Pre-eclampsia
A refresher and update for home birth midwives

Today’s Objectives
› Know 2 diagnostic symptoms of preeclampsia and 10 symptoms of severe preeclampsia.
› Be able to assess the current theories of preeclampsia etiology and apply this information to create recommendations to clients for potential prevention, or for early recognition of preeclampsia.
› Create a guideline for your practice by listing appropriate lab work and listing indications for consult with an OB when symptoms of preeclampsia arise.

What we will cover…
› Definitions & when it occurs
› Risk factors & incidence
› Case review
› Theories of Preeclampsia Etiologies
› Diagnosis
› Case review
› Implications
› Management for Home Birth Midwives
› Evaluation at OB Level
› Medical Management

We are lucky to have such healthy clients, but that doesn’t mean we should not be vigilant for signs of preeclampsia.
Even clients with no risk factors, healthy diets and healthy lifestyles can develop preeclampsia. Don’t fall asleep!
Definition: Preeclampsia
Refers to the onset of:
- hypertension and
- proteinuria
after 20 weeks in a previously normotensive woman.

Define: Hypertension
- >140 systolic OR
  >90 diastolic.
- The elevation in blood pressure should be sustained, which is generally regarded as two measurements at least six hours, but no more than seven days, apart.

Define: Proteinuria
- Proteinuria = ≥0.3 grams in a 24-hour urine specimen.
- A random urine protein of 30 mg/dL or 1+ on dipstick is suggestive, but not diagnostic, of the presence of this criterion.

Degrees of Preeclampsia
- Preeclampsia can be classified as ‘severe’ when severe hypertension, severe proteinuria, or other signs/symptoms of end-organ injury are present (next slide).
- In the absence of any of these above findings, preeclampsia can be classified as ‘mild.’
The presence of one or more qualifies as Severe Preeclampsia:

- Symptoms of CNS dysfunction
  - Visual disturbance*
  - Severe headache**
  - Altered mental status
- Symptoms of liver capsule distention:
  - RUQ or epigastric pain,
  - Nausea
  - Vomiting
- Hepatocellular injury:
  - Serum transaminase concentration ≥ twice normal
- Severe blood pressure elevation:
  - Systolic bp ≥ 160 mm Hg or
diastolic bp ≥ 110 mm Hg
  on two occasions at least
six hours apart
- Thrombocytopenia:
  - <100,000 platelets/microL
- Proteinuria:
  - ≥ 35 grams in 24 hours
- Oliguria:
  - <500 mL in 24 hours
- Fetal growth restriction
- Pulmonary edema or cyanosis

One of four major hypertensive disorders related to pregnancy:

- Preeclampsia, eclampsia, HELLP
- Chronic/preexisting hypertension
- Preeclampsia superimposed upon chronic/
preexisting hypertension
- Gestational hypertension

When does it occur? (1 of 2)

- The clinical sx can
  appear anytime from
the 2nd trimester to the
first few weeks
postpartum;
- however, the initial
pathological changes
begin in the late first
trimester and consist of
abnormal remodeling
of the spiral arteries.
When does it occur?

- Most often after 34 weeks of gestation, including when the woman is in labor (i.e., "late onset preeclampsia")
- In about 10% of women, hypertension and proteinuria develop before 34 weeks of gestation (i.e., "early onset preeclampsia")
- In about 5%, preeclampsia is first recognized postpartum (i.e., "postpartum preeclampsia"), usually within 48 hours of delivery

Risk Factors (slide 1 of 2)

- Nulliparity
- Preeclampsia in a previous pregnancy
- Age >40 years (<18 years)
- Family history of preeclampsia
- Chronic hypertension
- Chronic renal disease
- Antiphospholipid antibody syndrome or inherited thrombophilia
- Vascular or connective tissue disease (lupus)
- Diabetes mellitus (pregestational and gestational)
- Multiple gestation (twins, etc)
- High body mass index
- Black race

Risk Factors (slide 2 of 2)

- Male partner whose mother or previous partner had preeclampsia
- Hydrops fetalis
- Unexplained fetal growth restriction
- Woman herself was small for gestational age
- Fetal growth restriction, abruptio placentae, or fetal demise in a previous pregnancy
- Prolonged interpregnancy interval (>48-60 mos)
- Partner related factors (new partner, limited sperm exposure [e.g., previous use of barrier contraception])
- Hydatidiform mole
- Susceptibility genes
- Poor diet (midwifery addition)

