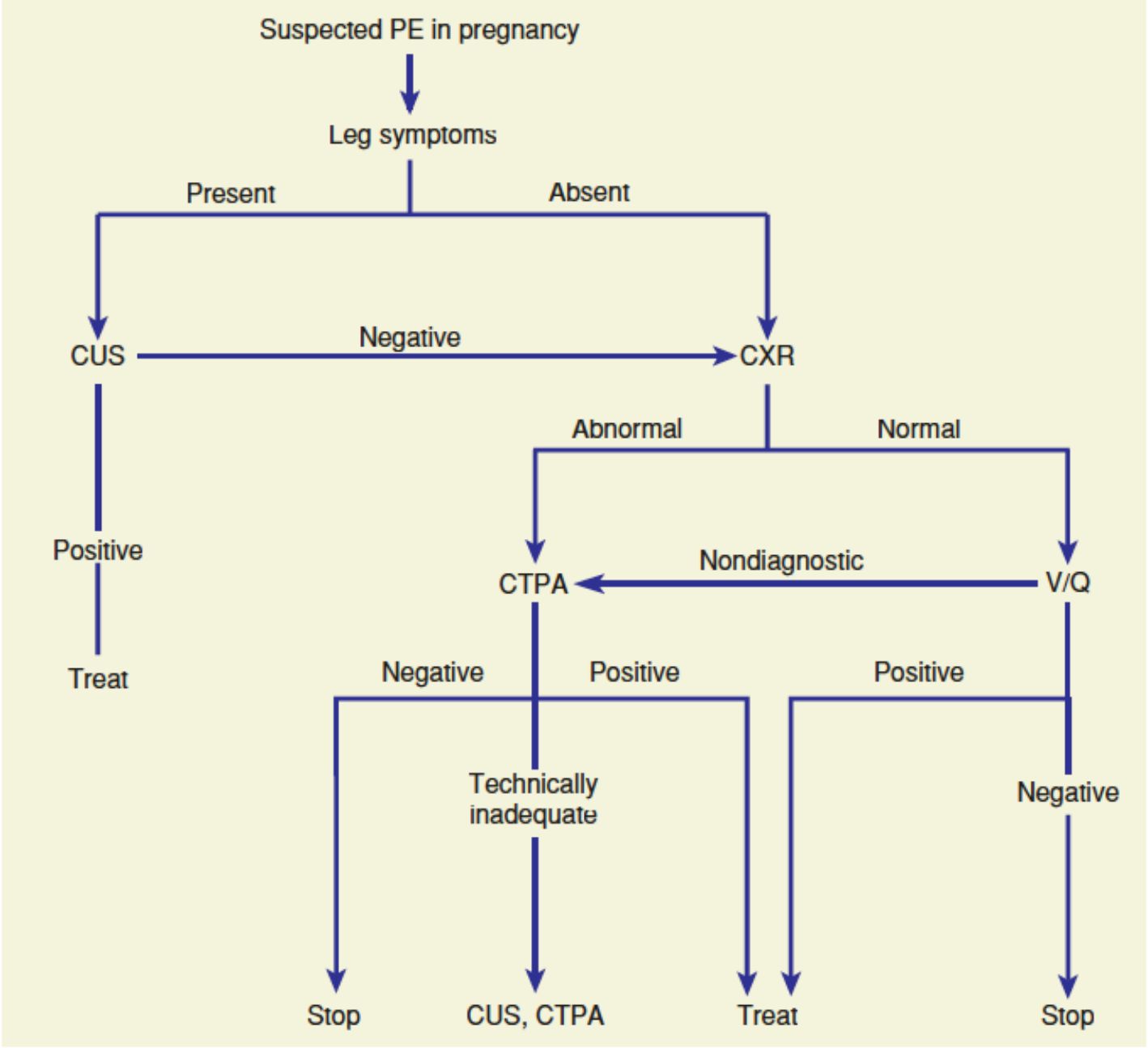

FIGURE 52-4 The American Thoracic Society and Society of Thoracic Radiology diagnostic algorithm for suspected pulmonary embolism during pregnancy. CTPA = computed tomographic pulmonary angiography; CUS = compression ultrasonography; CXR = chest x-ray; PE = pulmonary embolism; V/Q = ventilation/perfusion scintigraphy. (Redrawn from Leung, 2011, with permission.)

懷孕時的呼吸道疾病

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Management of Chronic Asthma

The management guidelines of the Working Group on Asthma and Pregnancy include:

1. Patient education—general asthma management and its effect on pregnancy
2. Environmental precipitating factors—avoidance or control Viral infections—including the common cold—are frequent triggering events (Murphy, 2013).
3. Objective assessment of pulmonary function and fetal well-being—monitor with PEFR or FEV_1
4. Pharmacological therapy—in appropriate combinations and doses to provide baseline control and treat exacerbations Compliance may be a problem, and periodic medication reviews are helpful (Sawicki, 2012).

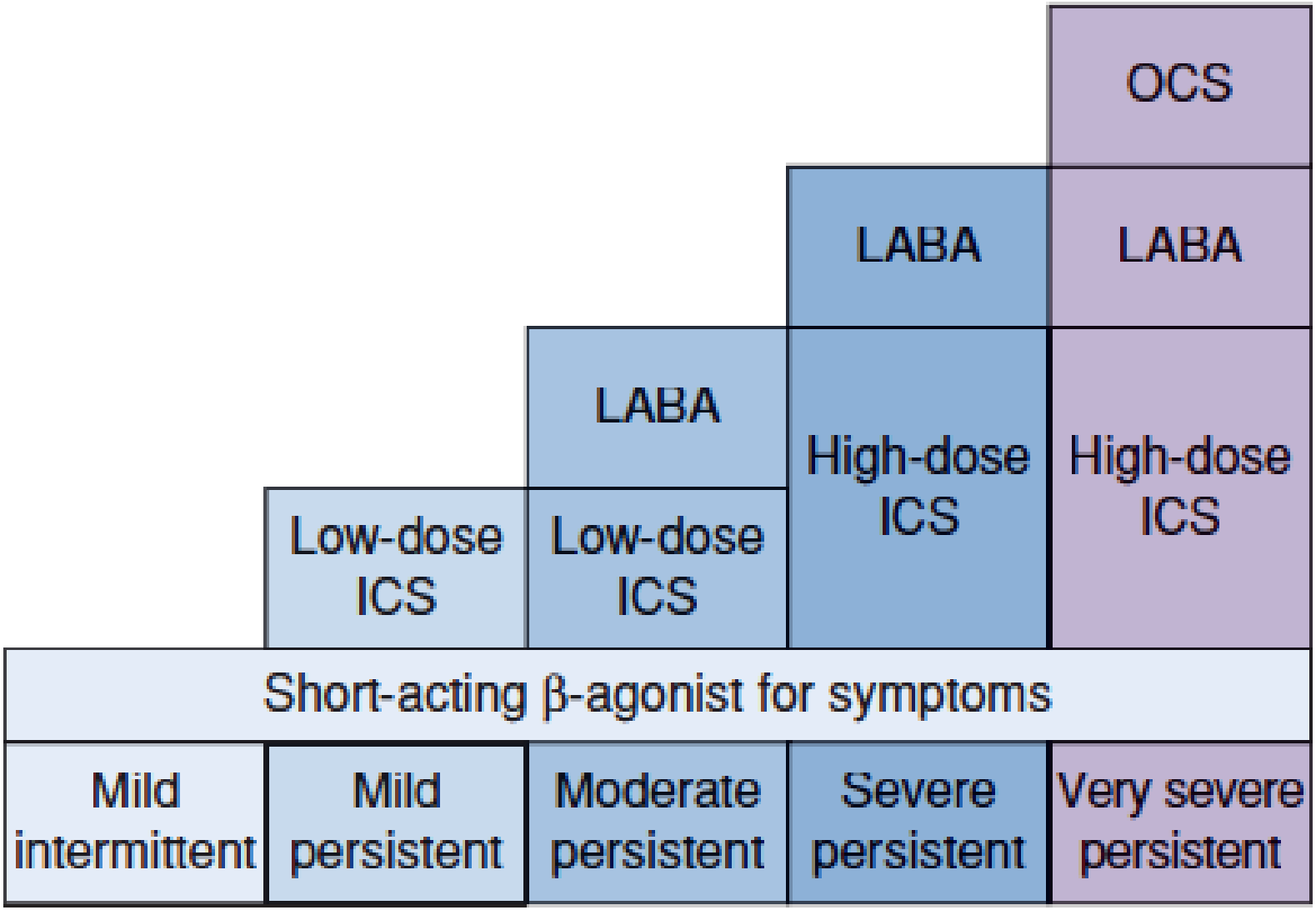

FIGURE 51-2 Stepwise approach to asthma treatment. ICS = inhaled corticosteroids; LABA = long-acting β-agonists; OCS = oral corticosteroids. (Modified from Barnes, 2012.)

TABLE 51-3. Criteria for Severe Community-Acquired Pneumonia[a]

Respiratory rate ≥ 30/min
Pa_{O_2}/Fi_{O_2} ratio ≤ 250
Multilobular infiltrates
Confusion/disorientation
Uremia
Leukopenia—WBC < 4000/μL
Thrombocytopenia—platelets < 100,000/μL
Hypothermia—core temperature < 36°C
Hypotension requiring aggressive fluid resuscitation

[a]Criteria of the Infectious Diseases Society of America/American Thoracic Society.
WBC = white blood cell.
Adapted from Mandell, 2007.

懷孕時的泌尿道疾病

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TABLE 53-1. Oral Antimicrobial Agents Used for Treatment of Pregnant Women with Asymptomatic Bacteriuria

Single-dose treatment
Amoxicillin, 3 g
Ampicillin, 2 g
Cephalosporin, 2 g
Nitrofurantoin, 200 mg
Trimethoprim-sulfamethoxazole, 320/1600 mg

TABLE 53-1. Oral Antimicrobial Agents Used for Treatment of Pregnant Women with Asymptomatic Bacteriuria

3-day course

Amoxicillin, 500 mg three times daily
Ampicillin, 250 mg four times daily
Cephalosporin, 250 mg four times daily
Ciprofloxacin, 250 mg twice daily
Levofloxacin, 250 or 500 mg daily
Nitrofurantoin, 50 to 100 mg four times daily or 100 mg twice daily
Trimethoprim-sulfamethoxazole, 160/800 mg two times daily

TABLE 53-1. Oral Antimicrobial Agents Used for Treatment of Pregnant Women with Asymptomatic Bacteriuria

Other

Nitrofurantoin, 100 mg four times daily for 10 days
Nitrofurantoin, 100 mg twice daily for 5 to 7 days
Nitrofurantoin, 100 mg at bedtime for 10 days

Treatment failures

Nitrofurantoin, 100 mg four times daily for 21 days

Suppression for bacterial persistence or recurrence

Nitrofurantoin, 100 mg at bedtime for pregnancy remainder

TABLE 53-2. Management of the Pregnant Woman with Acute Pyelonephritis

Hospitalize patient
Obtain urine and blood cultures
Evaluate hemogram, serum creatinine, and electrolytes
Monitor vital signs frequently, including urinary output—consider indwelling catheter
Establish urinary output ≥ 50 mL/hr with intravenous crystalloid solution
Administer intravenous antimicrobial therapy (see text)
Obtain chest radiograph if there is dyspnea or tachypnea
Repeat hematology and chemistry studies in 48 hours
Change to oral antimicrobials when afebrile
Discharge when afebrile 24 hours, consider antimicrobial therapy for 7 to 10 days
Repeat urine culture 1 to 2 weeks after antimicrobial therapy completed

TABLE 53-3. Patterns of Clinical Glomerulonephritis

Acute Nephritic Syndromes: poststreptococcal, infective endocarditis, SLE, antiglomerular basement membrane disease, IgA nephropathy, ANCA vasculitis, Henoch-Schönlein purpura, cryoglobulinemia, membranoproliferative and mesangioproliferative glomerulonephritis
Pulmonary-Renal Syndromes: Goodpasture, ANCA vasculitis, Henoch-Schönlein purpura, cryoglobulinemia
Nephrotic Syndromes: minimal change disease, focal segmental glomerulosclerosis, membranous glomerulonephritis, diabetes, amyloidosis, others
Basement Membrane Syndromes: anti-GBM disease, others
Glomerular Vascular Syndromes: atherosclerosis, chronic hypertension, sickle-cell disease, thrombotic microangiopathies, antiphospholipid antibody syndrome, ANCA vasculitis, others
Infectious Disease-Associated Syndromes: poststreptococcal, infective endocarditis, HIV, HBV, HCV, syphilis, others

ANCA = antineutrophilic cytoplasmic antibodies; anti-GBM = anti-glomerular basement membrane; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IgA = immunoglobulin A; SLE = systemic lupus erythematosus.

