Pharmacology

- General principles
- Organogenesis
- TGA pregnancy categories

Karen Whitfield
Pharmacy Team Leader
Women’s and Newborn Services RBWH
Medications in Pregnancy

• Use of a prescribed or non-prescribed medication 96-97% across trimesters

(Crowther HA. Patterns of medication use during and prior to pregnancy: the MAP study. Aust NZ J Obstet Gynaecol 2000;40:165-72)

• Pre-pregnancy chronic health conditions are on the rise (CDC USA) – including cardiac, metabolic, mental health and respiratory)

Australian Categorisation System for Prescribing Medicines in Pregnancy (TGA)

A: Taken by a large number of pregnant women without any proven increase in frequency of malformations or other direct or indirect harmful effects on fetus

B: Taken by only limited numbers of pregnancy women, without an increase in frequency of malformation other direct or indirect harmful effects on fetus

Studies in animals:

B1 Show no evidence of fetal damage

B2 Inadequate/lacking but available data show no evidence of fetal damage

B3 Have shown evidence of increased occurrence of fetal damage, but human significance uncertain

C: Drugs which owing to their pharmacological effects, have caused or suspected of causing, harmful effects on human fetus or neonate without causing malformations. Effects may be reversible

D: Have caused or suspected to cause, an increased incidence of human fetal malformations or irreversible damage

X: High risk of permanent damage in the fetus-contraindicated
Reference sources

TGA classification

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Category</th>
<th>Classification 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim</td>
<td>B3</td>
<td>Antimicrobial</td>
</tr>
</tbody>
</table>


**AMH 2017**

**Pregnancy**
Avoid in the first trimester as trimethoprim has been associated with congenital anomalies, e.g. cardiovascular and neural tube defects, oral clefts. It is unlikely to pose a risk in the second and third trimesters.

**Breastfeeding**
Safe to use.

**Product information Sheet**

**Use in pregnancy** (Category B3)
Trimethoprim may interfere with folic acid metabolism and animal experiments have shown that administration of very high doses of trimethoprim during organ development may give rise to birth defects typical of folic acid antagonism.

**Use in lactation** Trimethoprim is excreted in human milk. When Alprim is administered to a nursing mother, alternative arrangements should be made for feeding the infant.
Additional resources

• **Drugs in Pregnancy and Lactation** (Gerald G Briggs)
  – More complex monographs, Additional information with human/animal studies
  – USA – different pregnancy categorisation

• **Breast feeding – Medications in Mothers Milk** (Dr Thomas Hale and Dr Hilary Rowe)

• **Queensland Medicines Advice and Information Service (QMAIS)**
  – Email: QMAIS@health.qld.gov.au
  – Phone: 36467098 or 36467599
Metro North GP Alignment Program

MATUREITY WORKSHOP
Saturday, 25 MARCH 2017
Skills Development Centre, Royal Brisbane and Women’s Hospital

Case work 2: Complex cases
Kathy is 31 and planning her second pregnancy. You provided maternity shared care during her first pregnancy 5 years ago & diagnosed post natal depression, which responded well to Aropax (Paroxetine)

Despite several attempts at weaning her antidepressant medication, she copes much better when she is on it.

She has delayed having a second child due to fear of a return of depression, but now her first child is in school, she feels it is now or never

Does she need to stop the Aropax?
Outline your care during and after pregnancy
What resources are available to assist in planning her management?
Perinatal depression

• Antenatal depression
  ➢ More frequent during 2\textsuperscript{nd} and 3\textsuperscript{rd} trimesters

• Postnatal depression
  ➢ Greatest depression risk period
  ➢ Most common post-delivery complication of childbirth
### Perinatal depression

#### Risk factors for postnatal depression

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal depression</td>
<td></td>
</tr>
<tr>
<td>Hx infertility</td>
<td></td>
</tr>
<tr>
<td>Past Psych Hx</td>
<td></td>
</tr>
<tr>
<td>Lack of support</td>
<td></td>
</tr>
<tr>
<td>Adverse life events</td>
<td></td>
</tr>
<tr>
<td>Marital conflict</td>
<td></td>
</tr>
</tbody>
</table>

- Antenatal depression
- Hx infertility
- Past Psych Hx
- Lack of support
- Adverse life events
- Marital conflict

- Unplanned/unwanted
- Poor education
- Antidepressant discontinuation
- Younger/more children (≥ 4) closer together; birth trauma
- Medical co morbidity
- Recent loss

Only 20% of depressed pregnant women are taking an antidepressant.
### Perinatal depression consequences

<table>
<thead>
<tr>
<th>Mother</th>
<th>Baby</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine irritability</td>
<td>Decreased Apgar</td>
</tr>
<tr>
<td>Pregnancy induced Hypertension</td>
<td>Decreased breastfeeding</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Low birth weight</td>
</tr>
<tr>
<td>Antepartum haemorrhage</td>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Decreased uterine arterial flow</td>
<td>Increased NICU admissions</td>
</tr>
<tr>
<td>Pre-term delivery</td>
<td>Fetal distress</td>
</tr>
<tr>
<td>Increased LSCS rate</td>
<td>Prematurity</td>
</tr>
<tr>
<td>Post natal depression</td>
<td>Developmental delay</td>
</tr>
</tbody>
</table>
Antidepressant use during pregnancy

• Continue if depression severe & woman willing
• Slow withdrawal in low risk women pre-conception; recommence 2\textsuperscript{nd} trimester if necessary
• Avoid in 1\textsuperscript{st} trimester where possible
• Monotherapy if possible
• Avoid abrupt discontinuation
• Lowest effective dose
• Treat to remission
Antidepressant use during pregnancy

