Pregnancy Hypertension in Emergency Conditions

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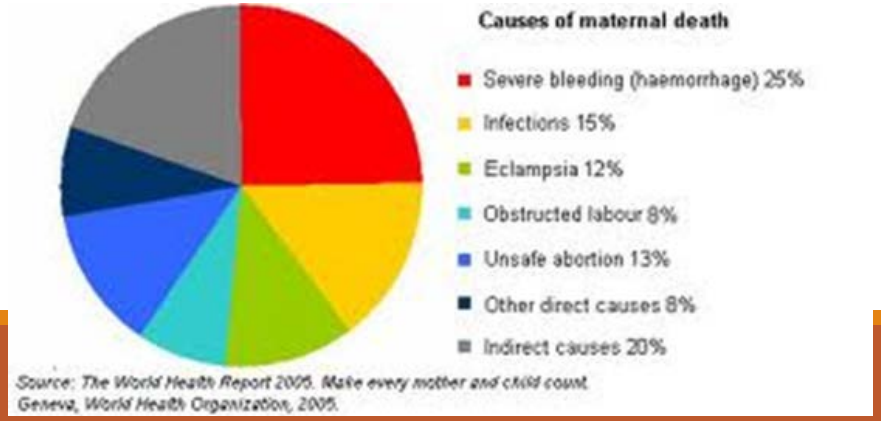
เมื่อท่านเจ้าคุณ ได้กลับมาถึงจวนเมื่อตอนย่ำค่ำ พบเห็นอีเย็น ที่กำลังตั้งครรภ์อยู่ 7 เดือน ดูจะอ้วนท้วนมากกว่าปกติ ขาก็ดูบวมคล้ายกับขาโต๊ะบิลเลียด หน้าตาก็ดูอวบอูมกว่าเดิมมาก จึงได้ถามอีเย็นว่า “เจ้าไปทำประการใด เจ้าจึงดูผิดไปจากเดิมมากถึงเพียงนี้” อีเย็นได้ตอบท่านเจ้าคุณไปว่า “อีชั้นรู้สึก ตึงๆตามใบหน้า ตามตัว และขา เจ้าข้า และวันนี้อีชั้นปวดอยู่ในกะโหลกของอีชั้นด้วยเจ้าข้า” เจ้าคุณเมื่อได้ยินอีเย็นบอกอย่างนั้น จึงได้พาอีเย็นไปหาหมอหลวงโดยพลัน

Outline

- Introduction
- Optimal blood pressure measurement
- Classification
- Prediction
- Prevention
- Management

Introduction

- 10% of pregnancies worldwide
- Leading cause of maternal and perinatal morbidity and mortality
- 50,000-60,000 preeclampsia-related deaths/year
- Major cause of prematurity
- Risk factor for future cardiovascular disease and metabolic disease
- Unclear etiology