慢性腎臟病婦女與懷孕

Hypertension (BP>= 140/90 mmHg)

CKD:

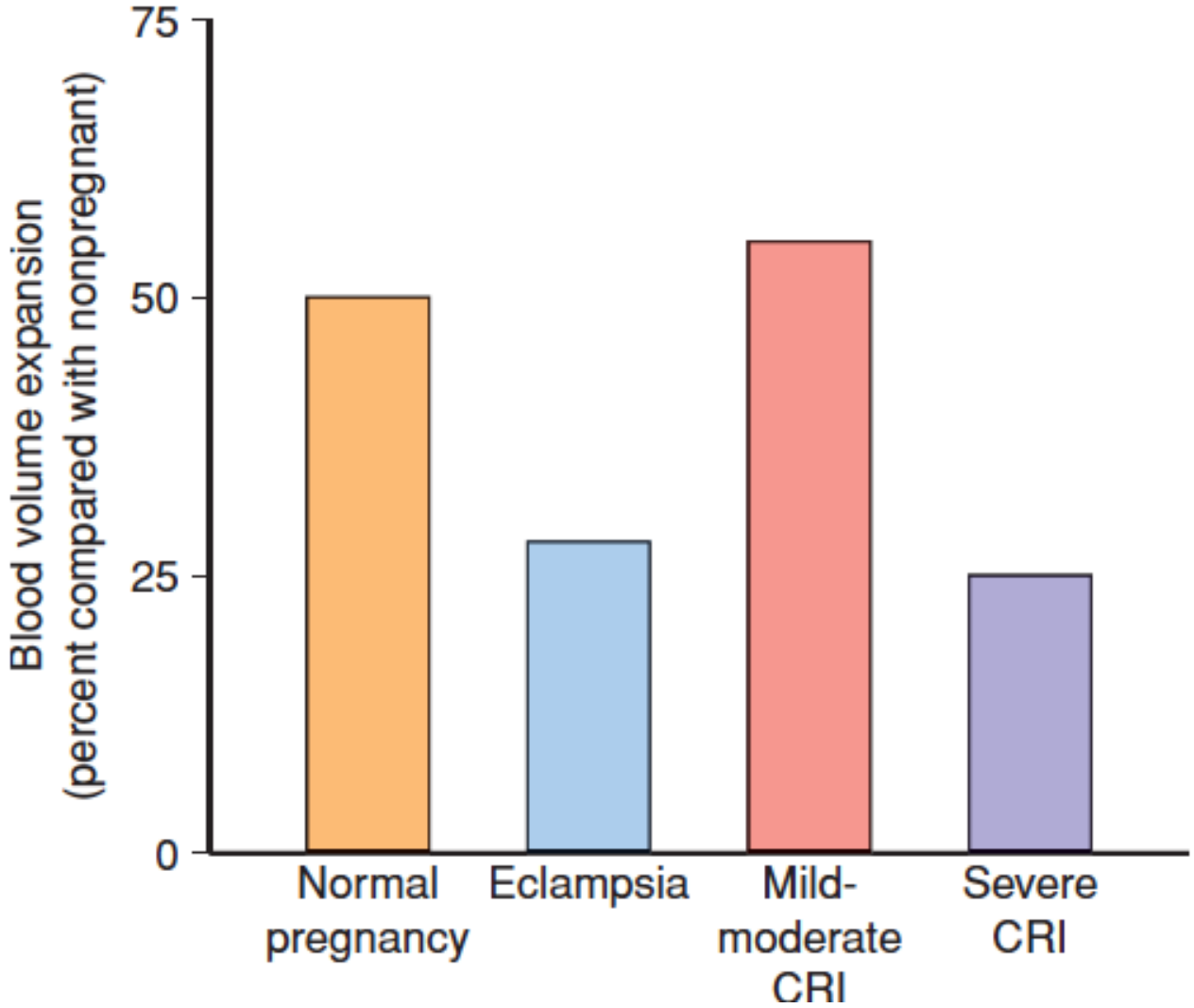
Stage 1 GFR >90 mL/min *(and signs of kidney*
Stage 2 GFR 90-60 mL/min *involvement)*
Stage 3a GFR 60-45 mL/min
Stage 3b GFR 45-30 mL/min
Stage 4 GFR 30-15 mL/min
Stage 5 GFR <15 mL/min or RRT

Proteinuria:

from
Micro-albuminuria 0.1- 0.3 g/day to
nephrotic proteinuria >= 3 g/day

G.B. Piccoli et al. / Best Practice & Research Clinical Obstetrics and Gynaecology 29 (2015) 625–642

王鵬惠



腎臟疾病婦女懷孕與一般婦女懷孕的血量比較

慢性腎臟病婦女懷孕的照護

- 頻繁及規則量血壓。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕的照護

- 頻繁及規則量血壓。
- 血中肌肝酸濃度測量。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕的照護

- 頻繁及規則量血壓。
- 血中肌肝酸濃度測量。
- 24小時小便蛋白尿偵測。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕的照護

- 頻繁及規則量血壓。
- 血中肌肝酸濃度測量。
- 24小時小便蛋白尿偵測。
- 小便檢查，並治療小便感染。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕的照護

- 不建議限制蛋白質飲食。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕的照護

- 不建議限制蛋白質飲食。
- 貧血時，可用血球生成素治療。
- 規則胎兒超音波檢查。
- 迅速治療伴隨的高血壓。

Peng-Hui Wang, M.D., Ph.D.

慢性腎臟病婦女懷孕後本身預後

- 高達三成在兩至三年內，演變成洗腎階段。

慢性腎臟病婦女懷孕後本身預後

- 高達三成在兩至三年內，演變成洗腎階段。
- 蛋白尿是一個有效的預測指標。

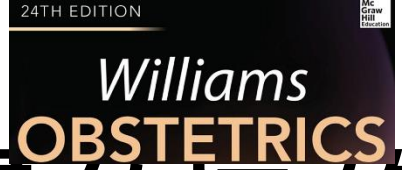
Table 3 | Drug safety in pregnancy

Safe	Not safe	Safety not determined
Immunosuppressants		
Tacrolimus	Cyclophosphamide	Sirolimus
Cyclosporin	Mycophenolate products	Everolimus
Azathioprine	Rituximab	
Corticosteroids		
Hydroxychloroquine		
Antihypertensives		
Labetalol	Angiotensin-converting enzyme inhibitors	
Calcium channel antagonists	Angiotensin receptor blockers	
Methyldopa	Minoxidil	
Hydralazine		
Furosemide		
Antibiotics commonly used in immunosuppressed patients		
Aciclovir	Ganciclovir	
Valaciclovir	Valganciclovir	
	Co-Trimoxazole	
Lamivudine	Quinolones	
Tenofovir		
Isoniazid		
Nystatin (topical)		

Kidney International (2017) **91,** 1047–1056

慢性腎臟病婦女懷孕藥物治療的安全性

Peng-Hui Wang, M.D., Ph.D.



洗腎婦女懷孕的預後

TABLE 53-6. Pregnancy Outcomes in 156 Women Undergoing Dialysis During Pregnancy

	Pregnancies			Pregnancy Outcomes (%)			
Study (Year)	N	Delivery (wk)	Birthweight (g)	Hypertension	Hydramnios	Perinatal Mortality	Surviving Infants
Toma (1999)	54	31.9	1545	35	44	33	67
Chao (2002)	13	32	1540	72	46	31	69
Tan (2006)	11	31	1390	36	18	18	82
Chou (2008)	13	30.8	1510	57	71	50	50
Luders (2010)	52	32.7	1555	67	40	13	87
Shahir (2013)	13	NS	2130	19[a]	14	22	78
Jesudason (2014)	77	33.8	1750	NS	NS	20	80
Approximate averages	233	~32	~1600	~45–5	~44	~20–5	~80

[a]Preeclampsia only.
NS = not stated.

洗腎婦女懷孕的預後

Table 2
Previous case series (>5 cases) of pregnancy in women on chronic dialysis after 1990

Number	Author	Dialysis	Case number (success rate%)
1	Romao et al. [2]	Hemodialysis	11/14 (78.6)
		Peritoneal dialysis	1/3 (33.3)
2	Bagon et al. [7]	Hemodialysis	9/15 (60)
3	Maruyama et al. [15]	Hemodialysis	4/5 (80)
4	Nakabayashi et al. [8]	Hemodialysis	11/15 (73.3)
5	Chao et al. [4]	Hemodialysis	9/13 (69)
6	Luciani et al. [10]	Hemodialysis	2/5 (40)
7	Eroğlu et al. [5]	Hemodialysis	6/7 (85.7)
8	Haase et al. [6]	Hemodialysis	5/5 (100)
9	Malik et al. [12]	Hemodialysis	7/12 (58)
10	Tan et al. [13]	Hemodialysis	8/10 (80)
		Peritoneal dialysis	1/1 (100)

Only cases series studies with more than five cases were listed above. Research using questionnaires was excluded. Patients who decided to terminate pregnancy electively were excluded. Only live infants or children were included in the group of successful deliveries.

European Journal of Obstetrics & Gynecology and Reproductive Biology 136 (2008) 165–170

台灣洗腎婦女懷孕的預後

Table 1
Brief data of the pregnant women on chronic dialysis in our hospital

Case no.	Age (years)	Complications	Gestational age (weeks)	Birth weight (g)	Long-term follow-up	Dialysis time before conception	Frequency (h × times/week)/ volume (l × times)	Renal disease	*Kt/V*	Residual urine (ml/day)	Hemoglobin (mg/dl)
1	28	PHA + IUGR + HTN + PT	34	1446	Healthy	26 gestational weeks[a]	3 h × 5	CGN	0.94	900 ml	8.6 ± 0.6
2	37	PHA + HTN + PT	31	1442	Healthy	10 years	4 h × 6	CGN	1.61	Auria	10.7 ± 1.8
3	42	PHA + PT	32	2092	Healthy[b]	6 years	4 h × 6	CGN	1.2	Auria	10.0 ± 2.5
4	26	HTN	31	1810	Healthy	4 years	4 h × 5	SLE	NA	Oliguria	9.4 ± 1.5
5	36	PHA + PT	27	1100	Death	7 years	4.5 h × 6	CGN	1.56	Auria	9.7 ± 0.1
6	39	IUGR + HTN + PT + still birth	30	1150	Still birth	26 gestational weeks[a]	4 h × 6	CGN	1.47	350 ml	11.9
7	36	PHA	31	1540	Still birth	7 months	5 h × 5	PRE	NA	NA	9.3 ± 0.0
8	39	PT	35	2388	Healthy	3 years	1.5 l (1.5%) × 6	SLE	3.36/1.13 (residual)	855 ml	8.9 ± 0.2
9	31	IUGR	34	1004	Still birth	2 years	2 l (1.5%) × 4 + 2 l (2.5%) × 1	SLE	1.71	Oliguria	11.1 ± 0.7
10	34	PHA + PT	22	440	Death	8 months	1.5 l (1.5%) × 4 + 1.5 l (2.5%) × 2	RPGN	2.77/0.31 (residual function)	400 ml	9.5 ± 0.5

EPO dosage (units × times/week)	Increased weight during pregnancy/dry weight (kg)
3000 × 3	10/53.3
Not use	12/61.3
4000 × 3	9/72.2
Not use	8.8/58.8
2000 × 4	13.5/53.5
2000 × 2	NA/45.6
2000 × 5	9/59
2000 × 2	11.9/64.9
Not use	10/61
2000 × 7	3.2/52

PHA = polyhydramnios; IUGR = intra-uterine growth restriction; HTN = hypertension; PT = preterm; HTN = hypertension; CGN = chronic glomerulonephritis; SLE = systemic lupus erythematosus; PRE = -preeclampsia; RPGN = rapid progressive glomerulonephritis; NA = not available.

[a] Patient started regular hemodialysis after conception.

[b] Time of follow up was less than 2 years.