• Dose requirements may increase in 3rd trimester
• Unlikely benefit from tapering/discontinuing before birth; also there is a risk of recurrence
• Close monitoring of mother
• Close monitoring of baby

<table>
<thead>
<tr>
<th>Signs of withdrawal or toxicity in baby</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Floppy</td>
</tr>
<tr>
<td>• Irritable</td>
</tr>
<tr>
<td>• Constant crying</td>
</tr>
<tr>
<td>• Tremor</td>
</tr>
<tr>
<td>• Shivering</td>
</tr>
<tr>
<td>• Restlessness</td>
</tr>
<tr>
<td>• Increased tone</td>
</tr>
<tr>
<td>• Poor feeding &amp; sleep changes</td>
</tr>
</tbody>
</table>
Management of perinatal mental illness

• Metro North HHS Perinatal Mental Health Service - Non-Acute
  – RBWH: 0417 819 949
  – Caboolture/Redcliffe: 0408 151 138
  – TPCH: 0413 482 684
  – Perinatal psychiatrist available

• 1300 MH CALL (1300 64 2255) - Acute
“Successful parenting is a principal key to the mental health of the next generation,” John Bowlby.

About us

The Queensland Centre for Perinatal and Infant Mental Health (QCPIMH) supports parents, caregivers and communities to have the confidence, knowledge, skills and resources to support their own wellbeing and raise emotionally healthy and resilient children.

QCPIMH aims to bring perinatal and infant mental health needs to the attention of policy-makers, decision-takers and the general community, to improve the mental health of the next generation.
Management of perinatal mental illness

- Consider options including lifestyle & facilitating supports
- Cognitive behavioural therapy (CBT), interpersonal psychotherapy (IPT) and psychodynamic therapy have been shown to improve depressive symptoms in postnatal period
- Psychotherapy involving mother and baby may improve mother - baby interaction
- Options include:
  - Pregnancy support counselling
  - No Mental Health Plan required
  - 3 Medicare funded visits.
  - Search for eligible psychologists at: [www.psychology.org.au](http://www.psychology.org.au)
Management of perinatal mental illness

• Mental health treatment plan
• Psychiatry referral
• Private Practice Specialist Suite RBWH offers a one off assessment service with recommendations for ongoing care with GP
  
  – Reception / General Enquiries: (07) 3646 8346 / (07) 3646 8848
Management of perinatal mental illness

www.beyondblue.org.au
Management of perinatal mental illness

APPROPRIATE RESPONSES TO VARIOUS EPDS SCORES

Provide EPDS questionnaire or administer face-to-face

- Woman scores 1, 2 or 3 on Q10
  - YES
  - Woman scores 10, 11 or 12
    - Repeat EPDS within 2-4 weeks
  - Woman scores 13 or more
    - Depending on clinical judgement:
      - Antenatal: Repeat EPDS within 2-4 weeks and if 13 or more refer to appropriate health professional
      - Postnatal: Refer to appropriate health professional
    - Assess current safety of woman, fetus or infant and other children in the woman’s care

Notes: Ideally, referral will be to a woman’s usual GP or health professional with mental health training and expertise; referral and information exchange require consent from the woman.
* See Sections 3.1 and 3.2.

www.beyondblue.org.au
The Perinatal Anxiety Screening Scale (PASS):

**Administration, Scoring and Interpretation Guidelines**

Scourfield, S., Devlin, K., Hagan, R., Coutts, B., Lock, G., Cuthbert, D., 
Archives of Women's Mental Health. DOI: 10.1007/s00739-014-0425-8

**Description of the Scale**

The PASS is a valid and reliable 31-item self-report instrument designed to screen for problematic anxiety in antenatal and postpartum women. It differentiates between high and low risk for presenting with an anxiety disorder by measuring four domains that address specific symptoms of anxiety as they present in perinatal women. These domains form subscales which include: 1) Excessive Worry and Specific Fears, 2) Perfectionism, Control and Trauma, 3) Social Anxiety, and 4) Acute Anxiety and Adjustment. The PASS was validated for perinatal (i.e., pregnant or less than 1 year postpartum) women who are English-speaking, illiterate, and aged 16 years and older. The average time taken for respondents to complete the PASS is 6 minutes.

**Administration and Scoring**

The PASS is suitable for use by researchers and clinicians in a variety of settings to screen for problematic perinatal anxiety. Respondents rate each of the four clusters of anxiety symptoms, indicating the frequency of the symptoms over the previous month. The items are on a scale ranging from 0 ("not at all") to 3 ("almost always"). Example scoring:

1. Worry about the baby/pregnancy
   - Not at all: 0
   - Sometimes: 1
   - Often: 2
   - Almost always: 3

**Total Score**

A total PASS score is obtained by adding all of the items on the PASS. A cut-off score of 28 is recommended to differentiate between high and low risk for presenting with an anxiety disorder.

**Recommended severity ranges:**

<table>
<thead>
<tr>
<th>Anxiety Severity</th>
<th>Range of scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>0 – 20</td>
</tr>
<tr>
<td>Mild-moderate symptoms</td>
<td>21 – 41</td>
</tr>
<tr>
<td>Severe symptoms</td>
<td>42 – 93</td>
</tr>
</tbody>
</table>

**Subscales**

Subscale items describe clusters of symptoms which are characteristic of various anxiety disorders. Rassled item scores indicate risk of types of anxiety disorder presentations as indicated in the table below.