Optimal blood pressure measurement

- EQUIPMENT
- POSITION
- METHOD

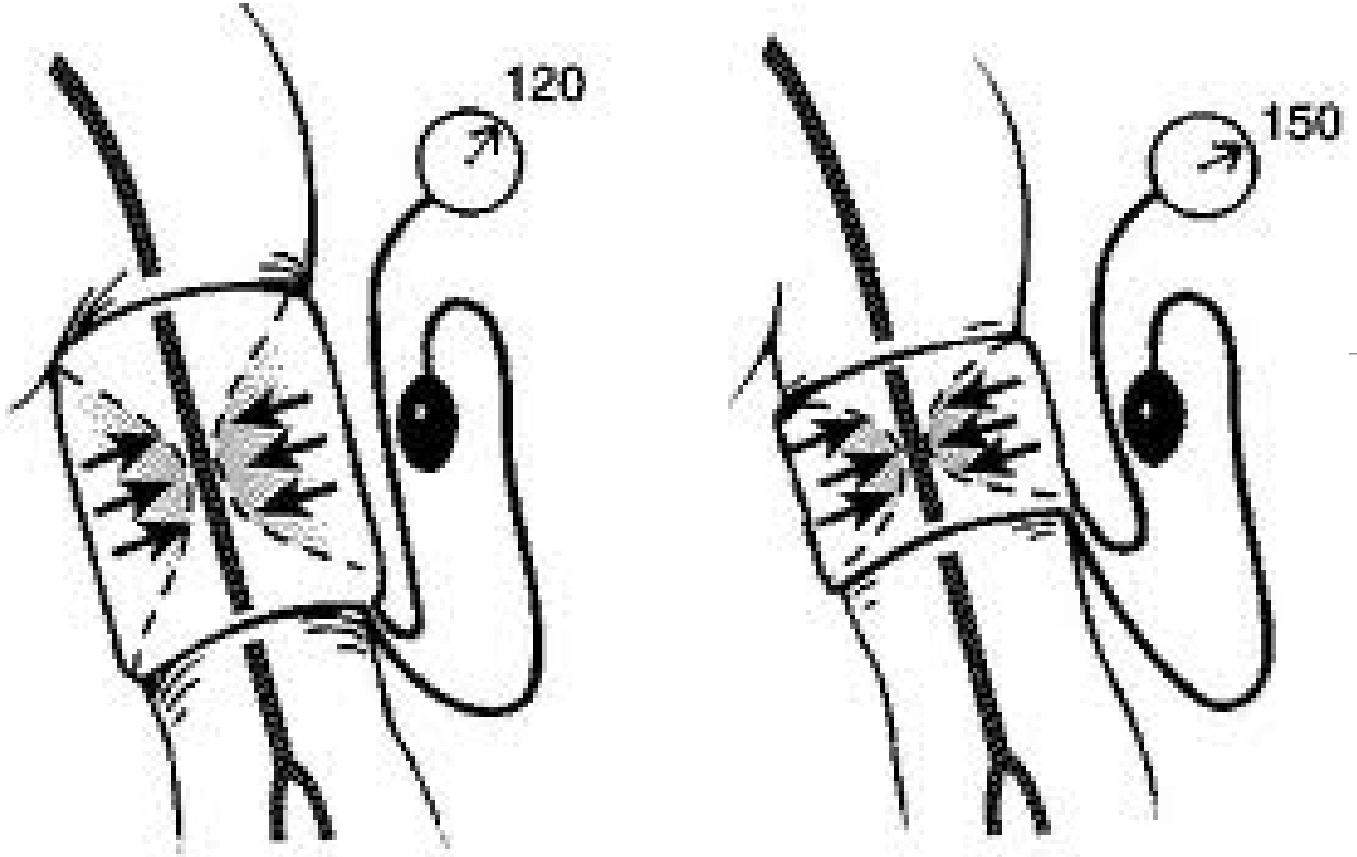

INDEX


110
84
59

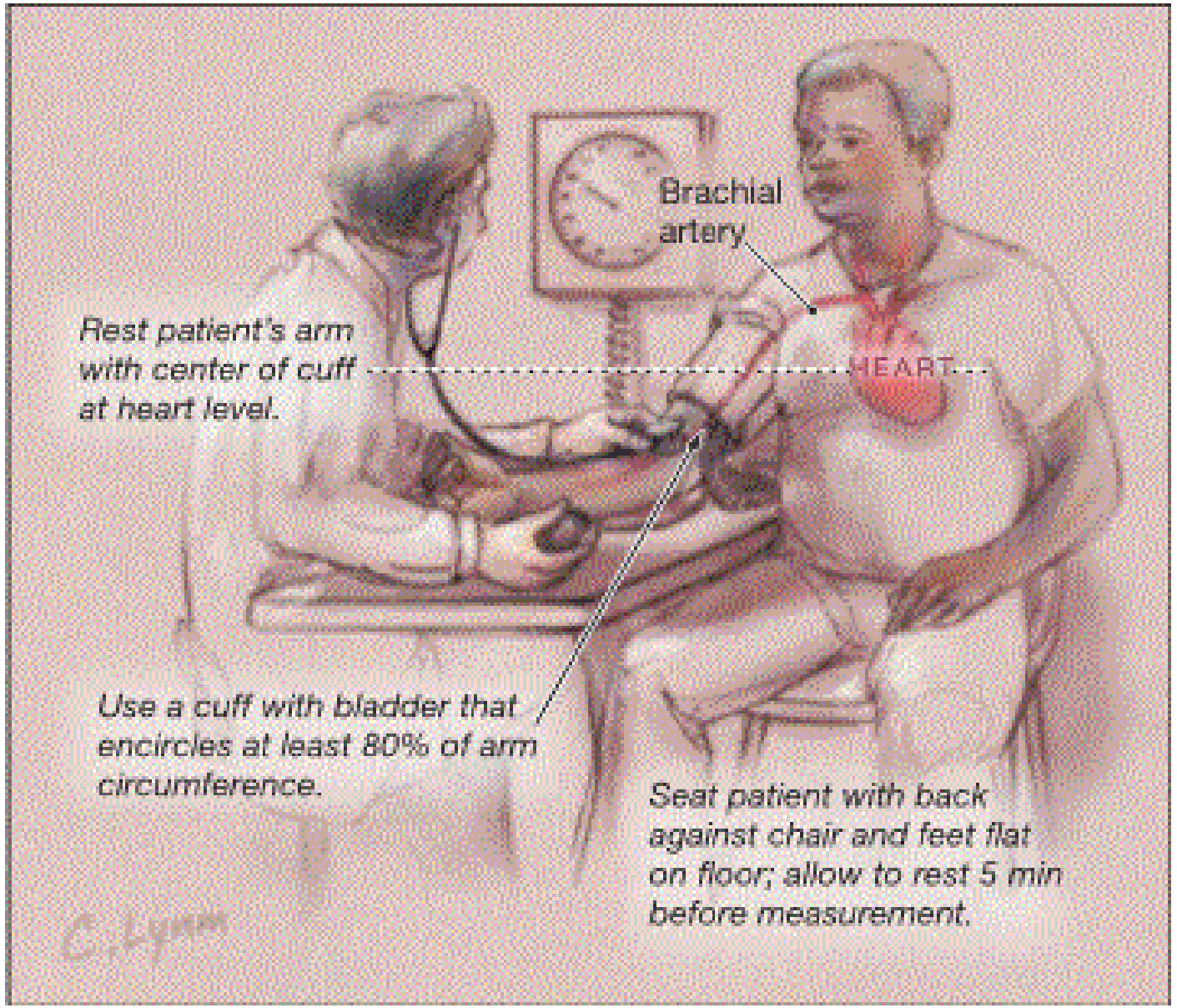
Recommended cuff size

Arm circumference(cm)	Cuff type	Cuff size(cm)
22-26	Small adult	12x22
27-34	Adult	16x30
35-44	Large adult	16x36
45-52	Adult thigh	16x42

American Heart Association



Unappropriated cuff size



Optimal blood pressure measurement

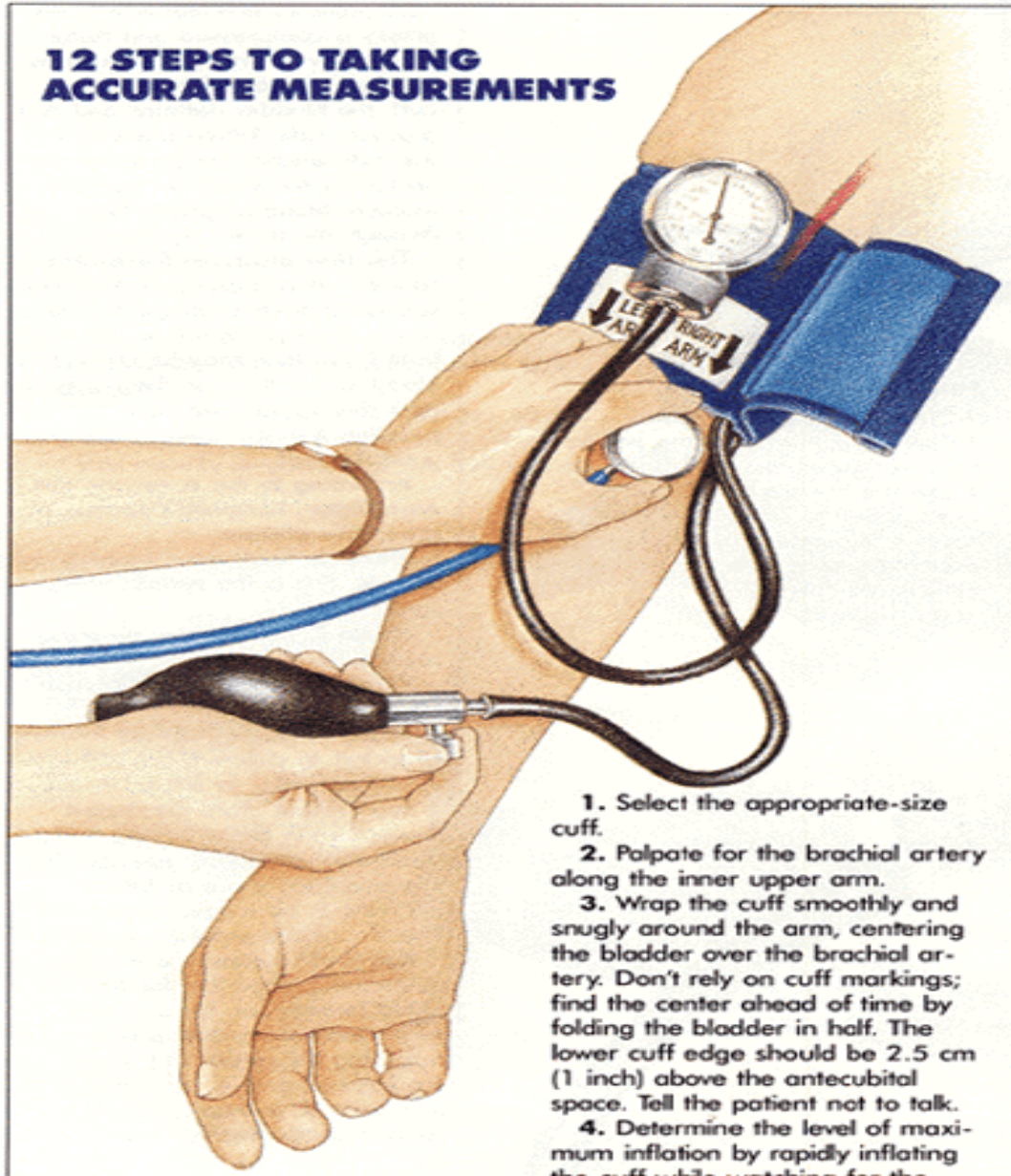
- Seated
- Leg uncrossed

  DBP ⇑ 6 mmHg
- Back&arm supported

  SBP ⇑ 2-8 mmHg
- Middle of the cuff=right atrium(midpoint of sternum)
- If in labor

→ Lt lateral recumbency

12 STEPS TO TAKING ACCURATE MEASUREMENTS



1. Select the appropriate-size cuff.

2. Palpate for the brachial artery along the inner upper arm.

3. Wrap the cuff smoothly and snugly around the arm, centering the bladder over the brachial artery. Don't rely on cuff markings; find the center ahead of time by folding the bladder in half. The lower cuff edge should be 2.5 cm (1 inch) above the antecubital space. Tell the patient not to talk.