European Journal of Obstetrics & Gynecology and Reproductive Biology 136 (2008) 165–170

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懷孕時的消化道疾病

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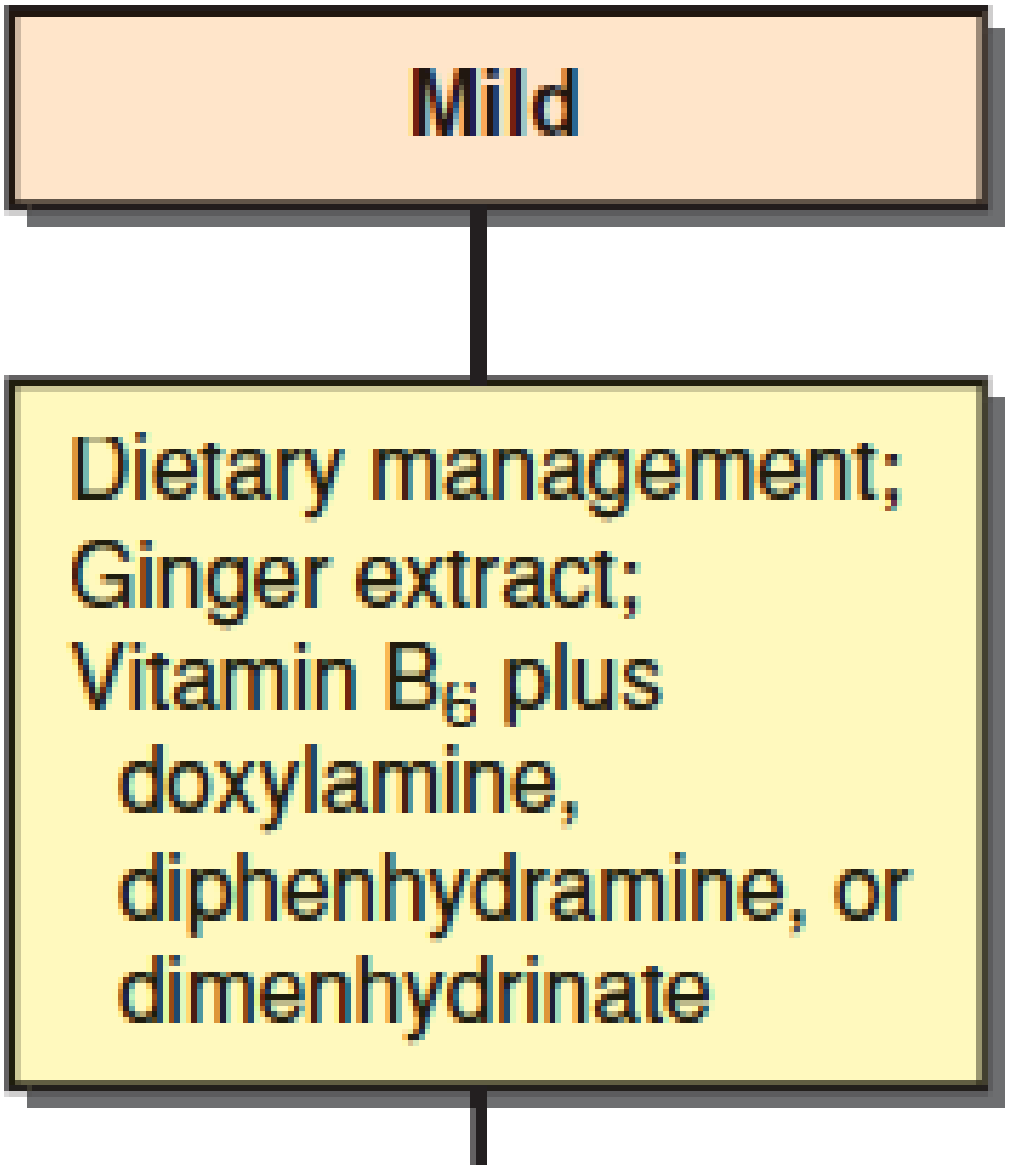
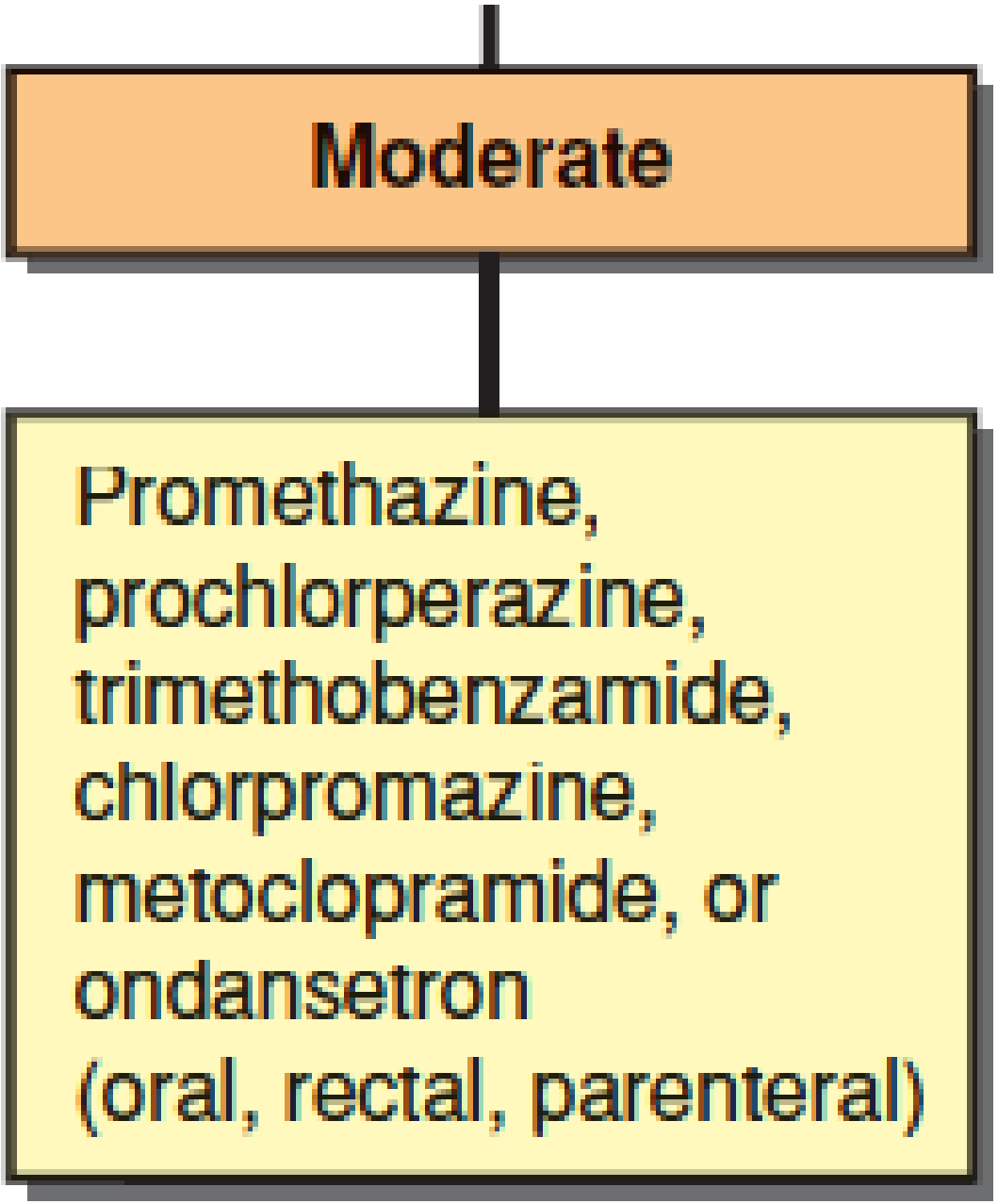
TABLE 54-2. Some Life-Threatening Complications of Recalcitrant Hyperemesis Gravidarum

Acute kidney injury—may require dialysis
Depression—cause versus effect?
Diaphragmatic rupture
Esophageal rupture—Boerhaave syndrome
Hypoprothrombinemia—vitamin K deficiency
Hyperalimentation complications
Mallory-Weiss tears—bleeding, pneumothorax, pneumomediastinum, pneumopericardium
Wernicke encephalopathy—thiamine deficiency


Mild
Dietary management;
Ginger extract;
Vitamin B_6 plus
doxylamine,
diphenhydramine, or
dimenhydrinate


Moderate
Promethazine, prochlorperazine, trimethobenzamide, chlorpromazine, metoclopramide, or ondansetron (oral, rectal, parenteral)

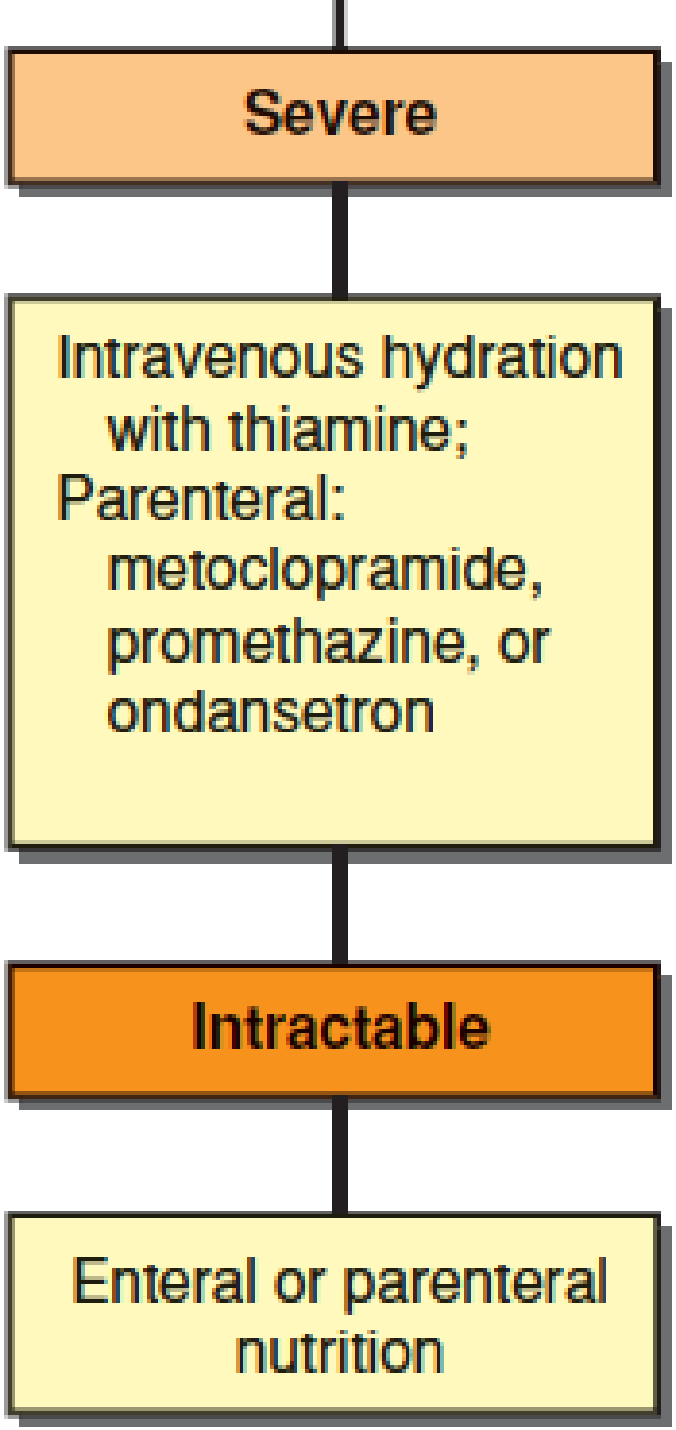

Severe
Intravenous hydration with thiamine;
Parenteral: metoclopramide, promethazine, or ondansetron
Intractable
Enteral or parenteral nutrition

TABLE 55-1. Clinical and Laboratory Findings with Acute Liver Diseases in Pregnancy

Disorder	Onset in Pregnancy	Clinical Findings	Hepatic		Renal	Hematological and Coagulation					
			AST (U/L)	Bili (mg/dL)	Cr (mg/dL)	Hct	Plat	Fib	DD	PT	Hemolysis
Hyperemesis	Early	Severe N&V	NL–300	NL–4	↑	↑↑	NL	NL	NL	NL	No
Cholestasis	Late	Pruritus, jaundice	NL–200	1–5	NL	NL	NL	NL	NL	NL	No
Fatty liver	Late	Moderate N&V, ± HTN, liver failure	200–800	4–10	↑↑↑	↑↑↑	↓↓	↓↓↓	↑	↑↑	↑↑↑
Preeclampsia	Mid to late	HA, HTN	NL–300	1–4	↑	↑	↓↓	NL	↑	NL	↑–↑↑
Hepatitis	Variable	Jaundice	2000+	5–20	NL	↑	↓	NL	NL	↑	No

↑ = increased levels; ↓ = decreased levels; AST = aspartate aminotransferase; Bili = bilirubin; Cr = creatinine; DD = D-dimers; Fib = fibrinogen; HA = headache; Hct = hematocrit; HTN = hypertension; N&V = nausea and vomiting; NL = normal; Plat = platelets; PT = prothrombin time.