The PASS is not a diagnostic scale. However for clinical purposes it can be useful to have some indication of the nature of the anxiety symptoms being experienced. In addition, the answers to items if should be considered individually, as this item is a clinical indicator of phobia

### PASS subscales and items

<table>
<thead>
<tr>
<th>Anxiety symptoms indicating risk of disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized or specific anxiety</td>
</tr>
<tr>
<td>Generalized anxiety, specific fears</td>
</tr>
<tr>
<td>Generalized anxiety, panic</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive-compulsive</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive-trauma</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive-compulsions</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive tendencies</td>
</tr>
<tr>
<td>Generalized anxiety, panic</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive tendencies</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive-compulsions</td>
</tr>
<tr>
<td>Generalized anxiety, obsessive tendencies</td>
</tr>
<tr>
<td>Generalized anxiety, panic</td>
</tr>
</tbody>
</table>

Source: Women and Newborn Health Service. King Edward Memorial Hospital. WA
Medication use for depression in pregnancy

• **SSRIs** - preferred medication with most evidence of safety
  – main risk is neonatal withdrawal

• **Paroxetine** is Cat D due to reported ↑ risk of cardiovascular complications (Septal defects)

• Less evidence exists for TCADs, however can be considered if previously effective

• Growing body of safety around SNRIs
Medication use for anxiety in pregnancy

- **Benzodiazepines (BZD)** can be used short term while awaiting onset of SSRI or TCAD
- Side effects include sedation, preterm birth, low birth weight and low Apgar
- Long acting BZD are to be avoided
Medication use for bipolar disorder

- **Sodium valproate** (Epilim) associated with major birth defects and cognitive deficits and **should not be used** without consulting a psychiatrist.

- **Lithium** associated with very small increased risk of birth defects and consultation with a psychiatrist is advised.
Medication use for bipolar disorder

• First-generation antipsychotics associated with:
  – low birth weight
  – low gestational age
  – preterm birth

• Risks associated with second-generation antipsychotics less clear, but clozapine (Clopine) should NOT be initiated during pregnancy or in women contemplating pregnancy, without consulting a psychiatrist
Breastfeeding

• Depression
  – Very low levels of SSRIs & TCADs pass into breast milk
  – No contraindications to SSRIs & TCADs
  – Fluoxetine (Prozac) can accumulate in baby & ‘jitteriness’ has been described
  – Venlafaxine (Efexor, an SNRI) may accumulate in breast milk in levels at higher end of accepted safe range

Source: Women’s and Newborn Services. RBWH
Breastfeeding

• Anxiety
  – Short-acting benzodiazepines - for a limited period
  – Long-acting benzodiazepines - avoid
  – Specific regimens around timing of breastfeed are not considered necessary as on balance, there is a very small exposure to baby via breast milk
Breastfeeding

• Bipolar disorder and puerperal psychosis
  – Limited evidence for safety of anticonvulsants during breastfeeding.
  – Passage of lithium into breast milk more variable than other psychotropic medications.
  – If mother chooses to breastfeed, lithium should be used with particular caution and as with sodium valproate and clozapine should NOT be used without consulting a psychiatrist.
Useful resources

• Massachusetts General Hospital Center for Women’s Mental Health
  https://womensmentalhealth.org/?doing_wp_cron=1482262772.0649859905242919921875

• Just speak up (beyondblue Support Service)
  justspeakup.com.au

• Black Dog Institute blackdoginstitute.org.au

• Panda Perinatal Anxiety & Depression Australia panda.org.au

• Centre of Perinatal Excellence cope.org.au

• MoodGYM Training Program www.moodgym.anu.edu.au

• Gold Coast Health - small talk EDITION 2

Useful resources

• Queensland Centre for Perinatal and Infant Mental Health Library Service
  http://qcpimh.libguides.com/Library/home

• Victorian Government – Better Health Channel

• PCL Women talk, we listen… http://www.pcl.org.au/

• Women’s Health Queensland Wide – Midwife Check-in
  http://womhealth.org.au/services/midwife-check-in

• Peach Tree http://peachtree.org.au/
Take home message

• Perinatal mental illness is a significant cause of morbidity and mortality, affecting maternal and neonatal outcomes, health of families and the community

• EPDS to be administered at hospital booking in, repeated by 34 weeks, at 6 weeks post partum and prn

• Identification & appropriate treatment essential

• Suicide is a leading cause of maternal death in the developed world

“In 2012 and 2013, the leading cause of death of women during pregnancy and within 365 days of the end of pregnancy was suicide”

Red group - complex

• Nicole is 9 weeks pregnant. She looks pale and ill at ease as she walks into the consulting room.

• Her partner, Shaun is with her, looking agitated. “She’s been spewing her guts up doc; you’ve got to help! The dumb chemist gave her some vitamins, which cost me money and haven’t helped at all”

• Her BP is 90/60 sitting, 80/55 standing, her PR is 104 and she reports that her urine output is down. You notice a suspicious bruise as you take her blood pressure.

• Outline your approach to her care.
Nausea and vomiting in pregnancy

- Nausea - most common GI symptom of pregnancy affecting 80-85% of women
- Vomiting occurs in about 52%
- ~ 90% will have symptoms settle by 16-20 weeks

Source: Clinical Practice Guidelines, Antenatal Care Module 1
Nausea and vomiting in pregnancy

- Only 11-18% of women have symptoms limited to the morning
- Hyperemesis gravidarum is not common, affecting 0.3-1.5% of women
- Decreasing iron supplementation can ease symptoms of severe nausea

Source: Clinical Practice Guidelines, Antenatal Care Module 1
Antenatal resources

Resources are designed to be used by health professionals.