4. Determine the level of maximum inflation by rapidly inflating the cuff while watching for the point where you can no longer feel the radial pulse (palpated systolic). To that reading, add 30 mm Hg.

5. Deflate the cuff rapidly and steadily, then wait 15 to 30 seconds before reinflating.

6. Insert the stethoscope earpieces, making sure they point forward. Apply the bell head lightly but with complete contact over the palpable brachial artery.

7. Inflate the cuff rapidly and steadily to the level of maximum inflation determined in step 4.

8. Release the air so the pressure falls at 2 to 3 mm Hg per second.

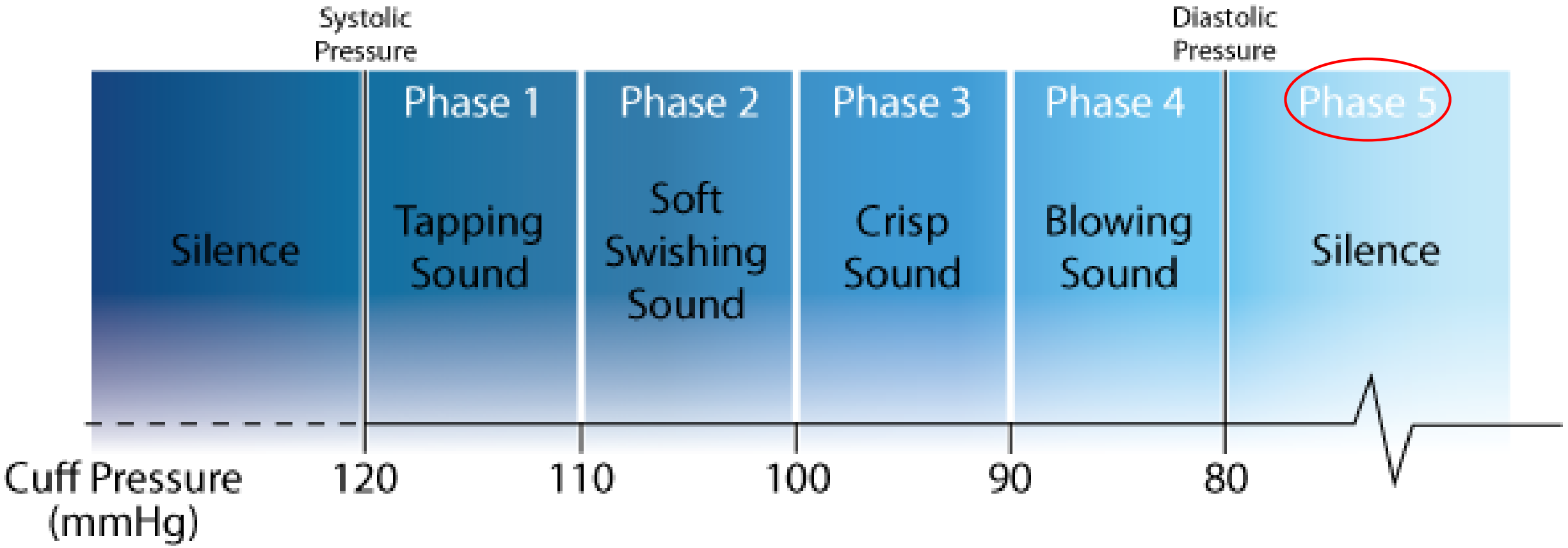
9. Listen for the onset of at least two consecutive beats (Korotkoff's sounds, phase 1). This is the systolic pressure. Note the closest mark on the manometer. Always record blood pressure measurements in even numbers.

10. Listen for a muffling sound (phase 4) with children or the cessation of sound (phase 5) with adults. This is the diastolic pressure. Continue listening for 10 to 20 mm Hg below the last sound to confirm your reading, then make sure to deflate the cuff rapidly and completely.

11. Record the patient's blood pressure, position (sitting or standing), cuff size, and the arm used for the measurement.

12. Wait 1 to 2 minutes before repeating the pressure measurement on the same arm, so the blood trapped in the arm veins can be released. If your patient's initial measurement is elevated, the American Heart Association recommends that you take two additional blood pressure measurements at 1- to 2-minute intervals. Refer the patient for treatment if the average of the second and third readings is elevated.

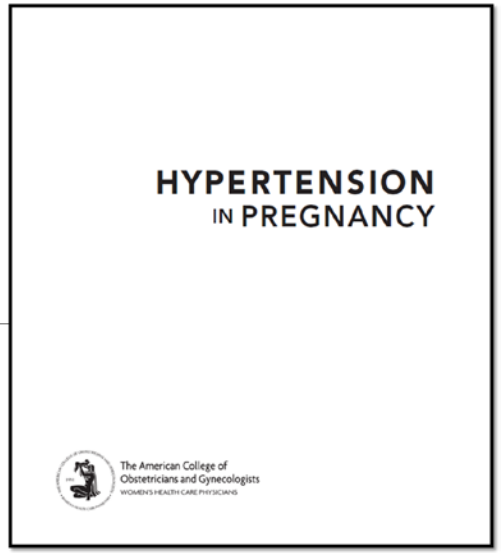
Korotkoff sound



เหตุเกิดเมื่อวานที่หน่วยฝากครรภ์ คุณหมอศตวรรษ ได้พาคุณนุชซึ่งตั้งครรภ์ได้ 6 เดือน มาพบคุณหมอทศวรรษ (เจมส์ ไป) ซึ่งเป็นสูตินรีแพทย์ที่ดูแลคุณนุชอยู่ เนื่องจากว่า เมื่อคืนก่อนคุณนุชบ่นว่ารู้สึกปวดศีรษะมาก รู้สึกมึนๆ บวมที่หน้าและแขนขา เนื่องจากนอนไม่หลับ มีเรื่องให้กังวลใจทั้งเรื่องพ่อที่จะต้อง เปลี่ยนไต ยังหาไตไม่ได้ และเรื่องหมอศตวรรษที่มีภาพหลุดกับโสม ทำให้มีความเครียด ถ้าคุณเป็นหมอทศวรรษ คิดว่าคุณจะดูแลคุณนุชอย่างไรดี

Classification

Classification



1. Preeclampsia-eclampsia
2. Chronic hypertension
3. Chronic hypertension with superimposed preeclampsia
4. Gestational hypertension

