THE NORTHERN HOSPITAL

PREECLAMPSIA

"Ariadne abandoned on Naxos" oil on canvas, Herbert James Draper, (1863-1920).

Adriane was the beautiful daughter of the all powerful King Minos of Crete and his wife Pasiphae. She was in a desperate dilemma as she had fallen in love with the Athenian hero Theseus who had come to Crete bringing seven boys and seven girls to be sacrificed to the terrifying Minotaur, a beast half human and half bull who inhabited the great Labyrinth. King Minos had demanded the sacrifices as part of his peace terms, when he had defeated Athens in a great war. The Athenians were desperate to escape from their horrific obligation and so had charged Theseus with a secret mission to kill the Minotaur. The Minotaur was the result of an unnatural union between Pasiphae and a fabulous white bull which the great god Poseidon had presented to Minos to sacrifice on the altar. Minos was so ashamed of his "step son", that he had him locked away from view in an impenetrable labyrinth designed by his architect Daedalus. Adriane wanted to assist Theseus in his secret mission and offered to help him in his task, providing he would marry her. Theseus agreed that he would elope with her after he had killed her half-brother, the horrible Minotaur. Adriane consulted Daedalus, who informed her that the labyrinth was so intricate that it was impossible for any mortal to ever find their way out of it. Ariadne however procured a long rope and had it secretly fixed at the entrance, so that when Theseus entered the labyrinth he would be able to find his way out by following the rope. Theseus was able to overcome and kill the Minotaur, and thanks to Ariadne's rope was then able to escape from the labyrinth. The two then escaped the wrath of King Minos by fleeing Crete and eloping together.

It is at this point that ancient sources became totally conflicting about the events that ensued from this point. Many different versions are recorded, but all say that because there were no witnesses nobody really knows what happened. All accounts agree that the couple rested on the island of Naxos, but then Adriane was abandoned on Naxos by Theseus or perhaps she was killed on the island. The great mystery is why Theseus left the island without her, and what in fact became of poor Ariadne? Some versions of what happened on Naxos are not complimentary to Theseus. Did he merely use Ariadne in order to achieve his mission of slaying the Minotaur? Homer was of the opinion that Theseus had no intention of marrying her and killed her on the island. Ariadne was however a very beautiful woman and so it is difficult to see how he would have so readily abandoned her on the island. Another common version of the story was that the god of wine Dionysus, one of the sons of Zeus, lusted after Ariadne and abducted her, threatening Theseus to remain silent on his intended abduction, and forcing him to return to Athens lonely and sad without his beloved Ariadne. Ariadne went to sleep for a rest and when she awoke Theseus was gone. Even the other gods of Olympus, began to wonder what had become of Ariadne. When they searched the island of Naxos all that they could find was her grass diadem, symbol of her noble kinship with the great king of Crete. Her diadem was sadly placed among the constellations of the northern skies in her memory. It can still be seen today as the small and faint Constellation of Corona Borealis, the Northern Crown...of Ariadne.

The gods were normally more than vigilant in their close monitoring of the affairs of humanity, but in the case of Ariadne they were quite negligent. The ancient writers were equally confused - was Theseus the villain in her disappearance - or was it really the god Dionysius who was the real villain? All this teaches us the importance of close monitoring of those who are vulnerable and at increased risk of harm when exposed to uncertain forces. Nowhere will this close vigilance be more important than in our patients who present with the uncertain forces of severe preeclampsia.

PREECLAMPSIA

Introduction

Pre-eclampsia is part of a spectrum of conditions known as the hypertensive disorders of pregnancy.

Its exact pathophysiology is uncertain.

It is diagnosed when there is hypertension and proteinuria that develop after 20 weeks of gestation.

It is best considered as a multisystem disorder as a range of other important associated complications may also be seen.

Pre-eclampsia is the commonest medical complication of pregnancy and is associated with substantial morbidity and mortality for both mother and baby.

Although outcome is usually good with proper management, pre-eclampsia can be a devastating and life threatening condition for both mother and baby.

The most severe manifestation of *pre*-eclampsia is **eclampsia**, which is characterised by the **onset of seizures.**

Patients who present with severe preeclampsia must be very closely monitored for impending eclampsia.

The most important initial therapy in severe pre-eclampsia is magnesium sulphate.

The only **definitive** cure is delivery.

See also document separate document for eclampsia.