### Approved nutrition education materials

<table>
<thead>
<tr>
<th>Resource</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate</td>
<td>Food Standards Australia &amp; New Zealand</td>
</tr>
<tr>
<td>Healthy eating and weight gain during pregnancy</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Healthy eating for breastfeeding mothers</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Iron for pregnant women</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Listeria</td>
<td>Food Standards Australia &amp; New Zealand</td>
</tr>
<tr>
<td>Nutrition for vegetarian pregnant &amp; breastfeeding mothers</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Nutrition for vegan pregnant &amp; breastfeeding mothers</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Managing morning sickness</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Mercury</td>
<td>Food Standards Australia &amp; New Zealand</td>
</tr>
<tr>
<td>Gestational diabetes mellitus large file 1MB</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Gestational diabetes presentation large file 4.2MB</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Pregnancy weight gain chart for BMI &lt; 25kg/m2 (PDF, 495KB)</td>
<td>NEMO Antenatal group</td>
</tr>
<tr>
<td>Pregnancy weight gain chart for BMI &gt; 25kg/m2 (PDF, 499KB)</td>
<td>NEMO Antenatal group</td>
</tr>
</tbody>
</table>
Hyperemesis gravidarum - assessment

<table>
<thead>
<tr>
<th>Exclude:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pyelonephritis</td>
<td>• Appendicitis</td>
</tr>
<tr>
<td>• Cholecystitis</td>
<td>• Intestinal obstruction</td>
</tr>
<tr>
<td>• Hepatitis</td>
<td>• Diabetes</td>
</tr>
<tr>
<td>• Pancreatitis</td>
<td>• Thyrotoxicosis</td>
</tr>
<tr>
<td>• Trophoblastic disease</td>
<td>• Twin pregnancy</td>
</tr>
<tr>
<td>• Pre eclampsia</td>
<td></td>
</tr>
</tbody>
</table>
Hyperemesis gravidarum

- Investigations:
  - Bloods (FBC, BHCG, ELFT, TFT, HbA1c, Serum Amylase), MSU, USS

- Review diet and supplements

- Weigh daily

- Admission - IV rehydration +/- parenteral nutrition

- Supplements - Vitamin B6 (Pyridoxine)

- Anti-emetics - Metoclopramide, Ondansetron, Chlorpromazine, Domperidone

- Anti-depressant - Mirtazapine

- Other - Corticosteroids
Recognising Domestic Violence

- Physical
  - Pushing, shoving, punching, injuring
- Verbal
  - Constant put downs, name calling
- Sexual
  - Forced or unwanted sexual contact
- Social
  - Controlling where you go and what you do
- Financial
  - Being denied/refused access to money
Recognising Domestic and Family Violence

• Physical
  – Direct assaults on the body, pushing, punching, causing or threatening personal injury using objects or weapons; assaults on children, being denied access to the home, deprivation of sleep or food.

• Verbal
  – Constant put downs, name calling, humiliation, focus of insults around sexuality, body image, intelligence or parenting skills.

• Sexual
  – ANY forced or unwanted sexual contact

• Social
  – Systematically controlling who one sees, who is speak to or receives phone calls, emails, text messages from. Control where one lives; social and geographic isolation.

• Financial
  – Being denied/refused access to money, prevented from seeking or holding a job.

https://www.dvconnect.org/mensline/what-is-domestic-and-family-violence/
Recognising Domestic and Family Violence

• **Damage to personal property**
  – Using physical strength or violence to intimidate by causing or threatening to cause damage to property and valuables. E.g. Kicking holes in walls, throwing things, pulling doors of hinges, or damaging furniture, car or personal belongings.

• **Psychological**
  – Behaviour and/or comments or taunts to undermine sense of self, personal security or which are likely to impose a sense of vulnerability around personal safety or mental health and well being. E.g. driving dangerously, threatening or causing injury to pets, making threats about custody of children, or asserting that no one or courts will believe the story.

• **Spiritual/Cultural**
  – Not allowing practise of chosen religion or cultural beliefs, misusing spiritual/religious traditions to justify physical or other abuse.

• **Stalking**
  – Constant worrying or frightening by following, watching, phoning or messaging and waiting outside home or workplace

https://www.dvconnect.org/mensline/what-is-domestic-and-family-violence/
Management

• Organise a follow up appointment
  – without partner if possible
• Resources (consider safety)
  – Domestic Violence Hotline
    1800 811 811 / http://www.dvconnect.org/
• Facilitate early referral to hospital
  – Flag concerns via referral to social work
directly Ph 3646 8268
Reporting responsibilities

• As a doctor or registered nurse, you are a mandatory reporter and have a:
  – legal responsibility to report physical or sexual abuse under \textit{s13E Child Protection Act 1999}
  – duty of care responsibility to report any other form of child abuse (emotional) and neglect under \textit{s13A Child Protection Act 1999}

• Child Safety Services Regional Intake
  Brisbane 1300 682 254 (business hours)
• Child Safety After Hours Service Centre 1800 177 135
Anna, age 32, presents anxiously for advice. Her 11 year old step-daughter, who stayed with her last weekend, has just been diagnosed with Chicken Pox. Anna is 17 weeks pregnant.

Outline your approach.