"Unclassified" → "Presumptive" preeclampsia

Preeclampsia

- **Pregnancy specific hypertensive disease with multisystem involvement**
- **After 20 weeks of gestation**
- **Classic definition → New onset HT plus new onset proteinuria**

TABLE 34-1. Diagnosis of Hypertensive Disorders Complicating Pregnancy

Gestational Hypertension:

- Systolic BP ≥140 or diastolic BP ≥90 mm Hg for first time during pregnancy
- No proteinuria
- BP returns to normal before 12 weeks postpartum
- Final diagnosis made only postpartum
- May have other signs or symptoms of preeclampsia, for example, epigastric discomfort or thrombocytopenia

Preeclampsia:

Minimum criteria:

- BP ≥ 140/90 mm Hg after 20 weeks' gestation
- Proteinuria ≥ 300 mg/24 hours or ≥ 1+ dipstick

Increased certainty of preeclampsia:

- BP ≥ 160/110 mm Hg
- Proteinuria 2.0 g/24 hours or ≥ 2+ dipstick
- Serum creatinine >1.2 mg/dL unless known to be previously elevated
- Platelets < 100,000/μL
- Microangiopathic hemolysis—increased LDH
- Elevated serum transaminase levels—ALT or AST
- Persistent headache or other cerebral or visual disturbance
- Persistent epigastric pain

Eclampsia:

- Seizures that cannot be attributed to other causes in a woman with preeclampsia

Superimposed Preeclampsia On Chronic Hypertension:

- New-onset proteinuria ≥ 300 mg/24 hours in hypertensive women but no proteinuria before 20 weeks' gestation
- A sudden increase in proteinuria or blood pressure or platelet count < 100,000/μL in women with hypertension and proteinuria before 20 weeks' gestation

Chronic Hypertension:

- BP ≥ 140/90 mm Hg before pregnancy or diagnosed before 20 weeks' gestation not attributable to gestational trophoblastic disease

or

- Hypertension first diagnosed after 20 weeks' gestation and persistent after 12 weeks postpartum

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BP = blood pressure; LDH = lactate dehydrogenase.

National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy (2000).

Blood pressure	• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure • Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy
and	
Proteinuria	• Greater than or equal to 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection) or • Protein/creatinine ratio greater than or equal to 0.3* • Dipstick reading of 1+ (used only if other quantitative methods not available)
Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:	
Thrombocytopenia	• Platelet count less than 100,000/microliter
Renal insufficiency	• Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
Impaired liver function	• Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual symptoms	

*Each measured as mg/dL.

Non-proteinuric pre-eclampsia: a novel risk indicator in women with gestational hypertension

Caroline S.E. Homer[a], Mark A. Brown[b,c,d], George Mangos[b,c,d] and Gregory K. Davis[b]

Journal of Hypertension 2008, 26:295–302

- **Objective:** To determine whether outcomes differed for women with pre-eclampsia according to the presence of proteinuria and whether non-proteinuric pre-eclampsia is similar to gestational hypertension.
- **Design:** From 1987 to 2005, at three hospitals in Sydney, Australia, women referred to the obstetric medicine team were recruited.
- **Outcomes** for three groups were compared:

  proteinuric pre-eclampsia, non-proteinuric pre-eclampsia and gestational hypertension

Non-proteinuric pre-eclampsia: a novel risk indicator in women with gestational hypertension

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- **Outcomes for three groups were compared:**

Severe hypertension, Preterm delivery, Perinatal mortality and morbidity rate

Proteinuric pre-eclampsia > Non-proteinuric pre-eclampsia > Gestational hypertension

Conclusion

- This study highlights differences between non-proteinuric pre-eclampsia and gestational hypertension.
- The subclassification of ‘non-proteinuric pre-eclampsia’ should be added to existing classification systems to alert clinicians to potential risks.

Preeclampsia

- ~~“Mild preeclampsia”~~
- “Preeclampsia without severe features”
- Even mild → increase morbidity & mortality

Severity of preeclampsia

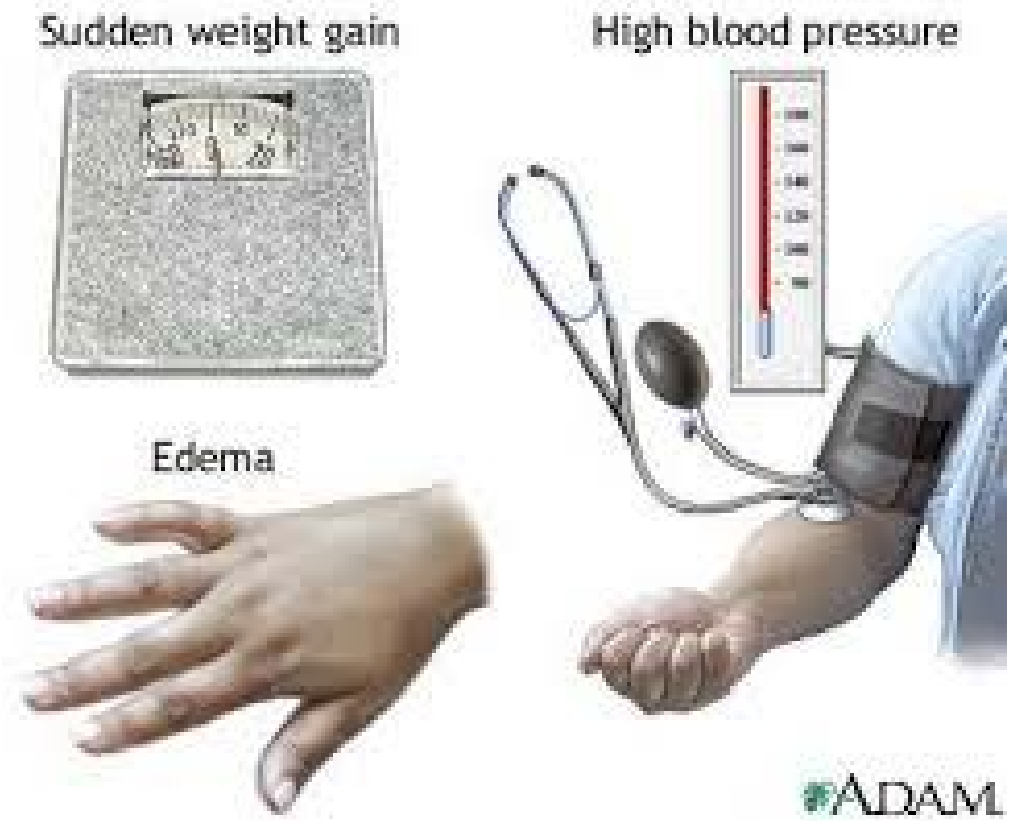
- Some clinical findings
- Laboratory
- ~~Quantity of urinary protein~~
- ~~FGR~~

Severe Features of Preeclampsia (Any of these findings)

- Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy is initiated before this time)
- Thrombocytopenia (platelet count less than 100,000/microliter)
- Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both
- Progressive renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- Pulmonary edema
- New-onset cerebral or visual disturbances

Pre-diagnostic findings of preeclampsia

- New onset of headache
- Visual disturbances
- Abdominal pain or epigastric pain
- Elevations in BP
- Edema, rapid weight gain or both
- FGR
- New onset proteinuria