Case Review 1 & 2: Risk Factors at Onset of Care

- G8P5
- 41yo
- No other risk factors
- High quality food, but possibly not always enough due to demands of mothering 5 kids

- G2P0
- 32 yo
- No other risk factors
- See diet recall
Incidence
- 2-6% of healthy nullip women in US
- 5-8% of all pregnancies in US
- 7.5% of pregnancies worldwide
- 75% of cases classified as mild
- 25% severe

Theories of Preeclampsia Etiologies
- Abnormal development of the placenta
- Systemic endothelial dysfunction
- Immunologic
- Genetic
- Diet
- Inflammation/infection
- Increased sensitivity to angiotensin II
Pathogenesis: overview

- Although the origins of pre-eclampsia remain unclear, a major cause is the failure to develop an adequate blood supply to the placenta, leading to placental oxidative stress.

Review of Normal Placental formation

- When the zygote enters the uterine cavity and fluid enters, it is called the blastocyst.
- The blastocyst has an outer layer called the trophoblast.
- The cells of the trophoblast differentiate into the placenta and the membranes.
- The trophoblast has 2 functions:
  - To invade the endometrial tissue providing communication between the mother and fetus
  - To produce hormones responsible for maintaining the PG; mainly hCG

Normal Placental Formation cont’d

- During the process of implantation the fingerlike projections (syncytiotrophoblast) on the trophoblast invade or burrow into the uterine lining or decidua.
- It is the syncytiotrophoblast that burrows in and becomes the placenta.
- Cytotrophoblasts are inner cells of the trophoblast that burrow through the decidua into the myometrium and alter the uterine blood vessels.
Normal placental development

- Normally, from wks 4-14, placenta burrows into the uterine lining and spiral arteries in uterus change from narrow, muscular and coiled vessels to wide, soft vessels that provide a low-pressure system for bountiful blood flow.
- At wks 16-20 there is a second wave of placental migration, this time deeper into the myometrium.

Pathogenesis: Placental formation

- In preeclampsia, the cytotrophoblast infiltrates the decidual portion of the spiral arteries, but fails to penetrate the myometrial portion. Thus, the large, vascular channels characteristic of the normal placenta do not develop; instead, the vessels remain narrow, resulting in hypoperfusion.
- Remodeling of the spiral arteries (whether nml or abnml) probably begins in the late first trimester and is completed by 18 to 20 weeks of gestation, long before clinical symptoms appear.
So what if the placental vessels are smaller…?

- Hypoperfusion of the placenta results in the excess release of placental factors*, into the maternal circulation, where they trigger an inflammatory response and endothelial dysfunction.
Placental perfusion and?
- Reduced placental perfusion alone is insufficient to explain preeclampsia.
- Conditions such as intrauterine growth restriction, and preterm birth are associated with the same implantation abnormality as preeclampsia, yet manifest none of the maternal signs and symptoms found in preeclampsia.
- This suggests that preeclampsia involves an interaction of reduced perfusion with maternal factors.

Immunologic Etiology
- Immunologic abnormalities, similar to those observed in organ rejection graft versus host disease, have been observed in preeclamptic women.
- In preeclampsia, conflict between maternal and paternal genes is believed to induce abnormal placental implantation through increased natural killer cell activity.
- Definitive evidence for this theory is lacking.

Genetic Etiology
Although most cases of preeclampsia are sporadic, genetic factors are thought to play a role in disease susceptibility. For example:
- Primigravid women with a family history of preeclampsia (e.g., affected mother or sister) have a two- to five-fold higher risk of the disease.
- The spouses of men who were the product of a pregnancy complicated by preeclampsia are more likely to develop preeclampsia than spouses of men without this history.
- A woman who becomes pregnant by a man whose previous partner had preeclampsia is at higher risk of developing the disorder than if the pregnancy with the previous partner was normotensive.