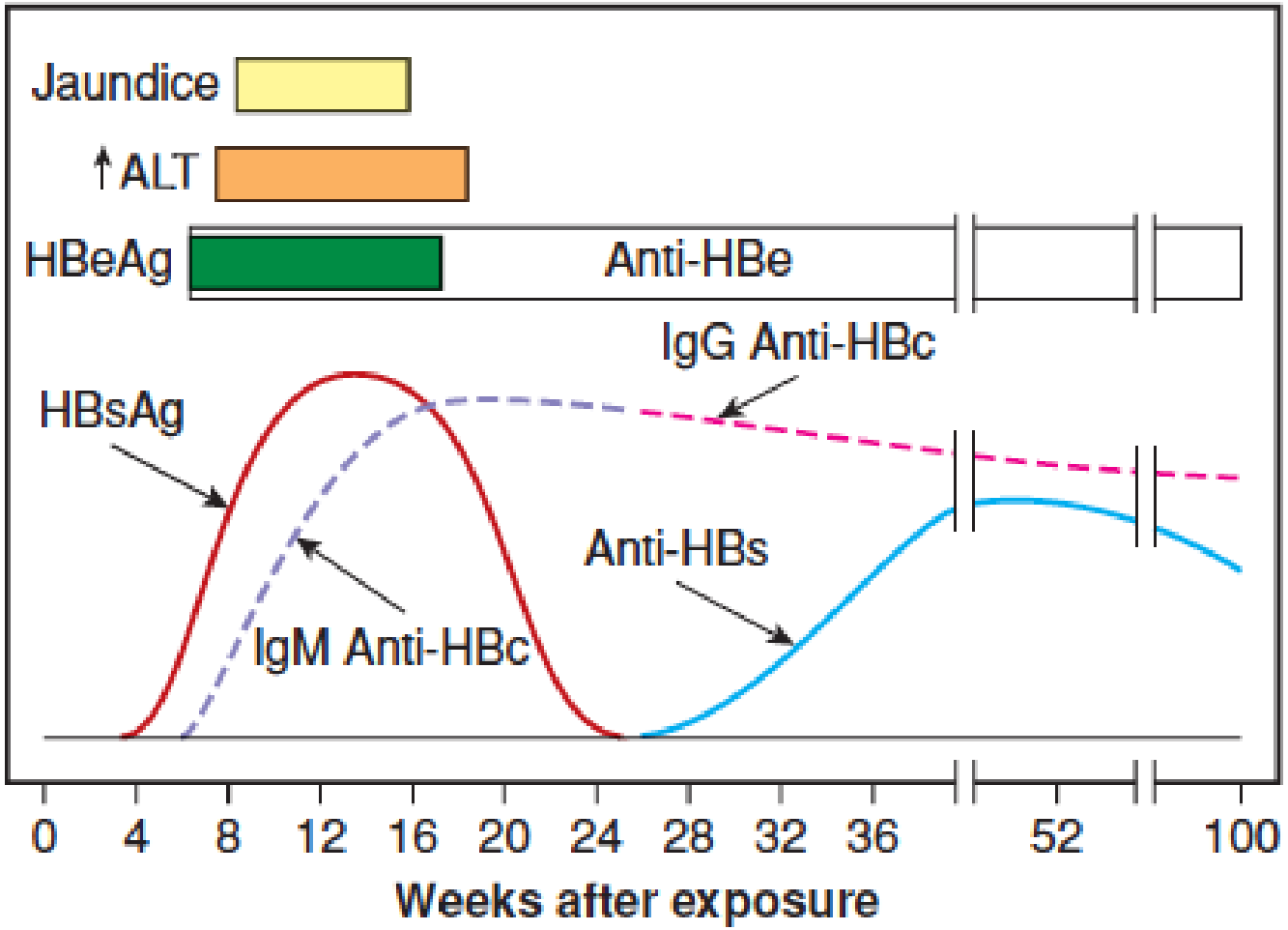


FIGURE 55-2 Sequence of various antigens and antibodies in acute hepatitis B. ALT = alanine aminotransferase; anti-HBc = antibody to hepatitis B core antigen; anti-HBe = antibody to hepatitis B e antigen; anti-HBs = antibody to hepatitis B surface antigen; HBeAg = hepatitis B e antigen; HBsAg = hepatitis B surface antigen. (Redrawn from Dienstag, 2012a.)

懷孕時的糖尿病

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王鵬惠

糖尿病的分類

TABLE 57-2. Classification Scheme Used from 1986 through 1994 for Diabetes Complicating Pregnancy

		Plasma Glucose Level		
Class	**Onset**	**Fasting**	**2-Hour Postprandial**	**Therapy**
A_1	Gestational	< 105 mg/dL	< 120 mg/dL	Diet
A_2	Gestational	> 105 mg/dL	> 120 mg/dL	Insulin
Class	**Age of Onset (yr)**	**Duration (yr)**	**Vascular Disease**	**Therapy**
B	Over 20	< 10	None	Insulin
C	10 to 19	10 to 19	None	Insulin
D	Before 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy[a]	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

[a]When diagnosed during pregnancy: proteinuria ≥ 500 mg/24 hr before 20 weeks' gestation.

糖尿病的分類

TABLE 57-3. Proposed Classification System for Diabetes in Pregnancy

Gestational diabetes: diabetes diagnosed during pregnancy that is not clearly overt (type 1 or type 2) diabetes

Type 1 Diabetes:
Diabetes resulting from β-cell destruction, usually leading to absolute insulin deficiency
a. Without vascular complications
b. With vascular complications (specify which)

Type 2 Diabetes:
Diabetes from inadequate insulin secretion in the face of increased insulin resistance
a. Without vascular complications
b. With vascular complications (specify which)

Other types of diabetes: genetic in origin, associated with pancreatic disease, drug-induced, or chemically induced

糖尿病的分類

TABLE 57-4. Diagnosis of Overt Diabetes in Pregnancy[a]

Measure of Glycemia	Threshold
Fasting plasma glucose	At least 7.0 mmol/L (126 mg/dL)
Hemoglobin A_{1c}	At least 6.5%
Random plasma glucose	At least 11.1 mmol/L (200 mg/dL) plus confirmation

空腹血糖 **> 126 mg/dl**

飯後血糖 **> 200 mg/dl**

糖化血色素 **> 6.5%**

2 小時 **75** 克糖水耐受試驗 **> 200 mg/dl**

PREGESTATIONAL DIABETES

- 有相當的比例的孕婦有糖尿病但未確診，許多確定患有妊娠糖尿病的女性可能先前就罹患第2型糖尿病
- 5%至10%有妊娠期糖尿病的女性在懷孕後被診斷為糖尿病

危險因子

- 懷孕初期須排除 **pre-gesational DM！**
- 前胎妊娠糖尿病
- 家族糖尿病史， 尤其一等親內
- 過重 **(BMI >24)**/肥胖 **(BMI >27)**
- 曾經生產過巨嬰 **(>4000 gm)**
- 高血壓、代謝症候群、 多囊性卵巢症候群、使用類固醇

- 子宮內環境對胎兒的影響：
- 在子宮內暴露於母體高血糖症導致胎兒高胰島素血症，導致胎兒脂肪細胞增加。
  - 這導致兒童期肥胖和胰島素抵抗
  - 導致成年期葡萄糖耐量降低和糖尿病

對懷孕的影響

- 自然流產
  - 早期流產與血糖控制不良有關
  - 高達**25**%的糖尿病孕婦有早期的**pregnancy loss**
  - **HbA1c > 12**%或其餐前葡萄糖濃度**> 120 mg / dL** 有更高的風險

對懷孕的影響

- 早產
- 畸形
  - 第**1**型糖尿病女性的懷孕畸形的發病率至少是一般女性的兩倍，接近**11**%
  - 心血管畸形佔一半以上的異常
  - 在懷孕前和懷孕早期，控制不佳的糖尿病被認為是這種高度嚴重畸形風險的基礎，母體**HbA1c**水平升高和畸形發病率明顯相關

- **Diminished growth of fetus :**
  - 先天性畸形
  - 母體血管的病變

TABLE 57-6. Congenital Anomalies in Fetuses of 91 Women with Type 1 Diabetes between 1999 and 2004 in Norway

Organ System	Babies Affected n (%)
Cardiovascular	47 (52)
Musculoskeletal	11 (12)
Urogenital	8 (9)
CNS	4 (4)
Gastrointestinal	2 (2)
Chromosomal	3 (3)
Others	9 (10)
Multiorgan	7 (8)

CNS = central nervous system.
Data from Eidem, 2010.

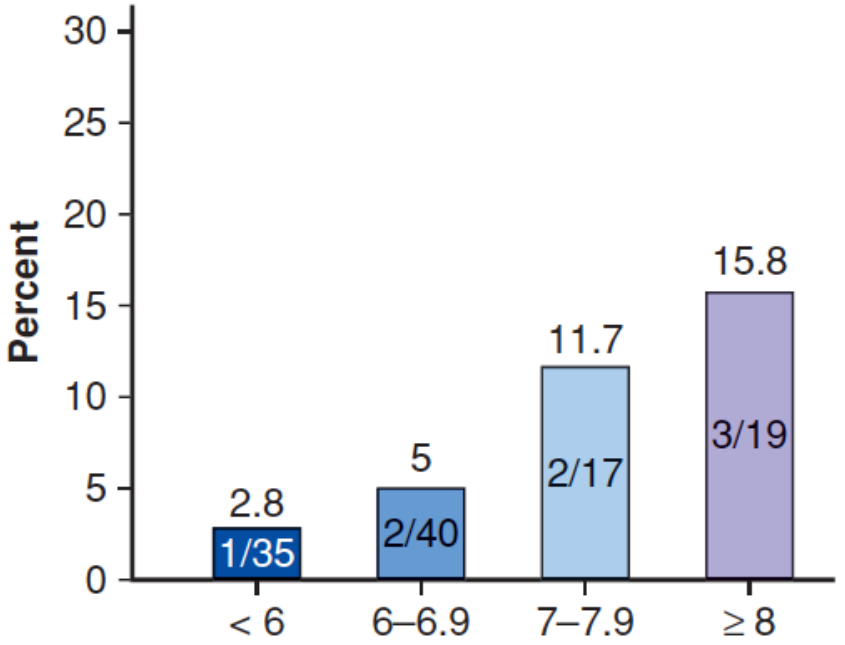


FIGURE 57-2 The frequency of major congenital malformations in newborns of women with pregestational diabetes stratified by hemoglobin A_{1c} levels at first prenatal visit. (Data from Galindo, 2006.)

- **overgrowth of fetus：**
  - 較典型的表現
  - 母親的高血糖症促使胎兒高胰島素血症，這反過來刺激過度體細胞生長。 除大腦外，大多數胎兒器官受**macrosomia**所影響
  - 這些新生兒的脂肪分布和一般新生兒不同：
    - 肩部和軀幹上的脂肪沉積過多，這可能會造成肩難產或剖腹產
  - 當平均母體血糖濃度長期超過**130 mg / dL**時，巨大兒的發病率顯著上升

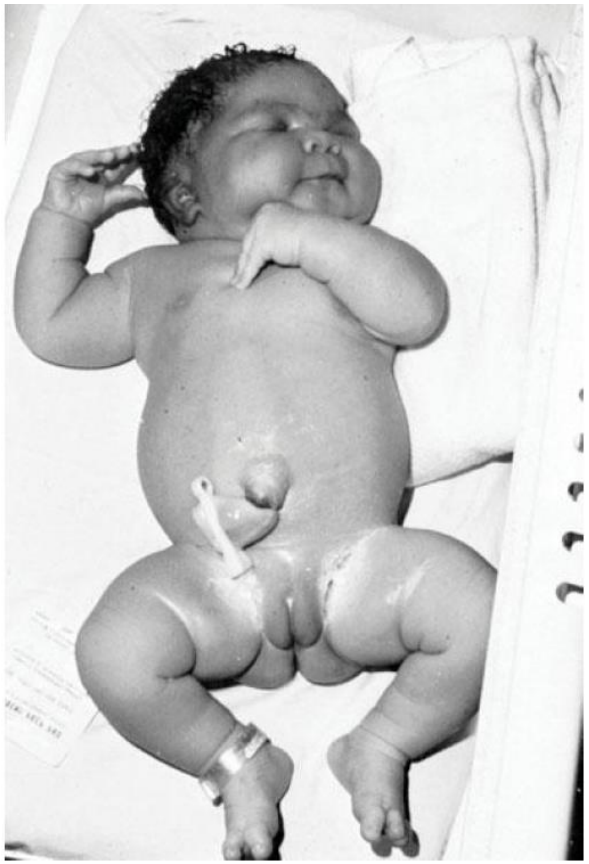


FIGURE 57-3 This 6050-g macrosomic infant was born to a woman with diabetes.