Classification of Hypertensive Disorders of Pregnancy

1. Chronic hypertension:

    - Hypertension that predates the pregnancy or arises prior to 20 weeks of gestation.

2. Gestational hypertension:

    - Onset of hypertension after 20 weeks gestation, but without any maternal or foetal features of preeclampsia (there is no proteinuria) and a return to normal blood pressure within 3 months of delivery.

      Note that the circulatory volume is normal in contrast to the situation in preeclampsia where it is contracted.

- Hypertension defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg

3. Preeclampsia /eclampsia:

   - Onset of hypertension after 20 weeks gestation, together with other features of end organ dysfunction.

     The hypertension resolves within 6 weeks of delivery.

4. Preeclampsia superimposed on chronic hypertension:

   - The development of end organ dysfunction after 20 weeks gestation in women with chronic hypertension.

Pathophysiology

The syndrome poses a threat to both mother and foetus.

Current theories suggest that PET/eclampsia is a placental disorder, resulting in a widespread endothelial dysfunction and coagulopathy.

- There is a generalized vasospasm resulting in hypertension and organ damage due to hypoxia, especially of the brain, liver and kidneys.

- There is a widespread increase in vascular permeability resulting in "third space" losses. There is a loss of albumin in the urine reducing intravascular osmotic pressures. The result is peripheral oedema in association with a "contracted" intravascular volume.

- The coagulopathy primarily manifests as a severe DIC or the HELLP syndrome.

Predisposing Clinical Factors:

These include:

1. Age:

   - > 40 years of age.

2. Obstetric history:

   - Pre-eclampsia in a previous pregnancy

   - Previous gestational hypertension.

   - Multiple pregnancy.

   - Primigravida

3. Preexisting conditions:

    - Chronic hypertension
    - Chronic renal disease
    - Diabetes
    - Presence of antiphospholipid antibodies or other thrombophilias
    - Some congenital heart conditions.
    - Obesity (Body mass index $\geq$ 35) at booking in.

4. Family history

Complications:

The disease process most commonly progresses from a "pre-clinical" stage, through a symptomless clinical stage (hypertension, oedema, proteinuria, but without symptoms) to a clinical stage with symptoms.

The clinical stage with symptoms ("imminent" preeclampsia) may lead to a number of possible clinical crises as listed below:

1. Eclampsia:

    - This is the encephalopathic complications of altered conscious state and seizures.

2. Hypertensive emergencies:

    - Such as SAH or intracerebral haemorrhage.

3. Hepatic:

    - This may range from mild impairment to fulminant failure.

4. Renal:

    - Acute renal impairment / failure
    - Oliguria

5. Haematological:

    - DIC

- HELLP syndrome:
  - ♥ "H" Haemolysis, "E" Elevated liver enzymes, "LP" Low platelets
- Haemolysis

6. Respiratory:
   - Acute pulmonary oedema
7. Foetal crisis:
   - Placental abruptions or infarctions.
   - Growth retardation.
   - FDIU

Rarely a clinical crises may occur without preceding clinical signs of PET, sudden onset of seizures for example.

However, within 24 hours the typical signs of oedema, hypertension and proteinuria are seen.

Clinical Features

All pregnant women should have regular assessment of their blood pressure and urinary analysis for proteinuria.

These checks should be routine minimums for any pregnant woman who presents to the ED

Establishing the diagnosis:

Pre-eclampsia is diagnosed when there is hypertension and proteinuria that develops after 20 weeks of gestation.

Hypertension defined as:

- Systolic blood pressure **≥ 140 mm Hg**

Or

- Diastolic blood pressure **≥ 90 mm Hg**

Proteinuria defined as:

- ≥ 1+ on dipstick screening

Or

- ≥ 300 mg/day, (a more sensitive indicator)

Or

- A ratio of protein to creatinine >30 mg/mmol. [2]

Generalized oedema:

- Note that oedema is **no longer** included in the diagnostic features of pre-eclampsia.

  It occurs equally in normal pregnancy and those with pre-eclampsia.

  The *rapid* development of *generalized* oedema however may be abnormal.

- Note that ankle oedema especially at the end of the day in pregnancy is normal.

  Morning ankle oedema and oedema of the hands and face are more suggestive features of abnormal oedema.