Eclampsia

- New onset “Grand mal seizures”
- Before, during, or after labor
- Others causes of seizures
  - Bleeding AVM
  - Ruptured aneurysm
  - Idiopathic seizure disorder
  - After 48-72 hr postpartum
  - During use of Mg

Classification

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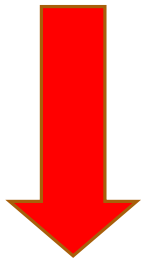
Chronic hypertension with superimposed preeclampsia

- Develop proteinuria after 20 weeks of gestation
- Proteinuria before 20 weeks of gestation plus

1. Symptoms such as RUQ pain, severe headache
2. Pulmonary congestion or edema
3. Sudden exacerbation of HT
4. ⇑ liver enzymes to abnormal level
5. Platelet < 100,000/microliters
6. Renal insufficiency (Doubling of Cr level or ≥ 1.1 mg/dL)
7. Sudden, substantial, and sustained increases in protein excretion

Chronic hypertension with superimposed preeclampsia

- **Elevation in BP but SBP<160 mmHg DBP<110 mmHg**
- **Plus proteinuria**



“Superimposed preeclampsia without severe features”

Prediction of preeclampsia

Prediction of preeclampsia

- Demographic factors
- Biochemical analyses
- Biological findings
- In combination

Risk factors

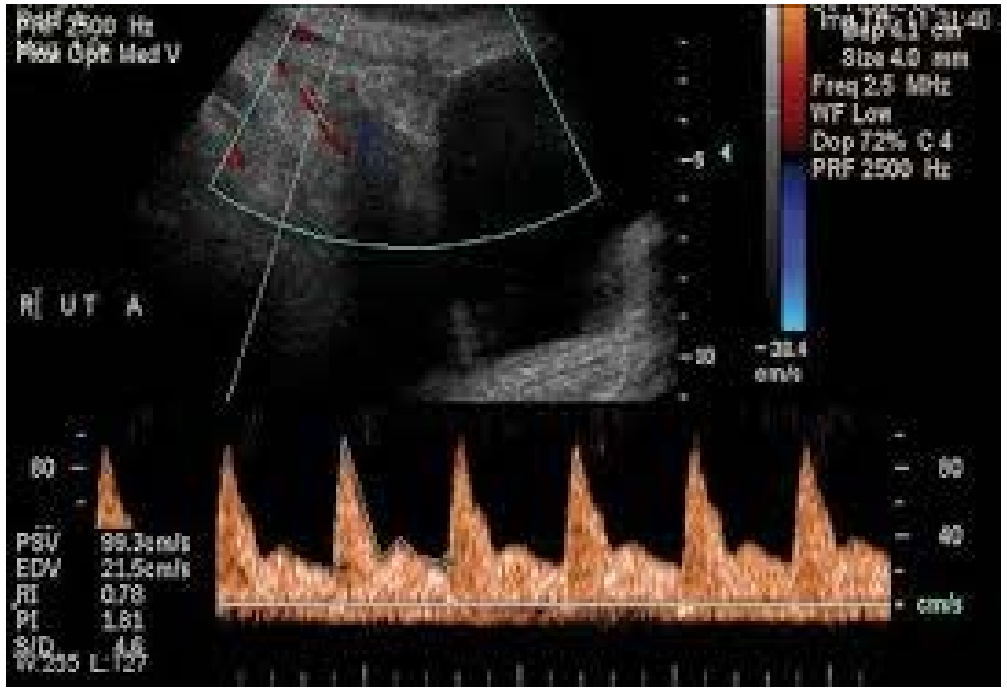
- Primiparity
- Previous preeclampsia
- CHT or CKD or both
- History of thrombophilia
- Multifetal pregnancy
- IVF
- Family history of preeclampsia
- DM
- Obesity
- SLE
- Advanced maternal age >40 years

Clinical risk factors

DR 37% early onset preeclampsia 29% late onset preeclampsia 20% GH

FPR 5%

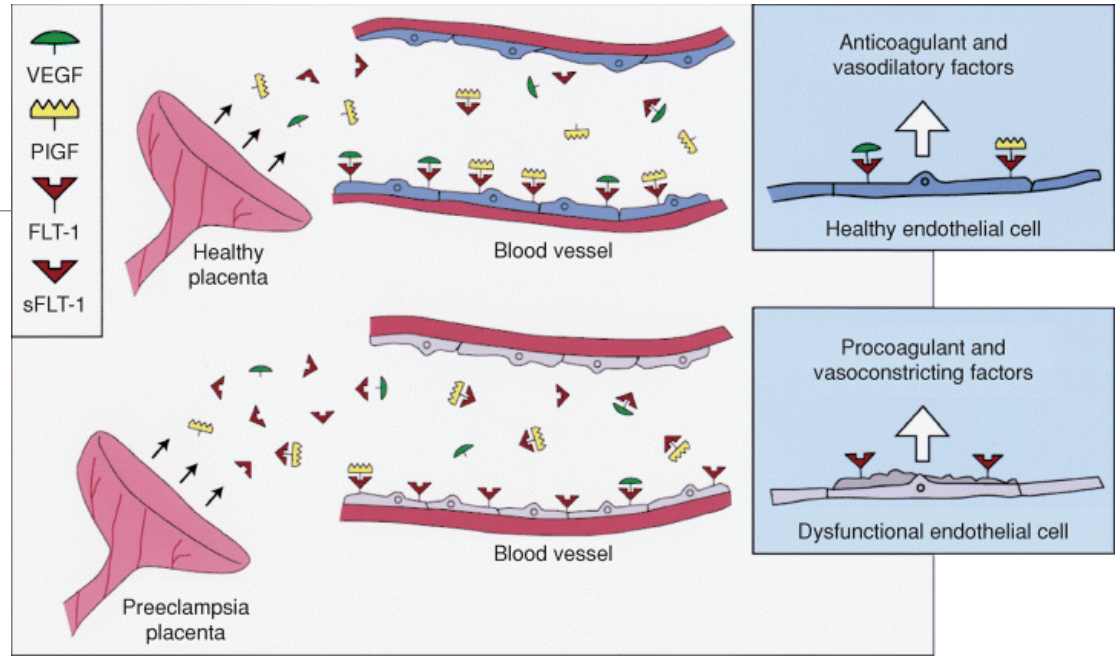
Uterine artery Doppler velocimetry



- **Early onset > term preeclampsia**
  - **LR+ 5-20**
  - **LR- 0.1-0.8**
- **Wide variability**
- **Poor predictive accuracy**
- **No RCT that demonstrated improved maternal or fetal outcomes**

Biomarkers

- sFlt-1
- PlGF
- Soluble endoglin
- PAPP-A
- Placental protein-13



-Not recommend using for clinical practice

-Evidence that maternal-fetal outcomes are improved by early screening is still lacking