Diet
- Healthy diets supply high amounts of antioxidants which help reduce endothelial damage.
- The placenta, receiving insufficient blood supply, releases free radicals into mother’s circulation, damaging the endothelial lining of all blood vessels (causing leakage, collecting platelets, and causing vasoconstriction and vasoospasm—sx of pre e).
- Increased dietary antioxidants can help counteract the action of free radicals.
- Antioxidants >> Less inflammation >> less free radicals, etc. Systemic inflammation can lead to shallow implantation.
Diet, continued

- Calcium-deficient diets may also be a risk; medical literature suggests supplementation for women at moderate to high risk of preeclampsia and women who are calcium deficient.
- Preeclamptic women seen to be deficient in Nitric Oxide, which mediates vasodilation and platelet aggregation. Aminic acid, L-arginine, is the substrate for synthesis of nitric oxide. Supplement bars of L-arginine had a modest effect on decreasing pre-E rates in a high risk population.*
- Foods high in protein are loaded with L-arginine. Meats, dairy, fish, nuts, oats, wheat germ have high levels of this amino acid.

Diet, blood volume expansion and the liver

- Inadequate nutrition affects the liver’s ability to expand blood volume, which is esp important if placenta implantation is abnl.
- Albumin, made in the liver is key protein for facilitating blood volume expansion. Liver makes albumin from dietary protein*. If caloric intake is low she will burn protein for energy needs.
- Adequate blood vol needed for nutrient/O2 transport to baby. With increased fetal and placental demands in 3rd trim more stress is placed on liver to meet blood vol needs.
- Liver demands also increased in pregnancy due to increased hormone metabolism and increased detoxification demands due to slowed digestion.
- All of this leads to liver, and then kidney damage as the kidneys try to reabsorb more fluid to make up for contracted blood vol.
- BP also increases to try to deliver this decreased blood to the fetus/placenta through smaller vessels.

Comments: Diet

- Is a bad diet alone enough to cause the defect in the trophoblast and subsequent abnormal placentation?
- Likely one of a few factors.
- However! Can diet prevent a women with abnormal placentation associated with preE prevent her from developing the disease? I would love to say yes!

Etiology: Inflammation/Infection

- Signs of maternal inflammation which appear to be present in normal pregnancies at term are exaggerated in preeclampsia.
- Trophoblastic debris and the microparticles shed during normal pregnancy are proinflammatory and this process is amplified in preeclampsia
- Not likely inflammation alone, as treatment with high doses of corticosteroids fails to improve maternal outcome in preeclampsia, despite suppressing inflammation.
Infection Continued

- A systematic review and metaanalysis of observational studies that examined the relationship between maternal infection and preeclampsia reported that the risk of preeclampsia was increased in pregnant women with urinary tract infection and periodontal disease.
- Other infections were studied and NOT found to contribute.*

Etiol: Increased Sensitivity to Angiotensin II*

- Angiotensin II is a peptide hormone that acts as a vasoconstrictor and stimulus for production/release of aldosterone. Thus raising blood pressure.
- This one I am still working on dissecting, however, it does appear that there is an auto-immune component at work here.
- Patients with preeclampsia have increased levels of antibodies to the angiotensin AT-1 receptor. Angiotensin II is the endogenous ligand for the AT-1 receptor, thus increased activation of this receptor by auto-antibodies could induce the hypertension and vascular injury observed in preeclampsia.

Pathophysiology and Etiology

In conclusion…

- The disease process appears to begin with abnormal placentation, which leads to hypoperfusion of the placenta and release of factors that cause oxidative stress and endothelial damage.
- Other maternal factors (immunological, genetic, dietary, etc) can contribute to the above to make preeclampsia.

Case 2 factors of etiology?

- Though at a glance, her history did not show conventional risks of preeclampsia, there was a history of chronic Lyme disease, still active in this pregnancy, for past 10 years. Chronic inflammation!
- Client began antibiotic treatment at 15 weeks through 36 weeks to reduce risk of transmission to baby. Liver stress!
- Poor nutrient absorption due to lack of normal gut flora?
Diagnosis: international criteria
- Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg**, and
- Proteinuria* ≥0.3 grams in a 24-hour urine specimen, or protein:creatinine ratio ≥0.3 mg/mg or >30 mg/mmol

Dx: History and Physical, sx/sxs
- Persistent and/or severe headache*
- Visual abnormalities (scotomata, photophobia, blurred vision, flashing lights or temporary blindness)
- Upper abdominal or epigastric pain**
- Nausea, vomiting
- Hyperreflexia
- Oliguria
- Dyspnea
- Altered mental status
- Fetal growth restriction
- Sudden, rapid weight gain (>5 lbs/wk) and facial edema