- 不明原因的胎兒死亡
  - 患有妊娠前糖尿病的女性患胎兒死亡的風險要高出三到四倍
  - 這些胎兒是通常是**large for gestational age**，通常發生在第三孕期晚期
  - 母體酮症酸中毒可導致胎兒死亡
- 羊水過多
  - 第三孕期**HbA1c**升高的患者更容易羊水過多

- **Respiratory Distress Syndrome** 呼吸窘迫
- 低血糖 **(**低葡萄糖濃度 **-** 定義為**<45 mg / dL)**
- 糖尿病母親的新生兒在分娩後經歷血漿葡萄糖濃度的快速下降。 這歸因於長期慢性母體高血糖誘導造成胎兒**β-islet cells**的增生
- 特別常見於待產過程血糖不穩定者

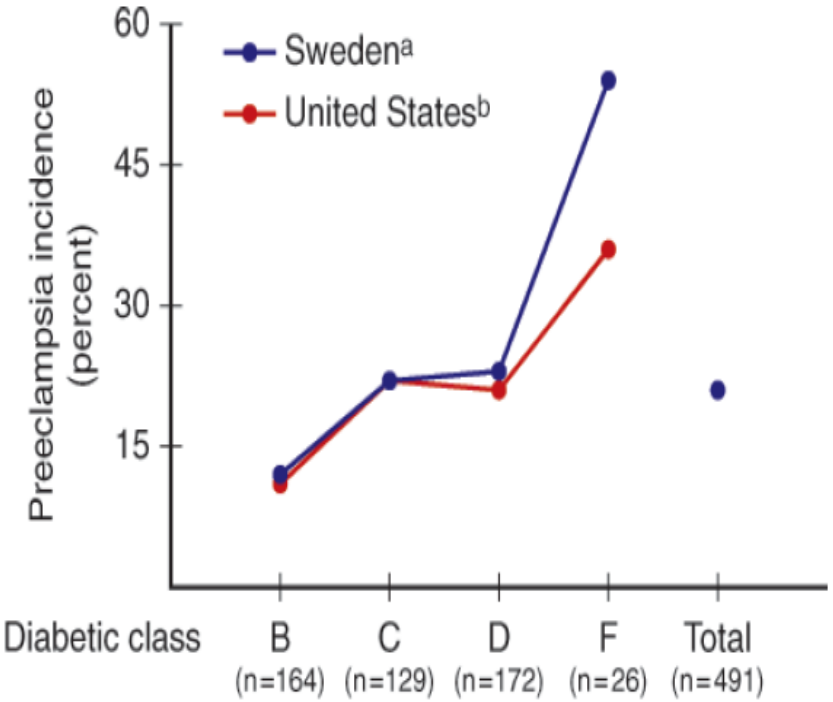
- 低鈣血症
  - 定義為足月新生兒的總血清鈣濃度**<8 mg / dL**
  - 其原因尚未明瞭
- 高膽紅素血症和紅細胞增多症
  - 糖尿病母親新生兒高膽紅素血症的發病機制尚不確定。 一個主要的促成因素是新生兒紅細胞增多症，它會升高膽紅素負荷
  - 紅細胞增多症被認為是對相對缺氧的胎兒反應

- **Cardiomyopathy**
  - 糖尿病妊娠的新生兒可能患有主要影響室間隔的肥厚性心肌病
- **Inheritance of Diabetes**

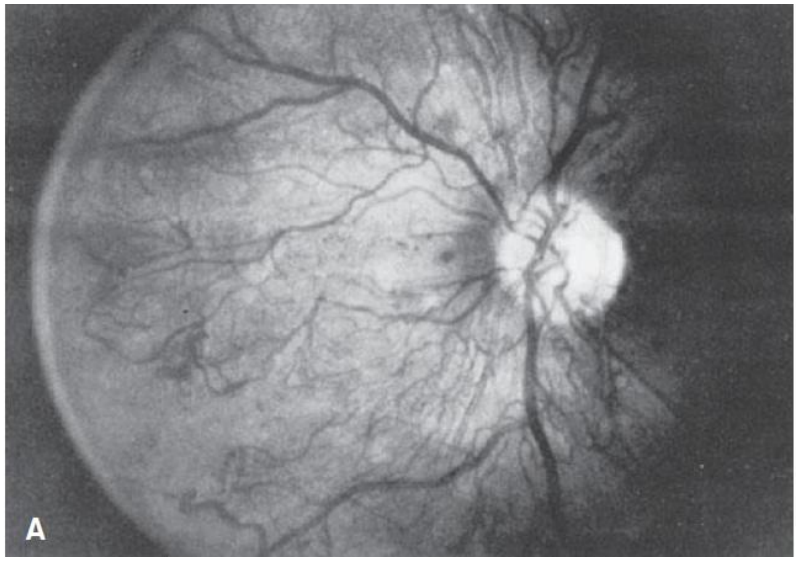
- 母體得到憂鬱症，高血壓，感染，心臟或呼吸系統併發症都比一般女性高
- 產婦死亡並不常見，但仍然高於一般女性 **(causes :**糖尿病酮症酸中毒，低血糖，高血壓和感染**)**
- 子癲前症機率顯著增加

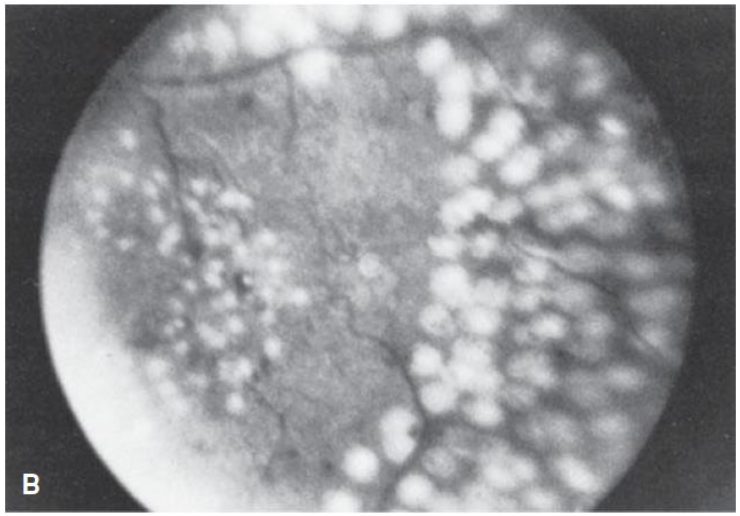
FIGURE 57-5

Incidence of preeclampsia in 491 type 1 diabetic women in Sweden and the United States. (Data from Hanson[a], 1993; Sibai[b], 2000.)



- 糖尿病性視網膜病變
- 糖尿病神經病變
  - 周邊對稱感覺運動糖尿病神經病變在孕婦中並不常見。但是糖尿病性胃病的形式可能導致噁心和嘔吐，營養問題以及控制血糖的困難。
  - **Treatment with metoclopramide and D2-receptor antagonists is sometimes successful.**





- 糖尿病酮症酸中毒
- 感染
- 糖尿病妊娠中許多感染率較高。常見的包括念珠菌性外陰陰道炎，尿路和呼吸道感染，和產**puerperal pelvic sepsis**

TABLE 57-7. Protocol Recommended by the American College of Obstetricians and Gynecologists (2012) for Management of Diabetic Ketoacidosis During Pregnancy

Laboratory assessment
Obtain arterial blood gases to document degree of acidosis present; measure glucose, ketones, and electrolyte levels at 1- to 2-hour intervals
Insulin
Low-dose, intravenous Loading dose: 0.2–0.4 U/kg Maintenance: 2–10 U/hr
Fluids
Isotonic sodium chloride Total replacement in first 12 hours of 4–6 L 1 L in first hour 500–1000 mL/hr for 2–4 hours 250 mL/hr until 80 percent replaced
Glucose
Begin 5-percent dextrose in normal saline when glucose plasma level reaches 250 mg/dL (14 mmol/L)
Potassium
If initially normal or reduced, an infusion rate up to 15–20 mEq/hr may be required; if elevated, wait until levels decrease into the normal range, then add to intravenous solution in a concentration of 20–30 mEq/L
Bicarbonate
Add one ampule (44 mEq) to 1 L of 0.45 normal saline if pH is < 7.1

From Landon, 2007, with permission.

妊娠期糖尿病的管理-
Preconceptional Care

- 由於妊娠併發症與母體血糖控制之間的密切關係， 管理最好應在懷孕前開始
- **HbA1c <6.5**%
- 餐前葡萄糖水平 **70**至**100 mg / dL**，餐後**2**小時**100**至**120 mg / dL**，平均每日葡萄糖濃度**<110 mg / dL**

妊娠期糖尿病的管理-
Preconceptional Care

- **overtly diabetic gravida**的孕婦最好用胰島素治療
- 雖然口服降糖藥已成功用於妊娠糖尿病，這些藥物目前不推薦用於**overtly diabetic gravida**

TABLE 57-2. Classification Scheme Used from 1986 through 1994 for Diabetes Complicating Pregnancy

Class	Onset	Plasma Glucose Level		Therapy
		Fasting	2-Hour Postprandial	
A_1	Gestational	< 105 mg/dL	< 120 mg/dL	Diet
A_2	Gestational	> 105 mg/dL	> 120 mg/dL	Insulin
Class	**Age of Onset (yr)**	**Duration (yr)**	**Vascular Disease**	**Therapy**
B	Over 20	< 10	None	Insulin
C	10 to 19	10 to 19	None	Insulin
D	Before 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy[a]	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

[a]When diagnosed during pregnancy: proteinuria ≥ 500 mg/24 hr before 20 weeks' gestation.

常用的短期和長期胰島素的作用概況

TABLE 57-8. Action Profiles of Commonly Used Insulins

Insulin Type	Onset	Peak (hr)	Duration (hr)
Short-acting (SC)			
Lispro	< 15 min	0.5–1.5	3–4
Glulisine	< 15 min	0.5–1.5	3–4
Aspart	< 15 min	0.5–1.5	3–4
Regular	30–60 min	2–3	4–6
Long-acting (SC)			
Detemir	1–4 hr	Minimal[a]	Up to 24
Glargine	1–4 hr	Minimal[a]	Up to 24
NPH	1–4 hr	6–10	10–16

[a]Minimal peak activity.
NPH = neutral protamine Hagedorn; SC = subcutaneous.
Modified from Powers, 2012.

Self-Monitored Capillary Blood Glucose Goals

TABLE 57-9. Self-Monitored Capillary Blood Glucose Goals

Specimen	Level (mg/dL)
Fasting	≤ 95
Premeal	≤ 100
1-hr postprandial	≤ 140
2-hr postprandial	≤ 120
0200–0600	≥ 60
Mean (average)	100
Hemoglobin A_{1c}	≤ 6%

- 妊娠前期糖尿病趨於不穩定，低血糖發生率在第一孕期達到最高
- 第二孕期進入血糖相對較穩定的時期
- **ACOG** 建議從**32~34**周開始要密切監測:胎兒狀況

- 妊娠晚期血糖控制更嚴格可能會減少胎兒晚期受損和剖腹產機率
- 生產時建議降低或暫停長效的胰島素
- 對胰島素需求在生產後會顯著降低
- 生產時須密切監測血糖狀態

Insulin Management During Labor and Delivery

TABLE 57-10. Insulin Management During Labor and Delivery

- Usual dose of intermediate-acting insulin is given at bedtime.
- Morning dose of insulin is withheld.
- Intravenous infusion of normal saline is begun.
- Once active labor begins or glucose levels decrease to < 70 mg/dL, the infusion is changed from saline to 5-percent dextrose and delivered at a rate of 100–150 mL/hr (2.5 mg/kg/min) to achieve a glucose level of approximately 100 mg/dL.
- Glucose levels are checked hourly using a bedside meter allowing for adjustment in the insulin or glucose infusion rate.
- Regular (short-acting) insulin is administered by intravenous infusion at a rate of 1.25 U/hr if glucose levels exceed 100 mg/dL.

Puerperium產褥期

- 在產後的前**24**小時左右，可能幾乎不需要胰島素
- 隨後，胰島素需求可能在接下來的幾天內顯著波動。 必須及時發現和治療，可以重新開始口服藥物

懷孕引起的糖尿病
GESTATIONAL DIABETES

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篩檢與診斷-
誰需要做？

Universal screening?