What are current Australian recommendations for preconception, antenatal and postnatal vaccination? (all vaccines, not just Varicella)
Varicella - exposure

• ‘Exposure’ = sharing home/face to face > 5 minutes
• Check serology if no reliable history of chicken pox or immunisation
• If negative IgG, and
  – Exposure < 96hrs, give ZIG (order through Red Cross 07 3838 9010)
  – Exposure > 96hrs, no ZIG, give aciclovir if risk factors for maternal complications (> 20/40, lung disease, immunocompromised, smoker)
Varicella in pregnancy

• **At risk times for baby:**
  - 12-20 weeks 2% risk of Fetal Varicella Syndrome (scarring of skin, low birth weight, prematurity, problems affecting limbs, brain and eyes)
  - ≤ 5 days before birth high risk as baby develops infection without maternal antibodies

• **At risk times for mother:**
  - Risk of maternal compromise throughout pregnancy e.g. Pneumonitis
  - Give aciclovir if seen within 24 hours of onset of symptoms
  - Risk higher if > 20 weeks gestation
Varicella in pregnancy

- Refer all women with Varicella in pregnancy
- Liaise by phone with the GP Liaison Midwife in first instance to reduce risk to other pregnant women (isolation will be required)
Vaccination before, during, after...

- **Preconception**
  - MMR, Varicella, (check status prn) dTpa, Influenza and Pneumococcus for at risk women (including smokers)

- **During pregnancy**
  - Influenza
  - dTpa in third trimester of each pregnancy
  - Other inactivated vaccines if benefits of protection from vaccination outweigh the risks; avoid fever
  - Only **absolute C/I** = smallpox, although all **live attenuated vaccines are C/I** because of hypothetical risk of harm

- **Post partum**
  - dTpa, MMR prn

Cytomegalovirus (CMV)

- Evidence limited to support screening for CMV during pregnancy
- As CMV may be transmitted to baby and can have serious consequences, the focus is on giving women advice about hygiene measures that reduce risk of infection

Source: Australian Health Ministers’ Advisory Council 2014, Clinical Practice Guidelines: Antenatal Care – Module II
Australian Government Department of Health, Canberra
Cytomegalovirus (CMV)

• Consensus-based recommendations
  – Advise pregnant women about hygiene measures to prevent CMV infection such as frequent hand washing, particularly after exposure to a child’s saliva or urine
  – Only offer screening to pregnant women if they come into frequent contact with large numbers of very young children (e.g. child care workers)

Source: Australian Health Ministers’ Advisory Council 2014, Clinical Practice Guidelines: Antenatal Care – Module II
Zika Virus

• Management of pregnant women
  – Inquire about travel history
  – If history of travel to a Zika virus affected country during/immediately prior to pregnancy → evaluate

• Remind travellers to all areas where mosquito borne diseases are present to use mosquito bite prevention measures

Zika Virus - Preventing sexual transmission

• Men who have travelled to Zika virus affected areas whose partner is pregnant:
  – Avoid unprotected sex for duration of pregnancy

• Men who have had a confirmed Zika virus infection, whose partner is not pregnant:
  – Defer pregnancy and unprotected sex for at least six months

Orange group - complex

• Janice G1P0 is stressed! Running late for your appointment (caught in traffic), to discover you are running late anyway; she must leave ASAP to get back to work in time for an important meeting.

• She's had a “stinker” of a headache all week and is not surprised that her BP is elevated at 162/97. However she is certain it will settle once she calms down. Now K28

• Despite her protests (must get to meeting!!), you take her BP again after 5 minutes and the best you can get is 153/92.

• Outline your approach.
Online resources

Hypertension in pregnancy

Pre-eclampsia

- Most common serious medical disorder of human pregnancy
- Most common in primiparous women
- Only occurs when a woman is pregnant
- Only cure is to end pregnancy, even if baby premature
## Pre-eclampsia

### Signs and symptoms...

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Hypertension</td>
<td>Oedema -hands, feet &amp; face</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>Proteinuria</td>
</tr>
</tbody>
</table>

### In severe cases ... 

<p>| | |</p>
<table>
<thead>
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<th></th>
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<tbody>
<tr>
<td>Dizziness</td>
<td>Visual disturbances</td>
</tr>
<tr>
<td>Headaches</td>
<td></td>
</tr>
</tbody>
</table>

### Left untreated can lead to ...

- Convulsions and other life-threatening problems for mother and baby
Pre-eclampsia

• In Australia
  – mild pre-eclampsia occurs in 5-10% of pregnancies
  – severe pre-eclampsia in 1-2% of pregnancies
  – pre-eclampsia and associated complications account for 15% of direct maternal mortality and 10% of perinatal mortality
  – is indication for 20% of labour inductions and 15% of caesarean sections
  – accounts for 5-10% of preterm births

Source: www.thewomens.org.au/Preeclampsia
2.2 Diagnosis of preeclampsia

Hypertension arising after 20 weeks gestation confirmed on 2 or more occasions and accompanied by one or more of the organ/system features identified in Table 3. Diagnosis of preeclampsia.

- Raised BP is common but not always the first manifestation
- Pre-existing hypertension is a strong risk factor for the development of preeclampsia\(^1\) and requires close clinical surveillance
- Proteinuria is common but should not be considered mandatory to make the clinical diagnosis\(^1\)