Assessing the degree of severity:

As a rough guide severity may be assessed according to the following:

Severity	**Blood Pressure**	**Proteinuria**	**Symptoms**	**Biochemistry**
Mild	140/90	None	None	Normal
Moderate	150/ 95	(+1)	None	Normal
Severe	160/110	(+2)	Maybe present	Abnormal
Imminent	160/110	(+3)	Present	Abnormal

The features of severe or "imminent" eclampsia include:

- Clinical signs of preeclampsia:

  - ♥ Hypertension, proteinuria, *severe* swelling of hands, face, or feet of *sudden* onset.

in addition to:

- Symptoms

and/or:

- Laboratory abnormalities (see Investigations below).

Symptoms may include:

1. Neurological:

    - Headache.
    - Drowsiness
    - Hyperactive reflexes and / or clonus.

    These neurological findings are precursors of convulsions, i.e. eclampsia, and require consideration of magnesium sulfate therapy and urgent delivery

2. Visual disturbances:

    - Blurred vision or diplopia
    - Visual scotomata

    These may signifying occipital cortical ischemia.

3. Hepatic dysfunction:

    - RUQ abdominal pain and tenderness.

Eclampsia (or other crises) on occasions may occur suddenly without preceding clinical signs and symptoms of preeclampsia.

Preeclampsia (especially if symptomatic) may *progress rapidly* to fulminating complications and eclampsia.

Preeclampsia is an inevitably progressive process. The rapidity of progression of signs and symptoms is also important in addition to absolute values.

Differential diagnoses:

These will essentially be those of the hypertensive disorders of pregnancy listed above.

Investigations

When preeclampsia is suspected the following investigations will be needed:

Blood tests:

1. FBE:
    - Look in particular for thrombocytopenia (platelets <100 x 10^9/L) which can be an early sign of DIC.
2. U&Es and glucose:
    - For renal impairment/ failure.
    - Serum/plasma creatinine ≥ 0.09 mmol/L is significant.
3. LFTs:
    - A rise in liver enzymes, especially aspartate aminotransferase (AST) to at least twice normal indicates hepatic cellular damage.
    - Bilirubin may be raised secondary to haemolysis.
4. Coagulation profile:
    - INR, APPT
    - Decreased fibrinogen and increased FDPs
5. Serum uric acid:
    - Uric acid clearance falls in pre-eclampsia, and there is a consequent rise in serum levels. A value exceeding 0.35 mmol/L is abnormal.

Urine:

- FWT (note that protein may also be due to infection or contamination)
- MSU for M&C (to rule out infection)
- Macroscopic haematuria and/or casts on microscopy suggest an underlying renal parenchymal disease.

CTG:

- To monitor foetal well-being.

Severe/Imminent PET is diagnosed when there are symptoms and/or laboratory abnormalities. Intrauterine growth restriction is also a significant finding.

Management

1. General nursing:

    - **Monitor vital signs closely**
    - Nurse in a calm and quite environment
    - Nurse in the left lateral position
    - Commence a strict fluid balance chart
    - Establish IV access.

2. Establish monitoring:

    The exact degree of monitoring required will be determined by how unwell the patient is.

    The following should be considered:

    - IDC (monitor for oliguria, a urine output of at least 0.5 mls/kg/hr is desirable)
    - Blood pressure (non-invasive/ arterial line)
    - ECG
    - Pulse oximeter
    - CTG monitoring

3. Oral antihypertensive drugs: [1]

    - Oral antihypertensive drugs are mandatory for systolic blood pressure ≥ 170 mm Hg or diastolic pressure ≥ 110 mm Hg, although lower thresholds are advisable if signs or symptoms are present.

    Options include:

    - Labetolol
    - Methyldopa
    - Nifedipine SR

Severe or imminent cases will require more aggressive treatment:

4. Magnesium sulphate:

- There is now good evidence that, for women with severe pre-eclampsia, magnesium sulphate more than halves the risk of progression to eclampsia and probably reduces the risk of maternal death as well

- Magnesium sulphate is the drug of choice for treating eclamptic fits.

- It should generally *precede* any antihypertensive therapy.

See Eclampsia Document for dosing details.

Note that prophylactic *phenytoin* is **not** recommended.

5. Parenteral antihypertensives:

There are two main options:

- IV labetalol:

  - **Intravenous labetalol is now considered to be the primary drug of choice for the urgent control of severe hypertension in pregnancy.**

- IV hydralazine:

  - Traditionally used in the past, but in fact is classified as a class C drug in pregnancy.