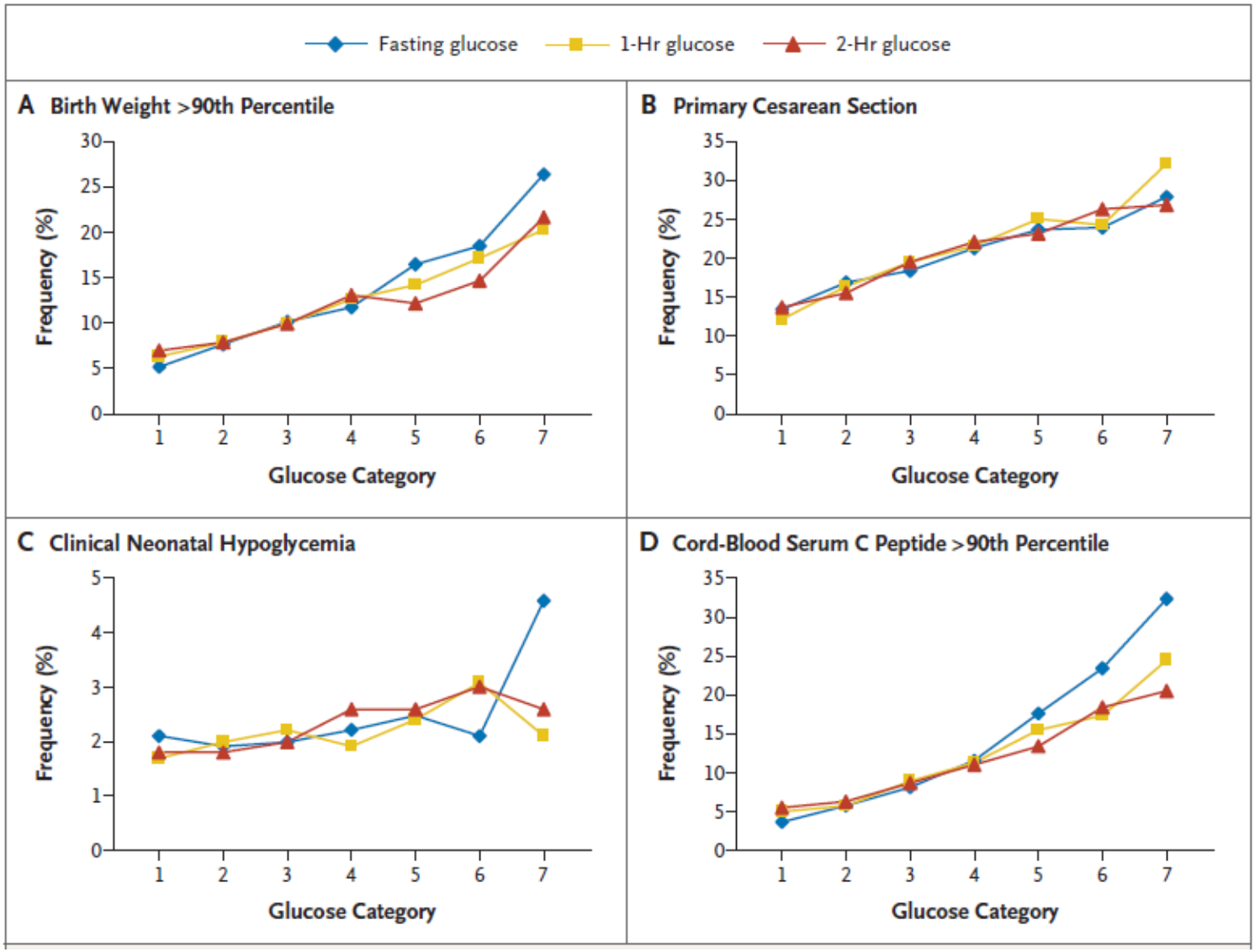
世界大不同~

Different GDM Diagnostic Criteria

TABLE 57-13. Fifth International Workshop Conference on Gestational Diabetes: Diagnostic Criteria of Gestational Diabetes by Oral Glucose Tolerance Testing

Time	Oral Glucose Load[a]			
	100-g Glucose[b]		75-g Glucose[b]	
Fasting	95 mg/dL	5.3 mmol/L	95 mg/dL	5.3 mmol/L
1-hr	180 mg/dL	10.0 mmol/L	180 mg/dL	10.0 mmol/L
2-hr	155 mg/dL	8.6 mmol/L	155 mg/dL	8.6 mmol/L
3-hr	140 mg/dL	7.8 mmol/L	—	—

The HAPO Study



HAPO Study 告訴我們

積極治療可減少
相關併發症！

血糖值↑
懷孕併發症↑

妊娠糖尿病對懷孕的影響

- 胎兒大
- 羊水多
- 剖腹產/器械生產
- 母體生產損傷
- 子癲前症
- 胎死腹中
- 新生兒生產損傷
- 新生兒呼吸窘迫
- 新生兒低血糖
- 新生兒高膽紅素
- 新生兒低血鈣

妊娠糖尿病的長期影響

- **母親未來懷孕的復發率：30-84%**
- **母親健康：糖尿病、心血管疾病**
- **胎兒：肥胖、代謝症候群**

Management

- **ACOG:**
  - 空腹血糖**<95 mg/dL or** 飯後兩小時血糖 **<120 mg/dL**
- 控制得宜可以顯著降低子癲前症，肩難產和**Macrosomia**的發病率

Management

- **ACOG:**
- 飲食：
  - 適當的碳水化合物以維持血糖正常和避免酮酸症
  - **daily caloric intake of 30 to 35 kcal/kg**
  - **ACOG** 建議**:**
  - 碳水化合物攝入量限制在總熱量的**40**%，剩餘的卡路里按比例分配為**20**%的蛋白質和**40**%的脂肪

- 運動：
  - **ACOG：**建議在懷孕期間定期進行有氧運動和力量訓練運動，並將其擴展到妊娠糖尿病
  - 減少懷孕期間的體重增加，甚至可以降低患妊娠糖尿病的風險
  - 妊娠期糖尿病婦女在懷孕期間運動也會降低血糖水平

胰島素治療

- 當目標葡萄糖水平不能持續時，胰島素被認為是妊娠期糖尿病女性的標準療法
- 它不會穿過胎盤
- 考慮使用胰島素治療：
  - 空腹血糖續超過**95 mg / dL**
  - 飯後一小時 > **140 mg / dL**
  - 飯後兩小時 > **120 mg / dL**

胰島素治療

- **ACOG:**
  - **If insulin is initiated, the starting dose is typically 0.7 to 1.0 units/kg/d and is given in divided doses**
  - **A combination of intermediate-acting and short-acting insulin may be used**

口服降血糖藥

- 胰島素是妊娠期糖尿病女性持續高血糖的首選一線藥物
- **ACOG & ADA：**
  - 支持**glyburide (Micronase)** 和 **metformin (Glucophage)**的安全性和有效性
  - 認為兩者都是妊娠期糖尿病婦女二線血糖控制的合理選擇
- 兩種藥物皆可通過胎盤
- 但仍有部分研究顯示和新生兒呼吸窘迫、低血糖、新生兒體重增加...等相關

口服降血糖藥

- **FDA：**尚未批准**glyburide (Micronase)**和 **metformin (Glucophage)**用於治療妊娠糖尿病

Obstetrical Management

- 一般而言，對於不需要胰島素的妊娠期糖尿病女性，很少需要早期分娩或其他干預措施。
- **ACOG：**
  - 對妊娠期糖尿病和血糖控制不佳的女性進行胎兒監測
- 胰島素治療的婦女在妊娠**34**週後接受住院治療，並且每週進行三次產前監測

- 要選擇催生或是自然發動目前仍有爭議

Obstetrical Management

- **ACOG:**
  - 在妊娠**39**週之前，不應該對患有飲食治療的妊娠糖尿病的女性進行常規引產
  - 用胰島素治療的患者在妊娠**38**週時分娩
  - 預估體重**≥4500g** 可考慮剖腹產

產後評估

- **ACOG**：
- 建議在產後**4**至**12**週使用空腹血糖或**75**克**2**小時**OGTT**來診斷**overt DM**

- **ADA：**
- 建議至少每**3**年檢測一次有妊娠期糖尿病史但產後血糖正常的女性

TABLE 57-14. Fifth International Workshop-Conference: Metabolic Assessments Recommended after Pregnancy with Gestational Diabetes

Time	Test	Purpose
Postdelivery (1–3 d)	Fasting or random plasma glucose	Detect persistent, overt diabetes
Early postpartum (6–12 wk)	75-g, 2-hr OGTT	Postpartum classification of glucose metabolism
1-yr postpartum	75-g, 2-hr OGTT	Assess glucose metabolism
Annually	Fasting plasma glucose	Assess glucose metabolism
Triannually	75-g, 2-hr OGTT	Assess glucose metabolism
Prepregnancy	75-g, 2-hr OGTT	Classify glucose metabolism
Classification of the American Diabetes Association (2013)		
Normal Values	**Impaired Fasting Glucose or Impaired Glucose Tolerance**	**Diabetes Mellitus**
Fasting < 100 mg/dL	100–125 mg/dL	≥ 126 mg/dL
2 hr < 140 mg/dL	2 hr ≥ 140–199 mg/dL	2 hr ≥ 200 mg/dL
Hemoglobin A_{1c} < 5.7%	5.7–6.4%	≥ 6.5%

OGTT = oral glucose tolerance test.
From American Diabetes Association, 2013; Metzger, 2007.

懷孕時的內分泌疾病

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甲狀腺疾病

Hypothyroidism

- **Clinical, or overt , hypothyroidism** 在懷孕中的比例 **: 2/1000**
- **Clinical hypothyroidism** 診斷**:**
  - 異常高的**TSH** 合併 低的**free T4**

- 最常見的原因**:** 自身抗體或橋本甲狀腺炎引起的腺體破壞
- 在**5~15%**的懷孕婦女中可 發現**Thyroid peroxidase (TPO) antibodies,** 其中有一半的女性可能之後會發展成**autoimmune thyroiditis**

Overt hypothyroidism

- 母體和胎兒的併發症風險會提升:
  - 子癲前症
  - 胎盤早期剝離
  - 心臟功能異常
  - 胎死腹中
  - 早產
- 若有適當治療，**perinatal outcomes** 通常正常

- **Replacement therapy：**
  - **Thyroxine, 50~100ug/day**
- **TSH** 和 **free T4** 建議每四到六個禮拜追蹤一次
- 每次調整劑量**dose：25~50ug,** 直到到達正常值
- 懷孕中通常需要較多的**thyroxine**
- 但治療需要個人化，並不是每位都需要**replacement therapy**

Subclinical hypothyroidism

- 定義:
  - 異常升高的**TSH**
  - 正常的**free T4**
  - 沒有症狀

- 在懷孕中所佔的比例：**2.3%**
- 遺傳是最大的**risk factor**
- 其他**risk factors:**
  - **Type 1 DM**
  - **Thyroid peroxidase antibodies**

Subclinical hypothyroidism

- 對懷孕**outcome**的影響目前仍不完全明瞭
- 會提高早產及胎盤早期剝離的風險

對胎兒的影響

- **Overt hypothyroidism or subclinical hypothyroidism** 都曾被提出會造成 **subnormal mental development**
- 和有良好控制的組別相比，母體血清中**TSH**濃度上升其後代的學校表現、認知能力、**IQ**分數都有較差的表現
- 因此有學者認為針對**subclinical hypothyroidism**需要**prenatal screening**和後續治療

對胎兒的影響

- **ACOG**：仍不建議常規篩檢
- 針對胎兒神經發育適當的碘攝取是必要的
  - 建議懷孕中攝取量**: 220ug/day**
- 嚴重缺乏碘和**endemic cretinism(**地方性呆小病**)**有關

Hyperthyroidism

- **Clinical hyperthyroidism, or thyrotoxicosis**在懷孕中的比例**: 1/1000**
- **Mild thyrotoxicosis** 在懷孕中很難診斷，有一些症狀可以協助：
  - 心跳加快
  - 甲狀腺腫大
  - 眼球突出
  - 體重難增加

Hyperthyroidism

- 診斷：
  - 異常低的**TSH**
  - 異常高的**fee T4**
- 很少情況**hyperthyroidism**是由於異常高的**T3**造成的 **(T3 toxicosis)**

- 懷孕中最常見的**hyperthyroidism：Graves disease**
- 和**thyroid-stimulating antibodies**有關
- 在很多女性中，**thyroid-stimulating antibody**的活性在懷孕中會降低

- 懷孕的預後和控制的狀況有關
- 控制不佳沒有治療，會增加以下風險：
- 子癲前症
- 心臟衰竭
- **Adverse perinatal outcomes**