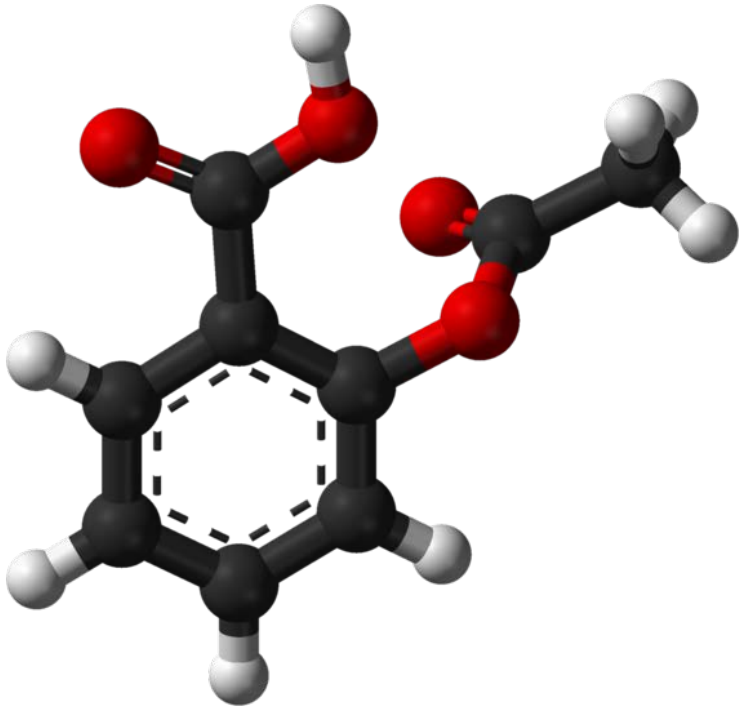
Prediction of preeclampsia

- **No single test reliably predicts preeclampsia**
- **Current evidence**
  - **Combination of biomarkers + UA Doppler studies → best predictive accuracy for identification of early onset preeclampsia**
- **Lack of standardization across various platforms**

Prevention

- **Low dose aspirin**
- **Antioxidant (Vit C and Vit E)**
- **Calcium**
- **Sodium restriction**
- **Lifestyle modification**

Aspirin



- Antiplatelet
- Block production of thromboxanes
- Low dose ≤81 mg
- 17% reduction in the risk of pre-eclampsia NNT 72

(Cochrane Database Syst Rev. 2007)

TABLE 4-1. PARIS number needed-to-treat with sample baseline event rates ⇦

	Sample baseline event rate	PARIS relative risk (95%CI)	Number needed-to-treat (95% CI)
Pre-eclampsia	18%	0·90 (0·84–0·97)	56 (35–185)
	6%		167 (104–556)
	2%		500 (313–1667)
Preterm <34 weeks	20%	0·90 (0·83–0·98)	50 (29–250)
	10%		100 (59–500)
	2%		500 (294–2500)
Perinatal death	7%	0·91 (0·81–1·03)	159 (75–476)
	4%		278 (132–833)
	1%		1111 (526–3333)
Small for gestational age baby	15%	0·90 (0·81–1·01)	67 (35–667)
	10%		100 (53–1000)
	1%		1000 (526–10 000)
Pregnancy with serious adverse outcome	25%	0·90 (0·85–0·96)	40 (27–100)
	15%		67 (44–167)
	7%		143 (95–357)

Reprinted from The Lancet, Vol. 369, Askie LM, Duley L, Henderson-Smart DJ, Stewart LA, Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data, PARIS Collaborative Group. 1791–98, Copyright 2007, with Permission from Elsevier.

Aspirin

- **Indication**
  - **History of early onset preeclampsia and preterm delivery at < 34 wks**
  - **Preeclampsia more than one prior pregnancy**
- **Low dose 60-80 mg**
- **Beginning in the late first trimester**

Antioxidant

- Oxidative stress – pathogenesis of preeclampsia
- Antioxidants may prevent preeclampsia
- Cochrane systematic review of 15 RCTs
  - Vit C and Vit E no benefit

Calcium

- **Meta-analysis of 13 trials (15,730 women)**
- **Significant reduction in preeclampsia risk (RR 0.45; 95%CI 0.31-0.65)**
- **Low baseline calcium intake (RR 0.36; 95%CI 0.20-0.65)**
- **Calcium supplementation 1.5-2 g**

Management of preeclampsia

Antepartum

- **Maternal evaluation**
  - History of severe preeclampsia
  - CBC, plt count
  - Cr
  - LFT
  - 24-hr urine protein or protein/creatinine ratio
- **Fetal evaluation**
  - FMC
  - Growth
  - Antenatal testing

Maternal and fetal assessment during expectant management

Maternal

- **Symptoms of severe preeclampsia**
- **Labor symptoms**
- **V/S, I/O, urine output**
- **Lab CBC with plt, Cr, LFT daily**

Fetal

- **FMC, NST daily**
- **BPP twice weekly**
- **Fetal growth q 2 weeks and UmA Doppler if FGR**

Indications for delivery

Maternal

- Recurrent severe HT
- Recurrent severe preeclampsia symptoms
- Progressive renal insufficiency
- Persistent thrombocytopenia or HELLP
- Pulmonary edema
- Eclampsia
- Abruptio placenta
- Progressive labor or rupture of membranes

Fetal

- GA 34 weeks
- Severe FGR less than 5th percentile
- Persistent oligohydramnios
- BPP of < or = 4/10 at least 6 hrs apart
- REDV of UmA
- Recurrent variable or late deceleration
- Death

Intrapartum management

- **Magnesium sulfate**
- **Antihypertensive to treat severe hypertension**
  - **Hydralazine = Labetalol = Nifedipine**
- **Route of delivery**
  - **GA, presentation, cervical status, maternal-fetal condition**

Intrapartum Magnesium sulfate

- **MgSO4 loading dose 4 g IV push slowly**
- **MgSO4 continuous dose 1-2 g/hr IV drip for 24 hour after delivery**
- **Monitors I/O, Vital signs, RR, Reflex**
- **Calcium gluconate in LR**

Monitor Mg level 4 - 8 **mg/dL therapeutic levels**

Intraoperative Magnesium sulfate

- **Induction of anesthesia and stress of delivery -- ⇑ seizure threshold**
- **Discontinuing Mg --⇑ postpartum eclampsia**

Postpartum hypertension and preeclampsia

- **Monitor BP at least 72 hours postpartum and again at 7-10 days**
- **Discharge instructions**
  - **Signs**
  - **Symptoms**
- **If new-onset HT with symptoms of severe preeclampsia or severe features– Magnesium sulfate**
- **Persistent postpartum hypertension**
  - **SBP ≥150 mmHg or DBP ≥100 mmHg – Antihypertensive drugs**
  - **If SBP ≥160 mmHg or DBP ≥100 mmHg should be treated within 1 hour**

Management of women with prior preeclampsia

BOX 6-1. Evaluation and Management of Women at Risk of Preeclampsia Recurrence ⇦

Preconception

- Identify risk factors (ie, type 2 diabetes mellitus, obesity, hypertension, and family history).
- Review outcome of previous pregnancy (abruptio placentae, fetal death, fetal growth restriction, and gestational age at delivery).
- Perform baseline metabolic profile and urinalysis.
- Optimize maternal health.
- Supplement with folic acid.

First Trimester

- Perform the following:
  - Ultrasonography for assessment of gestational age and fetal number
  - Baseline metabolic profile and complete blood count
  - Baseline urinalysis
- Continue folic acid supplementation.
- Offer first-trimester combined screening.
- For women with prior preeclampsia that led to delivery before 34 weeks of gestation or occurring in more than one pregnancy, offer low-dose aspirin late in the first trimester and discuss the risks and benefits of low-dose aspirin with other women.