Table 3. Diagnosis of preeclampsia

<table>
<thead>
<tr>
<th>Organ/System</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>- Random urine protein to creatinine ratio greater than or equal to 30 g/mmol</td>
</tr>
<tr>
<td></td>
<td>- Serum or plasma creatinine greater than or equal to 90 micromol/L or</td>
</tr>
<tr>
<td></td>
<td>- Oliguria</td>
</tr>
<tr>
<td>Renal</td>
<td>- Thrombocytopenia (platelets less than 100 x 10^9/L)</td>
</tr>
<tr>
<td></td>
<td>- Haemolysis: schistocytes or red cell fragments on blood film, raised bilirubin, raised lactate dehydrogenase (LDH), decreased haptoglobin</td>
</tr>
<tr>
<td></td>
<td>- Disseminated intravascular coagulation (DIC)</td>
</tr>
<tr>
<td>Haematological</td>
<td>- Raised transaminases</td>
</tr>
<tr>
<td></td>
<td>- Severe epigastric or right upper quadrant pain</td>
</tr>
<tr>
<td>Liver</td>
<td>- Severe headache</td>
</tr>
<tr>
<td></td>
<td>- Persistent visual disturbances (photopsia, scotomata, cortical blindness, retinal vasospasm)</td>
</tr>
<tr>
<td></td>
<td>- Hyperreflexia with sustained clonus</td>
</tr>
<tr>
<td></td>
<td>- Convulsions (eclampsia)</td>
</tr>
<tr>
<td></td>
<td>- Stroke</td>
</tr>
<tr>
<td>Neurological</td>
<td>- Pulmonary oedema</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>- Fetal growth restriction (FGR)</td>
</tr>
<tr>
<td>Uteroplacental</td>
<td></td>
</tr>
</tbody>
</table>
Anna presents at 35 weeks for an unscheduled appointment. Her pregnancy has been progressing smoothly, but she is clearly anxious. Her baby, who usually ‘kicks like a world cup soccer player’, has been noticeably quiet since yesterday afternoon. She asks “Is something wrong with my baby?”

- What do you say to her?
- What do you do if you can hear the fetal heart?
- What do you do if you cannot hear the fetal heart?
Obstetric Review Centre (ORC)

• Common presentations include:
  – Labour/Preterm labour
  – Uncertainty about ruptured membranes or premature rupture of membranes
  – Reduced or no fetal movements
  – Review of hypertensive women referred by their GP, obstetrician or midwife
  – Bleeding after 14 weeks
  – Headaches
  – Feeling unwell
MATERNITY WORKSHOP
Saturday, 25 MARCH 2017
Skills Development Centre, Royal Brisbane and Women’s Hospital

Antenatal testing for chromosomal abnormality

Pauline McGrath  
Senior Genetic Counsellor  
Churchill Fellow  
Genetic Health Queensland RBWH

pauline.mcgrath@health.qld.gov.au
Prenatal diagnosis and screening

- Screening
- Invasive testing
- PAPP-A
- Referrals
Assess knowledge and provide information

• Variable patient understanding of Down syndrome (trisomy 21), Edward syndrome (trisomy 18) and Patau syndrome (trisomy 13)

• Cultural and language barriers

• Information delivery in verbal and written forms

• Document
  – Information provided, offer of test/s, response of patient
Advantages of screening

• More accurate than age-related risk alone
• Screening in first trimester enables diagnostic testing
• Reduction in utilisation of invasive tests
• Highest detection rate
  – NIPT – 99% detection rate for trisomy 21
  – Combined first trimester screen - 85-90% detection rate
# Aneuploidy tests compared

<table>
<thead>
<tr>
<th>Test</th>
<th>Down Syndrome Detection Rate</th>
<th>Screen positive rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Invasive Prenatal Testing (NIPT)</td>
<td>99%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Nuchal translucency scan (NTS)</td>
<td>70%</td>
<td>5%</td>
</tr>
<tr>
<td>Combined NTS, Serum testing (B HCG, PAPP-A)</td>
<td>85-90%</td>
<td>5%</td>
</tr>
<tr>
<td>Second trimester serum test (Free B HCG, oestriol, AFP +/- Inhibin)</td>
<td>65-70%</td>
<td>5%</td>
</tr>
<tr>
<td>Morphology scan</td>
<td>20-50%</td>
<td>10-15%</td>
</tr>
</tbody>
</table>
Nuchal translucency scan
11 to 13^{+6} weeks

Sensitivity (detection rate) = 70%
Screen positive rate = 5% (1/20 screened ‘high risk’)
Nasal bone (NB)

Presence of NB increases screening sensitivity

Image source: Maternal Fetal Medicine RBWH
Absent nasal bone

What is it?

- Delayed ossification of NB
- It does NOT mean that baby does not have a nose

Image source: Maternal Fetal Medicine RBWH
Absent nasal bone

- At 11-13 weeks gestation, ~1-2% of normal fetuses have an absent nasal bone
- ~60% of fetuses with trisomy 21 have an absent nasal bone
- Overall effect on screening is increased detection and reduced screen positives
Combined First Trimester Screen

- Nuchal translucency scan and maternal serum -PAPP-A and fβhCG (9-13 weeks)
- Cut-off for high risk 1/300
- Test results should be ‘combined’ and not provided separately

<table>
<thead>
<tr>
<th>Trisomy 21</th>
<th>Trisomy 18</th>
<th>Trisomy 13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background risk:</strong> 1 : 267</td>
<td>1 : 640</td>
<td>1 : 2010</td>
</tr>
<tr>
<td><strong>Ultrasound risk:</strong> 1 : 2173</td>
<td>1 : 3215</td>
<td>1 : 25877</td>
</tr>
<tr>
<td><strong>Biochemistry risk:</strong> 1 : 626</td>
<td>1 : 4552</td>
<td>1 : 5169</td>
</tr>
<tr>
<td><strong>Adjusted risk:</strong> 1 : 5115</td>
<td>1 : 12794</td>
<td>1 : 40199</td>
</tr>
</tbody>
</table>
Example Report

Indication:
1st Trimester screening.

History:
Obstetric History: Gravida: 5. Para: 2. CMV infection.