- **Thyroid storm：**只會在沒有治療的**Graves disease**上發生且罕見
- 心臟衰竭比**thyroid storm**更常發生：由於**thyroxine**的**myocardial effects** → **high-output state**
- 子癇前症、貧血、敗血症可引起肺水腫

治療

- **Thionamide drugs：**
- **Propylthiouracial (PTU)** 和 **methimazole (Tapazole)**都是有效且安全的
- 暫時性白細胞減少症約佔**10%**，但這並不需要停止治療
- 但有**0.3%**會突然發生顆粒細胞缺乏症 **(agranulocytosis)** 並且使得藥物停止使用。
  - 因此，如果出現發燒或喉嚨痛，應指示女性立即停止服藥並抽血**complete blood count**

治療

- 一些臨床醫生更喜歡**PTU**，因為它部分地抑制了**T4**向**T3**的轉化，並且它比**methimazole**更不容易穿過胎盤
- **PTU**也與**esophageal/choanal atresia or aplasia cutis**無關，後者 **(**和**methimazole**有關**)**

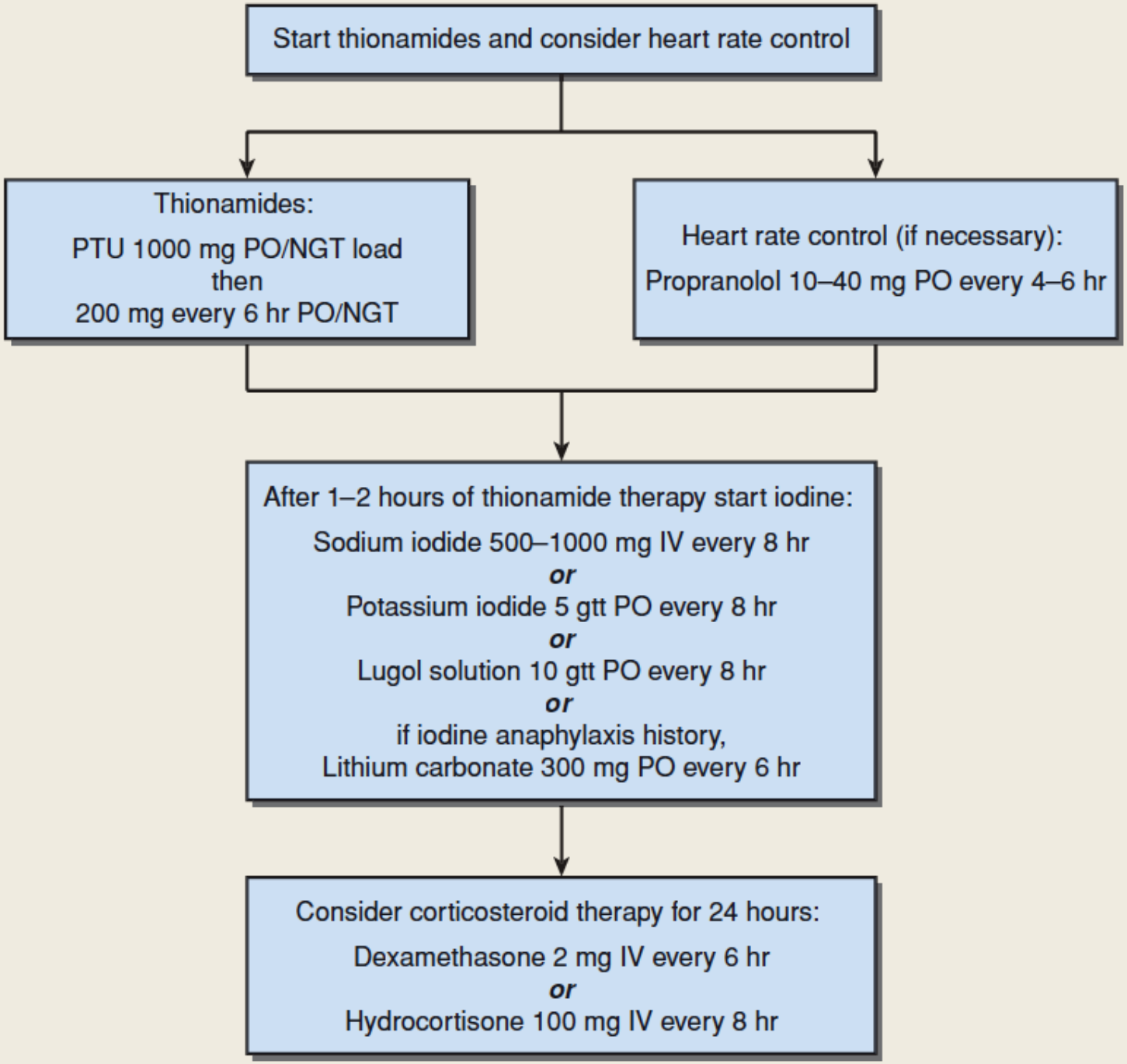
- **PTU**的劑量通常從每天**300**至**450mg**開始
- 游離**T4**回到正常值的時間大約是**7~8**週
- 其他治療方法包括在甲狀腺毒症受到抑制後，再進行甲狀腺切除術，但這在懷孕期間很少進行。

懷孕中發生甲狀腺風暴的處理

- 加護病房觀察
- **PTU 1g ST (oral or by NG tube) → PTU 200mg Q6H**
- **PTU**給後一小時，給予**iodide** 以抑制**T3**和**T4**從甲狀腺中被釋放 **(Q8H)**

懷孕中發生甲狀腺風暴的處理

- **Dexamethaxsone 2mg IV Q6H (**四個**dose) :** 以抑制周邊**T4**轉化為**T3**
- 使用**β-blocker IV,** 但要注意是否有心臟衰竭
- 治療的主要方向是支持治療和積極管理嚴重的高血壓，感染和貧血


Start thionamides and consider heart rate control
Thionamides:
PTU 1000 mg PO/NGT load
then
200 mg every 6 hr PO/NGT
Heart rate control (if necessary):
Propranolol 10–40 mg PO every 4–6 hr
After 1–2 hours of thionamide therapy start iodine:
Sodium iodide 500–1000 mg IV every 8 hr
or
Potassium iodide 5 gtt PO every 8 hr
or
Lugol solution 10 gtt PO every 8 hr
or
if iodine anaphylaxis history,
Lithium carbonate 300 mg PO every 6 hr
Consider corticosteroid therapy for 24 hours:
Dexamethasone 2 mg IV every 6 hr
or
Hydrocortisone 100 mg IV every 8 hr

Subclinical hyperthyroidism

- 定義:
  - 低的**TSH**
  - 正常的**thyroid hormone**
  - 沒有症狀
- 懷孕中發生率：**1~2%**
- 目前沒有發現和不良的懷孕預後有關
- 這些女性大約有一半會發展成正常的**TSH**
- **Long-term effects** 目前不清楚，定期監測是合理的

Maternal thyrotoxicosis
對胎兒的影響

- 新生兒可能表現出短暫的甲狀腺毒症，有時需要抗甲狀腺藥物治療
- 胎兒或新生兒甲狀腺毒症可以由母體甲狀腺刺激抗體的經胎盤傳代引起，並且發生在患有**Graves disease** 的女性所生的新生兒中，約**1**%
- 這種胎兒甲狀腺毒症通常對**thionamide**治療有反應，但也有發生胎兒死亡的狀況

Maternal thyrotoxicosis
對胎兒的影響

- 相反地，長期接觸**thionamide**可能會導致新生兒甲狀腺功能減退
- 評估在懷孕期間用這些藥物治療的甲狀腺炎母親所生孩子的智力和身體發育的長期研究，未發現對隨後的生長和發育產生不利影響。

懷孕時的結締組織及風濕疾病

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TABLE 59-1. Some Autoantibodies Produced in Patients with Systemic Lupus Erythematosus (SLE)

Antibody	Prevalence (%)	Clinical Associations
Antinuclear (ANA)	84–98	Best screening test, multiple antibodies; a second negative test makes SLE unlikely
Anti-double-stranded (ds)-DNA	62–70	High titers SLE-specific; may correlate with disease activity, nephritis, and vasculitis
Anti-Sm (Smith)	25–38	Specific for SLE
Anti-RNP	33–40	Not SLE-specific, high titers associated with rheumatic syndromes
Anti-Ro (SS-A)	30–49	Not SLE-specific; associated with Sjögren syndrome, predisposes to cutaneous lupus, neonatal lupus with heart block, reduced risk of nephritis
Anti-La (SS-B)	10–35	Associated with anti-Ro; possible decreased nephritis risk
Antihistone	70	Common in drug-induced lupus (95%)
Antiphospholipid	21–50	Lupus anticoagulant and anticardiolipin antibodies associated with thrombosis, fetal loss, thrombocytopenia, valvular heart disease; false-positive test for syphilis
Anti-erythrocyte	60	Small number develop hemolysis
Antiplatelet	30	Thrombocytopenia in 15%; poor clinical test

TABLE 59-4. Complications in 13,555 Pregnancies in Women with Systemic Lupus Erythematosus

Complications	Percent
Comorbid illness	
Pregestational diabetes	5.6
Thrombophilia	4.0
Hypertension	3.9
Renal failure	0.2
Pulmonary hypertension	0.2
Pregnancy complications	
Preeclampsia	22.5
Preterm labor	20.8
Fetal-growth restriction	5.6
Eclampsia	0.5
Medical complications	
Anemia	12.6
Thrombocytopenia	4.3
Thrombotic—stroke, pulmonary embolism, deep-vein thrombosis	1.7
Infections—pneumonia, sepsis syndrome	2.2
Maternal morbidity-mortality rate	325/100,000

懷孕時的神經及精神系統疾病

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TABLE 60-2. Teratogenic Effects of Common Anticonvulsant Medications

Drug (Brand Name)	Abnormalities Described	Affected	Embryo-Fetal Risk[a]
Valproate (Depakote)	Neural-tube defects, clefts, cardiac anomalies; associated developmental delay	10% with monotherapy; higher with polytherapy	Yes
Phenytoin (Dilantin)	Fetal hydantoin syndrome—craniofacial anomalies, fingernail hypoplasia, growth deficiency, developmental delay, cardiac anomalies, clefts	5–11%	Yes
Carbamazepine; oxcarbazepine (Tegretol; Trileptal)	Fetal hydantoin syndrome, as above; spina bifida	1–2%	Yes
Phenobarbital	Clefts, cardiac anomalies, urinary tract malformations	10–20%	Suggested
Lamotrigine (Lamictal)	Increased risk for clefts (Registry data)	Up to 1% (4- to 10-fold higher than expected)	Suggested
Topiramate (Topamax)	Clefts	2–3% (15- to 20-fold higher than expected)	Suggested
Levetiracetam (Keppra)	Theoretical—skeletal abnormalities; impaired growth in animals	Preliminary observations	Suggested

TABLE 60-3. Some Associated Disorders or Causes of Ischemic and Hemorrhagic Strokes During Pregnancy or the Puerperium

Ischemic Stroke	Hemorrhagic Stroke
Preeclampsia syndrome	Chronic hypertension
Arterial thrombosis	Preeclampsia syndrome
Venous thrombosis	Arteriovenous malformation
Lupus anticoagulant	Saccular aneurysm
Antiphospholipid antibodies	Angioma
Thrombophilias	Cocaine, methamphetamines
Migraine induced	Vasculopathy
Paradoxical embolus	
Cardioembolic	
Sickle hemoglobinopathy	
Arterial dissection	
Vasculitis	
Moyamoya disease	
Cocaine, amphetamines	