Case Review: No diagnosis based on H&P prenatally → Case 1
- Nml weight gain this pg
- Normal fetal growth
- Evidence of good blood vol expansion– hgb from 13.7 to 11.7
- BP at initial 9wk visit 110/82; next 3 visits 102/58, 110/72, 90/62, 28 wks 110/82; next 3 visits 104/76, 120/82, 122/76, 38 wks [last PN visit] 136/76.
- Visual disturbances noted (“floaters when standing”) 1x at 24 wks, 28 wks and 1x at 31 wks. No h/a’s.
- Minimal and slight ankle swelling at 37 and 38 wks
- Urine normal at each PN visit
Case 1 Continued: Sxs

- Early/pre labor at 40 wks, one BP reading of 140/90 and 134/86, Labor stopped.
- Later in day, ctx resumed; 148/98, 120/80, 128/80, 132/84 over 3 hours.
- Altered mental status (confusion/agitation, not remembering events of early in the day).
- No protein in urine.
- 8lb 2oz baby born at arrival at hospital following seizure.
- Unusual polyuria.
- Severe maternal hyponatremia — atypical presentation of preeclampsia/eclampsia.

Atypical presentations

- Onset of signs/symptoms at <20 weeks of gestation: usually associated with a complete or partial molar pregnancy
- Hypertension or proteinuria (but not both) with or without characteristic signs and symptoms of severe preeclampsia*
- Delayed postpartum onset or exacerbation of disease (>2 days postpartum)

Case Review: Diagnosis based on H&P at 39+ wks ➔ Case 2

- BP at 10 wk initial visit: 118/86;
- Next 3 visits 120/66, 124/68, 132/84 and 122/72;
- 28wks 118/82; 32wks 122/84; 34 wks 128/76;
- 37wks 132/86; 38wks 138/92; 39wks 138/92 and 118/78
- Nml wt gain
- Slight swelling, WNL from 31 wks on

Case Review: Diagnosis based on H&P at 39+ wks ➔ Case 2

- Measured small from 34 wks on (32 cm at 34 wks, 33 cm at 37 wks, 34 cm at 38, 36 at 39 wks)
- Reported spots/floaters in peripheral vision 2x at 37 wks
- +1 protein in urine and severe h/a at 39 wk visit
- Sxs in middle of night at 39+ wks: severe h/a, N&V, epigastric pain
Dx: Labs
- Platelet count (<100,000/microL)
- Serum creatinine (>1.3 mg/dL)
- Elevated liver enzymes; Serum aspartate aminotransferase, AST or alanine aminotransferase, ALT. (twice the upper limit of normal)
- Severe proteinuria (≥5 grams in 24 hours)
- Hemoconcentration (high hct)
- Serum uric acid (>6 mg/dL)

Case 2: Labs drawn 39+
- CBC
  - Hgb 15.3
  - Platelets 123,000
- Liver Panel
  - AST 3x the upper nml (146)
  - ALT 6x the upper nml (290)
- Kidney Panel
  - normal creatinine
  - Uric acid not done

Differential Diagnosis
- Preexisting hypertension
- Gestational hypertension (PIH)
- Acute Fatty Liver of Pregnancy
- Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS)
- Exacerbation of systemic lupus erythematosus (SLE).

Implications:
Increases risk of ...
- placental abruption (<1% in mild, 3% in severe)
- acute renal failure
- cerebral hemorrhage
- oligohydramnios
- hepatic failure or rupture
- pulmonary edema
- disseminated intravascular coagulation
- progression to eclampsia 1/400 in mild. 1/50 severe
... During this current pregnancy/labor/birth
Implications, cont’d

- Maternal death due to preeclampsia/ecl:
  - Worldwide, 10 to 15% of maternal deaths
  - In US, one of four leading causes of maternal death
  - approx one maternal death per 100,000 live births
  - 6.4 deaths per 10,000 cases

- Greater risk of restricted fetal growth and its associated problems* (greatest decrease in birth rate with early onset and severe)

- Greater risk of preterm birth

Long-term Maternal Implications

- Cardiovascular disease—preeclampsia is predictive of future cardiovascular and cerebrovascular disease. (17.8% risk with hx, vs 8.3% risk w/ no hx at age 50-59)