EDD by ultrasound: 7 January 2011.
Gestational age: 13 weeks + 3 days

First Trimester Ultrasound:
Fetal heart action present. Frequency 149 bpm.
Crown-rump length (CRL) 75.0 mm 50th%Nuchal translucency (NT) 1.92 mm
Nasal bone present
Fetal anatomy: skull/brain appears normal, heart not examined, spine appears normal, abdomen appears normal, stomach visible, bladder visible, hands both visible, feet both visible.
Additional Markers for Risk Assessment: Ductus Venosus (a-wave): positive.
Cervix length 46 mm.

Summary of ultrasound findings: normal intrauterine pregnancy.
Size agrees with dates. I could not see any fetal abnormality on today’s scan. Ultrasound is unable to detect all fetal abnormalities.

Maternal Serum Biochemistry:
Sample taken on 30 June 2010.
Free beta hCG: 99,000 IU/L, equivalent to 2.7078 MoM.
PAPP-A: 2,000 IU/L, equivalent to 0.5254 MoM.

Estimated risk for chromosomal abnormalities:

<table>
<thead>
<tr>
<th></th>
<th>Trisomy 21</th>
<th>Trisomy 18</th>
<th>Trisomy 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background risk</td>
<td>1 : 360</td>
<td>1 : 924</td>
<td>1 : 2886</td>
</tr>
<tr>
<td>Adjusted risk</td>
<td>1 : 110</td>
<td>1 : 18484</td>
<td>1 : 57726</td>
</tr>
</tbody>
</table>
What else can be detected with cFTS?

• Increased nuchal translucency (>3.5mm)
  – cardiac malformations, genetic syndromes
  – Recommend tertiary morphology scan 18-20 weeks gestation

• Low PAPP-A (<0.4 MoM)
  – associated with pre-eclampsia, growth restriction & stillbirth
  – fetal growth & uterine artery doppler assessment at 22-24 weeks gestation
Non-invasive Prenatal Testing (NIPT)

- Fetal cell-free DNA found in plasma of pregnant women from 10 weeks gestation
- Testing of fetal DNA in maternal blood poses no risk to pregnancy
- Major benefit is significant reduction in need to perform invasive test
- 96.6% positive predictive value
- 100% negative predictive value
- Not a diagnostic test, abnormal results should be confirmed via invasive testing
Benefits and limitations of NIPT

- Highest sensitivity and specificity
- Reduces invasive testing
- Beneficial for women unable to access cFTS or later gestation
- No Medicare rebate, costs vary
- Abnormal results require confirmation by invasive testing
- Advantages of cFTS
  - assess number of fetuses, structural abnormalities and PAPP-A
Contingent screening model

All women offered combined first trimester screening as primary test

Low-risk women (risk <1 in 1000) (86.9% of women)
- negative NIPT result (estimate 98%)
  - No further testing (a total of 98.6% of women)

Intermediate-risk women (risk <1 in 50 to ≥1 in 1000) (11.9% of women)
- Positive NIPT result or 'no call' (estimate 2%)
  - Invasive test (a total of 1.4% of women)
  - Overall detection of trisomy 21 is 97%

High-risk women (risk ≥1 in 50) (1.2% of women)
- Invasive test (a total of 1.4% of women)
  - Overall detection of trisomy 21 is 97%
Triple test

- Rarely used
- Blood test at 15-20 weeks gestation
- $fβhCG + Oestriol + alpha fetoprotein (AFP)$
- Detection rate 70%
- Provided risk assessment for open neural tube defects (AFP)
- Used 1 in 250 cut-off for high risk for chromosomal abnormalities
- Provides an option for screening later in gestation
Purpose of the 18-20 week morphology ultrasound scan

- **Confirm**
  - viability
  - gestational age by measuring fetal biometry

- **Assess**
  - number of fetuses
  - placental site
  - amniotic fluid volume
  - fetal anatomy

Source: Women’s and Newborn Services RBWH
Detection rates for fetal abnormalities at 18-20 week morphology scan

- Neural tube defects (>90%)
- Cardiac abnormalities (major 40-75%)
- Cleft lip (>75%)
- Trisomy 21 (20-50%)
- Trisomy 13 (>90%)
- Trisomy 18 (>90%)
Morphology scan as Down syndrome screen

• Detection rates reported as low as 17% (Finland)

• Markers on morphology scan that are useful
  – thickened nuchal fold >6mm
    • short or absent nasal bone
    • Echogenic bowel

• Echogenic bowel
  – associated with early onset growth restriction, CMV and cystic fibrosis
When should 3D/4D ultrasound be used in pregnancy?

- Main application is for ‘entertainment’ or ‘keepsake’ imaging
- Fetal anomaly detection not enhanced
- Can assist for surface anatomy abnormalities e.g. facial cleft
- Not used in screening for chromosomal abnormalities
Down Syndrome

Down syndrome is more likely if your baby has a small nuchal fluid at 10 weeks of pregnancy. If the nuchal fluid is not seen in the ultrasound, there may be a problem with the baby's heart, brain, or body. Down syndrome is a genetic condition that affects the development of the brain and other organs. It is caused by the presence of an extra copy of chromosome 21.

Screening tests for Down Syndrome

Screening tests are available to help detect Down syndrome. These tests can be performed during the first, second, or third trimester of pregnancy. The tests can help you decide whether to continue with the pregnancy or to consider other options.

First trimester Combined test / First test

This is a blood test that can be done between 11 and 14 weeks of pregnancy. It is a combination of a maternal serum alpha-fetoprotein (MSAFP) test and a maternal serum peptide (MSA-P) test. The test can help detect Down syndrome and other abnormalities.