Second Trimester

- Counsel patient about signs and symptoms of preeclampsia beginning at 20 weeks of gestation; reinforce this information with printed handouts.
- Monitor for signs and
- Monitor blood pressu
- Perform ultrasonograp
  molar gestation.
- Hospitalize for severe

Third Trimester

- Monitor for signs and
- Monitor blood pressu
- Perform the following
  - Laboratory testing
  - Serial ultrasonograp
  - Umbilical artery Dop
- Hospitalize for severe

BOX 6-2. Symptoms of Preeclampsia

- Swelling of the face or hands
- Headache that will not go away
- Seeing spots or changes in eyesight
- Pain in upper right quadrant or stomach
- Nausea or vomiting (in second half of pregnancy)
- Sudden weight gain
- Difficulty breathing

Modified from Barton JR, Siba

stet Gynecol 2008;112:359–72.

Management of chronic hypertension

Antihypertensive therapy

- **SBP > 160 mmHg, DBP > 105 mmHg**
- **Keep SBP 120-160 mmHg, DBP 80-105 mmHg**
- **End organ damage SBP<140 mmHg DBP<90 mmHg**

Antihypertensive therapy

TABLE 7-1. Antihypertensive Agents Used for Urgent Blood Pressure Control in Pregnancy

Drug	Dose	Comments
Labetalol	10–20 mg IV, then 20–80 mg every 20–30 min to a maximum dose of 300 mg or Constant infusion 1–2 mg/min IV	Considered a first-line agent Tachycardia is less common and fewer adverse effects Contraindicated in patients with asthma, heart disease, or congestive heart failure
Hydralazine	5 mg IV or IM, then 5–10 mg IV every 20–40 min or Constant infusion 0.5–10 mg/h	Higher or frequent dosage associated with maternal hypotension, headaches, and fetal distress—may be more common than other agents
Nifedipine	10–20 mg orally, repeat in 30 minutes if needed; then 10–20 mg every 2–6 hours	May observe reflex tachycardia and headaches

Abbreviations: IM, intramuscularly; IV, intravenously.

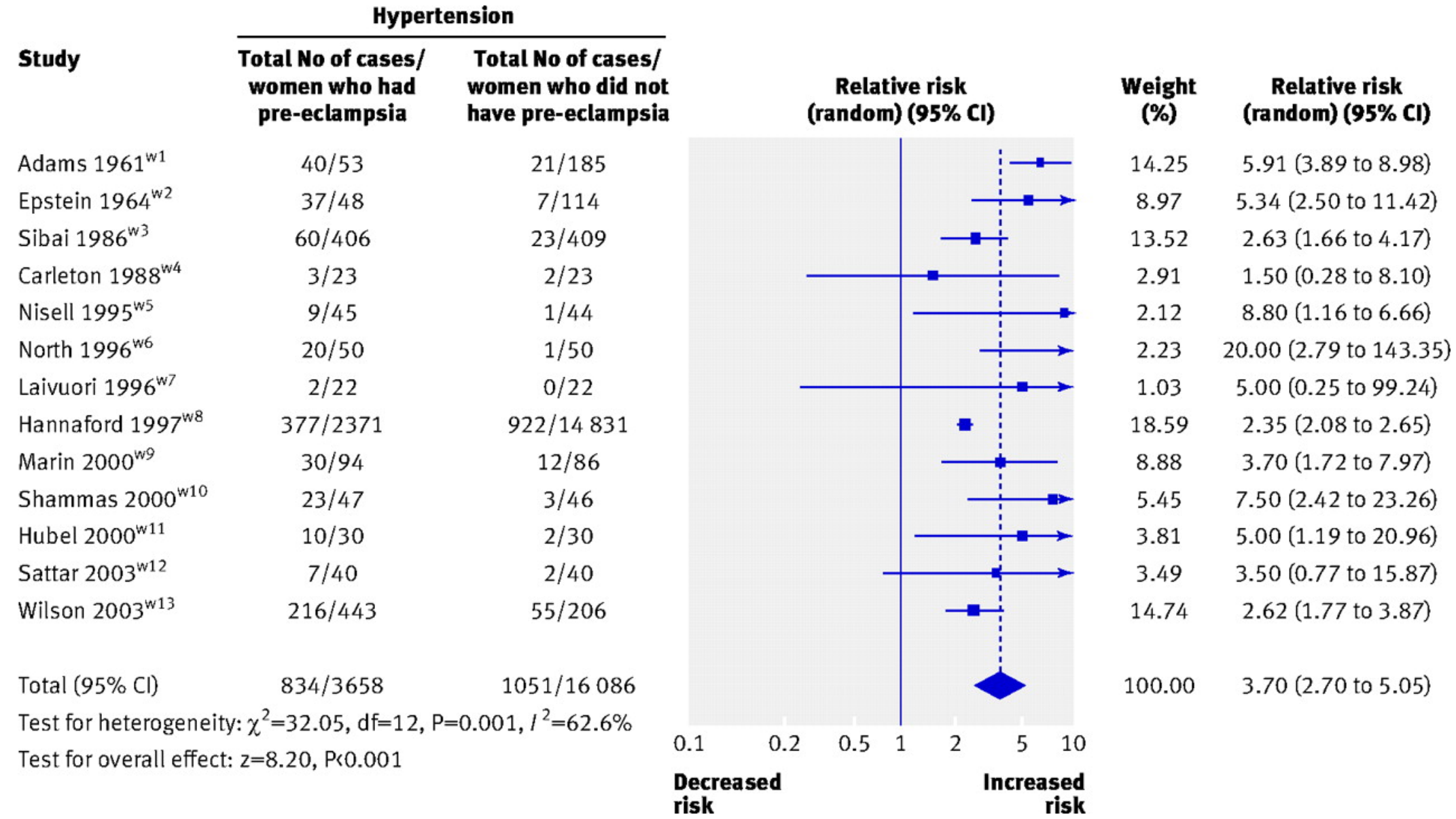
Antihypertensive therapy

TABLE 7-2. Common Oral Antihypertensive Agents in Pregnancy

Drug	Dosage	Comments
Labetalol	200–2,400 mg/d orally in two to three divided doses	Well tolerated Potential bronchoconstrictive effects Avoid in patients with asthma and congestive heart failure
Nifedipine	30–120 mg/d orally of a slow-release preparation	Do not use sublingual form
Methyldopa	0.5–3 g/d orally in two to three divided doses	Childhood safety data up to 7 years of age May not be as effective in control of severe hypertension
Thiazide diuretics	Depends on agent	Second-line agent
Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers		Associated with fetal anomalies Contraindicated in pregnancy and preconception period

Later life in women with prior preeclampsia

- Increase risk of cardiovascular diseases
- Greater risk if
  - Recurrent preeclampsia
  - Preterm delivery <37 weeks
  - FGR
- Equal risk with obesity or smoking
- Lifestyle modification
- Yearly checkup
  - BP, Lipid, FBS, BMI