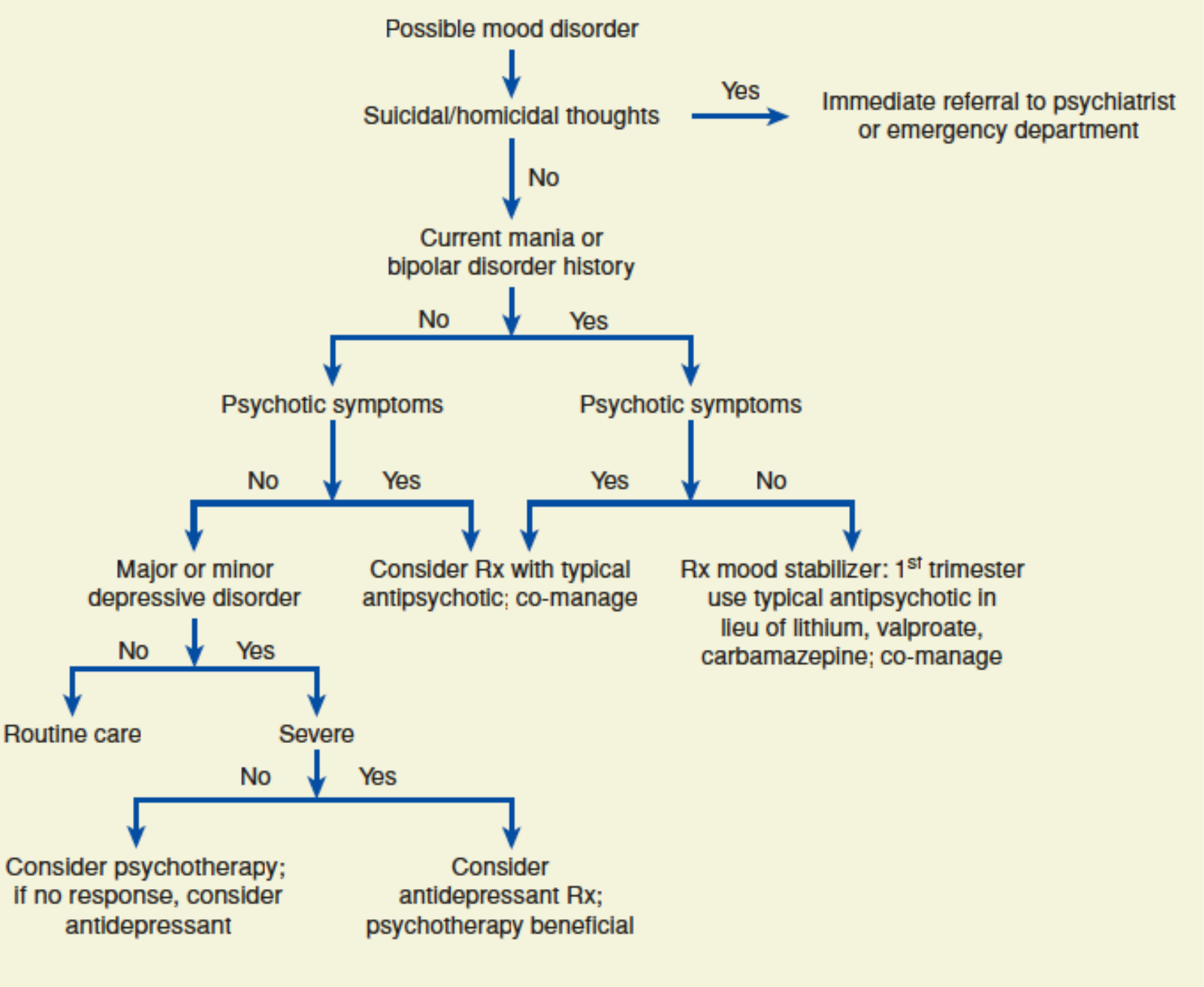
Possible mood disorder
Suicidal/homicidal thoughts
Yes
Immediate referral to psychiatrist or emergency department
No
Current mania or bipolar disorder history
No
Yes
Psychotic symptoms
Psychotic symptoms
No
Yes
Yes
No
Major or minor depressive disorder
Consider Rx with typical antipsychotic; co-manage
Rx mood stabilizer: 1st trimester use typical antipsychotic in lieu of lithium, valproate, carbamazepine; co-manage
No
Yes
Routine care
Severe
No
Yes
Consider psychotherapy; if no response, consider antidepressant
Consider antidepressant Rx; psychotherapy beneficial

TABLE 61-3. Some Drugs Used for Treatment of Major Mental Disorders in Pregnancy

Indication of Class	Examples	Comments
Antidepressants		
SSRIs[a]	Citalopram, fluoxetine, paroxetine, sertraline	*Possible* link with heart defects; neonatal withdrawal syndrome; *possible* persistent pulmonary hypertension[a]; paroxetine use avoided by some
Others	Bupropion, duloxetine, nefazodone, venlafaxine	
Tricyclics	Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	Not commonly used currently; no evidence of teratogenicity
Antipsychotics		
Typical	Chlorpromazine, fluphenazine, haloperidol, thiothixene	
Atypical	Aripiprazole, clozapine, olanzapine, risperidone, ziprasidone	
Bipolar Disorders		
Lithium[a]	Lithium carbonate	Tx manic episodes; teratogen—heart defects, viz., Ebstein anomaly; few data after 12 wks
Valproic acid[b]		
Carbamazepine[b]		
Antipsychotics	See above	

TABLE 62-1. Pregnancy-specific Dermatoses

Disorder	Frequency	Characteristic Lesion	Adverse Pregnancy Effects	Treatment
Cholestasis of pregnancy	Common	No primary lesions, secondary excoriations from scratching	Increased perinatal morbidity	Antipruritics, cholestyramine, ursodeoxycholic acid
Pruritic urticarial papules and plaques of pregnancy (PUPPP)	Common	Erythematous pruritic papules or plaques; patchy or generalized on abdomen, thighs, buttocks, especially within striae, but with umbilical sparing	None	Antipruritics, emollients, topical corticosteroids, oral steroids if severe
Atopic eruptions of pregnancy (AEP)			None	
Eczema of pregnancy	Common	Dry, red scaly patches on extremity flexures, neck, face		
Prurigo of pregnancy	Common	1–5 mm pruritic red papules on extensor surfaces, trunk		
Pruritic folliculitis of pregnancy	Rare	Small red papules, sterile pustules on trunk		
Pemphigoid gestationis	Rare	Erythematous pruritic papules, plaques, vesicles, and bullae; abdomen often with umbilical involvement, extremities	Preterm birth, fetal-growth restriction, transient neonatal lesions	

懷孕時的癌症

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懷孕時的感染

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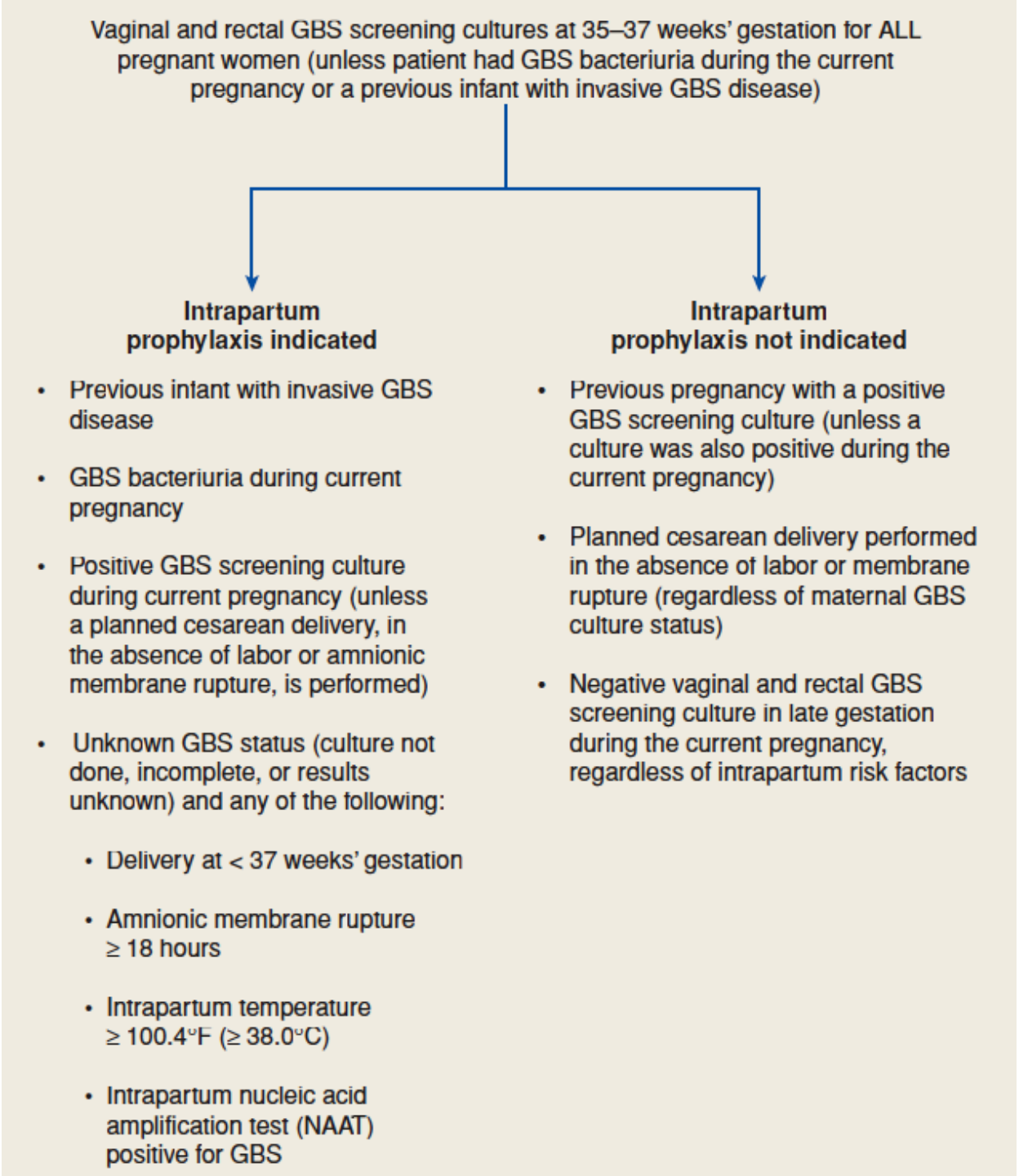
Vaginal and rectal GBS screening cultures at 35–37 weeks' gestation for ALL pregnant women (unless patient had GBS bacteriuria during the current pregnancy or a previous infant with invasive GBS disease)
Intrapartum prophylaxis indicated
Previous infant with invasive GBS disease
GBS bacteriuria during current pregnancy
Positive GBS screening culture during current pregnancy (unless a planned cesarean delivery, in the absence of labor or amnionic membrane rupture, is performed)
Unknown GBS status (culture not done, incomplete, or results unknown) and any of the following:
Delivery at < 37 weeks' gestation
Amnionic membrane rupture ≥ 18 hours
Intrapartum temperature ≥ 100.4°F (≥ 38.0°C)
Intrapartum nucleic acid amplification test (NAAT) positive for GBS
Intrapartum prophylaxis not indicated
Previous pregnancy with a positive GBS screening culture (unless a culture was also positive during the current pregnancy)
Planned cesarean delivery performed in the absence of labor or membrane rupture (regardless of maternal GBS culture status)
Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors

TABLE 65-1. Recommended Treatment for Pregnant Women with Syphilis

Category	Treatment
Early syphilis[a]	Benzathine penicillin G, 2.4 million units intramuscularly as a single injection—some recommend a second dose 1 week later
More than 1-year duration[b]	Benzathine penicillin G, 2.4 million units intramuscularly weekly for three doses
Neurosyphilis[c]	Aqueous crystalline penicillin G, 3–4 million units intravenously every 4 hours for 10–14 days ***or*** Aqueous procaine penicillin, 2.4 million units intramuscularly daily, plus probenecid 500 mg orally four times daily, both for 10–14 days

TABLE 65-3. Treatment of Uncomplicated Gonococcal Infections During Pregnancy

Ceftriaxone, 250 mg intramuscularly as a single dose ***plus*** Azithromycin, 1 gram orally as a single dose

TABLE 65-4. Treatment of *Chlamydia trachomatis* Infections During Pregnancy

Regimen	Drug and Dosage
Preferred choice	Azithromycin, 1000 mg orally as a single dose ***or*** Amoxicillin, 500 mg orally three times daily for 7 days
Alternatives	Erythromycin base, 500 mg orally four times daily for 7 days ***or*** Erythromycin ethylsuccinate, 800 mg orally four times daily for 7 days ***or*** Erythromycin base, 250 mg orally four times daily for 14 days ***or*** Erythromycin ethylsuccinate, 400 mg orally four times daily for 14 days

TABLE 65-5. Antiviral Medications for Herpesvirus Infection in Pregnancy

Indication	Pregnancy Recommendation
Primary or first episode infection	Acyclovir, 400 mg orally three times daily for 7–10 days ***or*** Valacyclovir, 1 g orally twice daily for 7–10 days
Symptomatic recurrent infection (episodic therapy)	Acyclovir, 400 mg orally three times daily for 5 days ***or*** Acyclovir, 800 mg orally twice daily for 5 days ***or*** Valacyclovir, 500 mg orally twice daily for 3 days ***or*** Valacyclovir, 1 g orally once daily for 5 days
Daily suppression	Acyclovir, 400 mg orally three times daily from 36 weeks until delivery ***or*** Valacyclovir, 500 mg orally twice daily from 36 weeks until delivery

太多東西，要有概念，懂得求助

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