Second trimester Trisomy 21 screening test / Trisomy 18 screening test / Trisomy 13 screening test

This is a blood test that can be done between 15 and 20 weeks of pregnancy. It is a combination of a maternal serum alpha-fetoprotein (MSAFP) test and a maternal serum peptide (MSA-P) test. The test can help detect Down syndrome and other abnormalities.

Diagnostic tests

Diagnostic tests include amniocentesis, chorionic villus sampling, and ultrasound. These tests can help detect Down syndrome and other abnormalities.

What should I do if my screening test shows a risk?

If your screening test shows a risk of Down syndrome, you should talk to your doctor about the options available to you. You may choose to have more tests to confirm the diagnosis.

What is the risk of having a baby with Down syndrome?

The risk of having a baby with Down syndrome is 1 in 700 for all women. The risk is higher for women who are older than 35 years. The risk is also higher for women who have had a previous child with Down syndrome.

Did you know that .......

Most pregnant women and partners can expect to have a healthy baby. However, every pregnancy carries a small risk of having a baby with Down syndrome or other chromosomal problems.

Key points to remember

1. Your baby is at increased risk of having Down syndrome.
2. Your baby is at increased risk of having Down syndrome.
3. Your baby is at increased risk of having Down syndrome.
4. Your baby is at increased risk of having Down syndrome.
5. Your baby is at increased risk of having Down syndrome.
6. Your baby is at increased risk of having Down syndrome.
7. Your baby is at increased risk of having Down syndrome.
8. Your baby is at increased risk of having Down syndrome.
9. Your baby is at increased risk of having Down syndrome.
10. Your baby is at increased risk of having Down syndrome.

Contact your local health service for more information.

Download from:
Screening summary

- *Inform and offer* screening tests for chromosomal abnormality to **ALL** pregnant women
- NIPT has best detection rate for trisomy 21
  - No Medicare rebate
- cFTS – reliable detection rate and offers additional morphological findings
  - Medicare rebate available
Post screening appointment

• Explain risk results using different methods e.g. 1 in 100 = 1% percent
• Offer diagnostic testing by CVS or amniocentesis where appropriate
• Provide referral to Maternal Fetal Medicine for CVS or amniocentesis or additional counselling
• Provide written information
Chorionic Villus Sampling (CVS) (from 11 weeks)
Amniocentesis (from 16 weeks)

Pregnancy loss rate of 0.5-1% for both transabdominal CVS and amniocentesis
Benefits vs. Risks of testing

• Invasive testing – only method of diagnosis in pregnancy
• Some parents will choose to terminate for fetal abnormality
  – In 2007-08 50.4% of pregnancies affected by Down Syndrome were terminated prior to 20 weeks gestation in Queensland (Howell, 2009)
• Preparation for birth is a valid reason for testing
• Monitoring
  – T21 has 30% risk of fetal demise between 12 – 40 weeks
  – Fetal echocardiography (50% T21 have cardiac anomaly)
What is PAPP-A?

- Pregnancy associated plasma protein - A
- Measured in IU/L, which is what is shown on blood test results
- In the first trimester screen, the result is in **MoM** (multiple of the median) as the value changes with gestation
Role of PAPP-A

• Produced by the placenta
• Multiple roles including in angiogenesis
• A low PAPP-A represents a poor placentation which may result in adverse pregnancy outcomes
Adverse pregnancy outcomes

• Association with
  – IUGR  \((2x <0.4, 5x <0.3)\)
  – PET
  – Premature delivery
  – IUFD

• With PAPP-A <0.20MoM and abnormal uterine artery dopplers; there is >65% risk of poor outcome
Low PAPP–A protocol

Women’s Imaging and MFM – RBWH – May 2015

LOW PAPP–A PROTOCOL

LOW PAPP–A <0.4 MoM
Regardless of first trimester risk

↓

19 WEEK MORPHOLOGY SCAN
Can be done privately

↓

23–24 WEEK GROWTH AND WELLBEING SCAN
INCLUDING DOPPLER OF BOTH UTERINE ARTERIES

NORMAL
- No protodiastolic notching
- PI <0.7
- Normal growth

ABNORMAL
- Notching – uni or bilateral
- PI >0.7
- Abnormal growth

↓

Further scans only if clinically indicated

28 WEEKS and 34 WEEKS GROWTH AND WELLBEING SCANS
More often if indicated by USS findings
Low PAPP-A

- Cut-off for intervention varies depending on centres
- 0.37 is the 5% and 0.20 is 1% in SA
- 0.40 is the 5% in FASTER trial

- A low PAPP-A is more frequent in IVF pregnancies
Why an ultrasound at 23-24 weeks?

- 14% of patients with low PAPP-A have an adverse outcome
- Improves the PPV of the screening
Referral

- RBWH Maternal Fetal Medicine
- Genetic Health Queensland

Include all relevant clinical information

<table>
<thead>
<tr>
<th>Time</th>
<th>Task</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 am</td>
<td>Diabetes in pregnancy</td>
<td>Dr Amanda Love</td>
</tr>
<tr>
<td>11.30 am</td>
<td>Pharmacy</td>
<td>Karen Whitfield</td>
</tr>
<tr>
<td>11.40 am</td>
<td>Case work 2: Complex</td>
<td>All</td>
</tr>
<tr>
<td>12.40 pm</td>
<td>Antenatal testing for chromosomal abnormality</td>
<td>Pauline McGrath</td>
</tr>
<tr>
<td>1.10 pm</td>
<td>Lunch (30 minutes)</td>
<td>All</td>
</tr>
</tbody>
</table>