Study	Hypertension: Total No of cases/ women who had pre-eclampsia	Hypertension: Total No of cases/ women who did not have pre-eclampsia	Relative risk (random) (95% CI)	Weight (%)	Relative risk (random) (95% CI)
Adams 1961[w1]	40/53	21/185		14.25	5.91 (3.89 to 8.98)
Epstein 1964[w2]	37/48	7/114		8.97	5.34 (2.50 to 11.42)
Sibai 1986[w3]	60/406	23/409		13.52	2.63 (1.66 to 4.17)
Carleton 1988[w4]	3/23	2/23		2.91	1.50 (0.28 to 8.10)
Nisell 1995[w5]	9/45	1/44		2.12	8.80 (1.16 to 6.66)
North 1996[w6]	20/50	1/50		2.23	20.00 (2.79 to 143.35)
Laivuori 1996[w7]	2/22	0/22		1.03	5.00 (0.25 to 99.24)
Hannaford 1997[w8]	377/2371	922/14 831		18.59	2.35 (2.08 to 2.65)
Marin 2000[w9]	30/94	12/86		8.88	3.70 (1.72 to 7.97)
Shammas 2000[w10]	23/47	3/46		5.45	7.50 (2.42 to 23.26)
Hubel 2000[w11]	10/30	2/30		3.81	5.00 (1.19 to 20.96)
Sattar 2003[w12]	7/40	2/40		3.49	3.50 (0.77 to 15.87)
Wilson 2003[w13]	216/443	55/206		14.74	2.62 (1.77 to 3.87)
Total (95% CI)	834/3658	1051/16 086		100.00	3.70 (2.70 to 5.05)

Test for heterogeneity: χ^2=32.05, df=12, P=0.001, I^2=62.6%

Test for overall effect: z=8.20, P<0.001

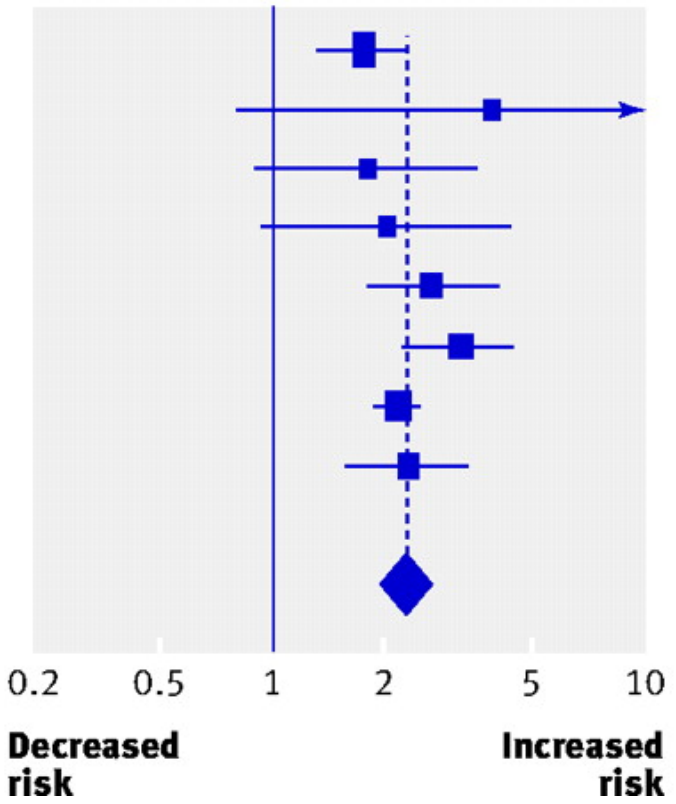
Pre-eclampsia and risk of hypertension in later life

Bellamy L, et al . BMJ 2007;335:974

Study	Ischaemic heart disease: Total No of cases/ women who had pre-eclampsia	Ischaemic heart disease: Total No of cases/ women who did not have pre-eclampsia	Relative risk (random) (95% CI)
Hannaford 1997[w8]	69/2371	216/14 831	1.65 (1.26 to 2.16)
Irgens 2001[w15]	27/24 155	325/602 117	3.61 (0.76 to 17.18)*
Smith 2001[w16]	12/22 781	31/106 509	1.70 (0.86 to 3.35)
Wilson 2003[w13]	26/1043	10/796	1.95 (0.90 to 4.22)
Kestenbaum 2003[w14]	35/20 552	64/92 902	2.55 (1.70 to 3.83)†
Funai 2005[w17]	41/1070	269/35 991	3.01 (2.18 to 4.33)
Ray 2005[w18]	228/36 982‡	1262/950 885	2.10 (1.82 to 2.42)
Wirkstrom 2005[w19]	176/12 533	2306/383 081	2.21 (1.56 to 3.31)†
Total (95% CI)	614/121 487	4483/2 187 112	2.16 (1.86 to 2.52)

Test for heterogeneity: χ^2=9.60, df=7, P=0.21, I^2=27.1%

Test for overall effect: z=10.00, P=0.001



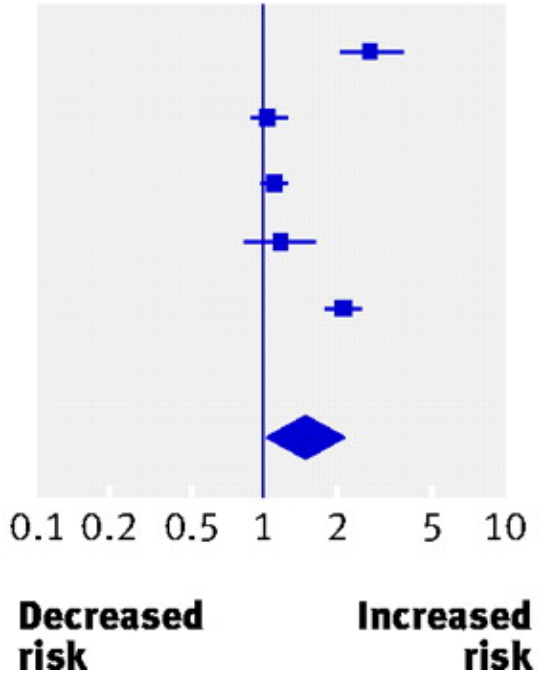
Pre-eclampsia and risk of fatal and non-fatal ischaemic heart disease events in later life.

Bellamy L, et al . BMJ 2007;335:974

	All cause mortality			
	Total No of cases/ women who had pre-eclampsia	Total No of cases/ women who did not have pre-eclampsia	Relative risk (random) (95% CI)	Relative risk (random) (95% CI)
Irgens 2001[w15] (early pre-eclampsia)	41/2649	284/26 018		2.71 (1.99 to 3.68)
Irgens 2001[w15] (late pre-eclampsia)	143/21 506	3882/576 099		1.04 (0.88 to 1.23)
Smith 2001[w16]	223/22 781	888/106 509		1.10 (0.96 to 1.25)
Wilson 2003[w13]	104/1043	72/796		1.17 (0.83 to 1.64)
Funai 2005[w17]	148/1070	1752/35 991		2.13 (1.79 to 2.53)
Total (95% CI)	659/49 049	6878/745 413		1.49 (1.05 to 2.14)

Test for heterogeneity: χ^2=65.87, df=4, P<0.001, I^2=93.9%

Test for overall effect: z=2.21, P=0.03



Pre-eclampsia and risk of death from any cause in later life

Bellamy L, et al . BMJ 2007;335:974

HYPERTENSION IN PREGNANCY

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

THANK YOU FOR YOURS ATTENTION