- Diabetes mellitus—gestational hypertension or preeclampsia in a first pregnancy was associated with a three- to four-fold increase in risk

- Subclinical hypothyroidism (not as strong evidence)

- Preeclampsia in subsequent preg

Prevention for clients with risk factors

- Adequate calories and protein* (80-100g daily)

- At least 50% of her diet should be high antioxidant vegetables and fruits – an anti-inflammatory diet

- Consider elimination of foods that trigger inflammation such as gluten and sugar

- Supplemental calcium* (1500-2000mg/day)

- Exercise at least 20 minutes 3-4 x per week

- Stress reduction activities: yoga, meditation, visualization

- Liver support herbs such as dandelion and milk thistle

- Nettles infusions to support the kidneys

- Consider WHO reco of 75 mg/day of aspirin for high risk women*

Creeping Blood Pressure:

Brainstorm ideas for midwifery management to prevent worsening of symptoms...
Okay, so you suspect preeclampsia. Now what?

Management: Homebirth MWs
- Consult with OB if:
  - 2 readings of BP over 140/90
  - One reading of >140/90 with +1 protein in urine
  - Concurrently draw labs (CBC, renal and hepatic panels, uric acid)
  - If anytime +1 or greater protein in urine, send client home with 24hr urine collection. Consult/refer if >.3 mg/dl.
  - Refer immediately if high BP in combination with any of the sx of severe preeclampsia (with or without proteinuria)

Evaluation: OB Level
- Repeat labs
- Obstetrical ultrasound (fetal weight, amniotic fluid volume)
- Fetal assessment (biophysical profile or nonstress test)
*The goal of the post-diagnostic evaluation is to determine the severity of disease and assess maternal and fetal well-being.*

Overview of management: OB
- The definitive treatment is delivery to prevent development of maternal or fetal complications from disease progression.
- Whether or not to “deliver the fetus” is based upon gestational age, the severity of preeclampsia, and maternal and fetal condition
Management: Early mild preeclampsia
- Expectant management until 37 weeks or signs of severe preeclampsia present
- Monitor labs every twice weekly
- Monitor fetus twice weekly
- Monitor blood pressure twice weekly
- Clear instructions to mom re reporting any sx's of severe
- Antenatal corticosteroids for lung maturity in case of progression to severe
- Induction or C/S at 37 weeks or sx's of severe preeclampsia

Management: Mild preeclampsia at term
- Current standard is to induce labor at 37 weeks with cervical ripening agent and then pitocin (grade B).
- Routine induction was associated with a significant reduction in composite adverse maternal outcome (no significant differences in neonatal outcome).

Management: Severe from 34 wks on
- Delivery
- The recommendation regarding severe preeclampsia is based largely on expert opinion; however, higher-level evidence is not likely to be forthcoming because this condition is believed to carry significant maternal risk with limited potential fetal benefit from expectant management after 34 weeks

Intrapartum Management
- Continuous fetal monitor (not evidence based)
- Repeat labs q 2-3 hours
- Strict fluid balance monitoring
- Magnesium sulfate (seizure prophylaxis until 24hrs pp)
- Management of hypertension
Case 2 Review: Medical Management

- Transfer to hospital upon receipt of stat labs at 39+4. Labor had spontaneously begun at home—very early labor on admission to hospital, enough to prevent induction.
- IV Magnesium Sulfate started for prevention of seizures.
- No BP management during labor (below 160/110).
- Labs repeat q 2-3 hours showed ongoing doubling of liver enzymes and dropping of platelet count to 40,000.

- Labor augmented with pitocin after 6 hours at 6-7 cms [c/tx slowed to q 7-10 mins, likely due to Mg Sulfate].
- Headache and liver pain treated with tylenol and antacids (ineffective).
- Vaginal birth 4-5 hours after onset of pitocin.
- Apgars 7 and 9 (low tone due to MgSO4)
- Despite therapeutic levels of maternal MgSO4, maternal seizures at 2 minutes and 4 hours postpartum. Sedation and ICU care following 2nd seizure. EEG, CT scan and continued lab monitoring. MgSO4 x 48 hrs pp and resumed for another 2 days following recurrence of BP spike and severe h/a, 6-day hospitalization. BP meds x 2 weeks.