  - Hydralazine may still be considered for women with a contraindication to IV beta blockers such as a history of significant asthma or congestive heart failure. [2]

See eclampsia document for further dosing details.

6. Delivery:

The only definitive "cure" for pre-eclampsia is to deliver the placenta.

Delivery is generally indicated in severe pre-eclampsia or in a foetus of greater than 37 weeks gestation.

Decisions about the exact timing on this as well as the mode of delivery (i.e. induced labour or caesarean section) can be complex, and are assessed on a case by case basis by the treating Obstetric Unit.

Factors that come into consideration will include

- The well-being of the mother
- The well-being of the baby
- The maturity of the baby
- The informed wishes of the mother

It should be noted however that the risks of pre-eclampsia do not resolve *immediately* upon delivery and that in fact both pre-eclampsia and eclampsia can occasionally present for the first time *after* the birth.

As a general rule most women will show signs of recovery within the first 24 hours of delivery.

Syntocinon may be used, but ergometrine should **not** be used.

Disposition

Any woman who presents to the ED with preeclampsia must be discussed with the Obstetric Unit.

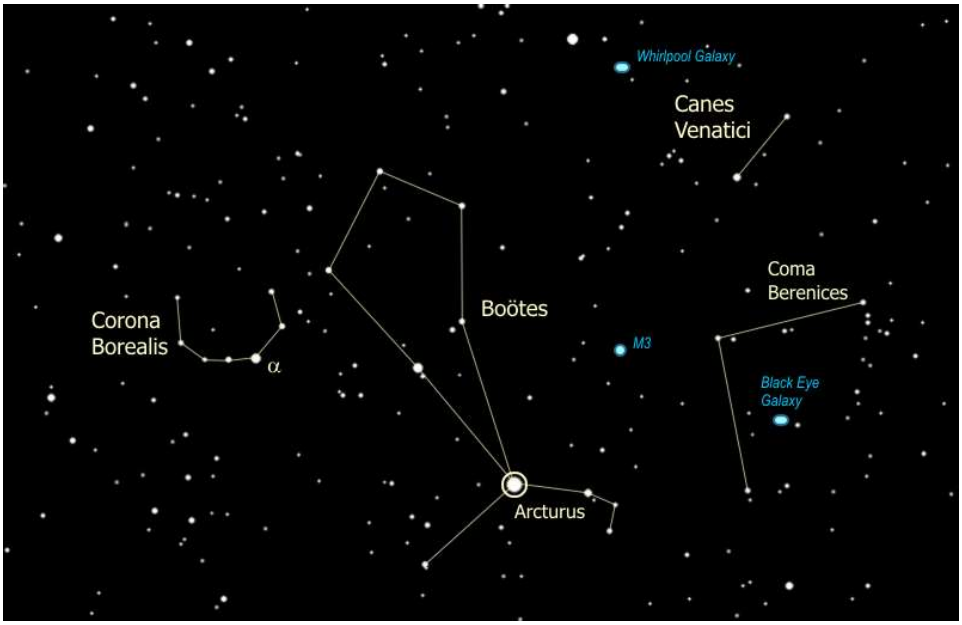
Those with moderate to severe preeclampsia are admitted to hospital. Mild cases may also be admitted depending on individual associated factors.

Patients with severe preeclampsia must be monitored, and admission should be to a High Dependency Unit, or Birthing Suite where this can occur.

After a pregnancy complicated by pre-eclampsia, women should be advised of the risk of recurrence and assessed for chronic hypertension and other underlying conditions

Women who have had pre-eclampsia are at increased risk of developing it again in subsequent pregnancies and need to be advised of this.

"Sleeping Ariadne", in marble, Roman copy of a Hellenistic sculpture of the Pergamene school, 2nd century BC, Vatican Museums.



The faint Northern Constellation of Corona Borealis, lies near the red giant star Arcturus in the Constellation of Bootes. It represents the diadem or crown of Ariadne.

References:

1. Duley L, Meher S and Abalos E, Management of pre-eclampsia. BMJ 332: 25 February 2006; 463-468

2. RWH Clinical Guidelines Pre-eclampsia, March 2013

3. eTG - March 2015

4. Marian Lee, Preeclampsia and Eclampsia, in Textbook of Adult Emergency Medicine, Cameron et al 4th ed 2015.

Dr J Hayes
Reviewed June 2014