ubomi buhle
Life is beautiful

Safer prescribing in pregnancy and common teratogenic medications

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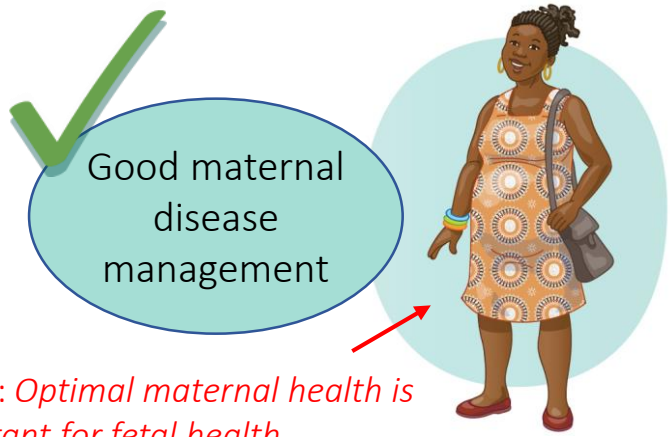
OBJECTIVES

By the end of the session you should:

- Know what factors to consider when prescribing medicines for pregnant clients and girls/women of childbearing potential
- Know some common teratogenic medications
- Know how to practice safer prescribing *in partnership* with the client
- Know how to manage patients who are on potentially teratogenic medicines

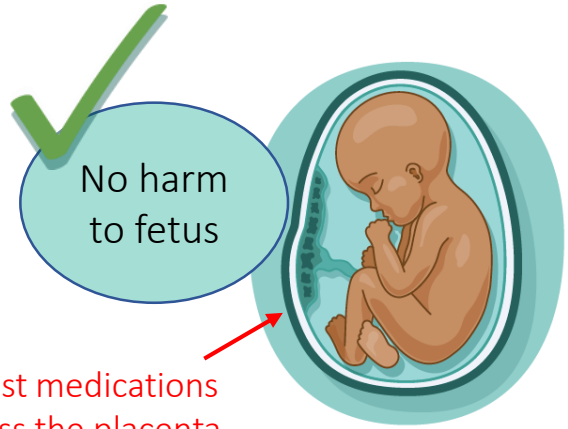
CONSIDERATIONS WHEN PRESCRIBING IN PREGNANCY

Each time we prescribe a medication during pregnancy, the ideal goals are:



Remember: *Optimal maternal health is very important for fetal health*

AND



Most medications cross the placenta

This means when we look after maternal health, we are also caring for the fetus

Consider:
- Is this medication important for this client's health?
- Will it interact with any other medication she is taking?
- Is her chronic disease well-controlled?

We just need to make sure the medicine that treats the mom, doesn't hurt the fetus

Consider:
- Is this medication safe for the fetus at this gestation?
- Are there effective alternatives that are safer?

MATERNAL HEALTH AND DISEASE MANAGEMENT

Some examples of chronic health conditions that may need treatment in pregnancy?

E.g.

HIV

Diabetes

Epilepsy

Hypertension

Asthma

Thyroid disease

Autoimmune conditions

Pregnant women with chronic conditions often need to take medication throughout pregnancy

- Chronic medication may have an effect on fetal development/ growth
- Medicines may need to be added, changed or dose-adjusted

Consider referral to secondary care for review

MATERNAL HEALTH AND DISEASE MANAGEMENT

It is very important not simply to stop the client's chronic medication when she's pregnant. Why?

- Often the period of risk to the fetus has already passed
- Untreated maternal illness is a major contributor to maternal and therefore fetal mortality

Changing medication during pregnancy can be problematic

- The "safer" medication may not work, and client's condition could de-stabilise
- Client (and fetus) may be exposed to additional meds whilst making the change

Management of pregnant women on chronic medications:

- If the client has stable hypertension, consider changing antihypertensives to Methyldopa
- For other chronic conditions, refer her to secondary care for review of her medication

When is the best time to review/change a client's chronic medication?

- *BEFORE* a client falls pregnant
- In other words, when prescribing to *any girl/woman of childbearing potential (WoCBP)*

FETAL SAFETY WHEN PRESCRIBING MEDICINES

Some medicines potentially have a teratogenic effect on the fetus

Teratogen

What is a teratogen?

Anything (e.g. a maternal illness, alcohol, a medicine) that causes an abnormality in the fetus following exposure during pregnancy

(In this talk we will concentrate on teratogenic *medications*)

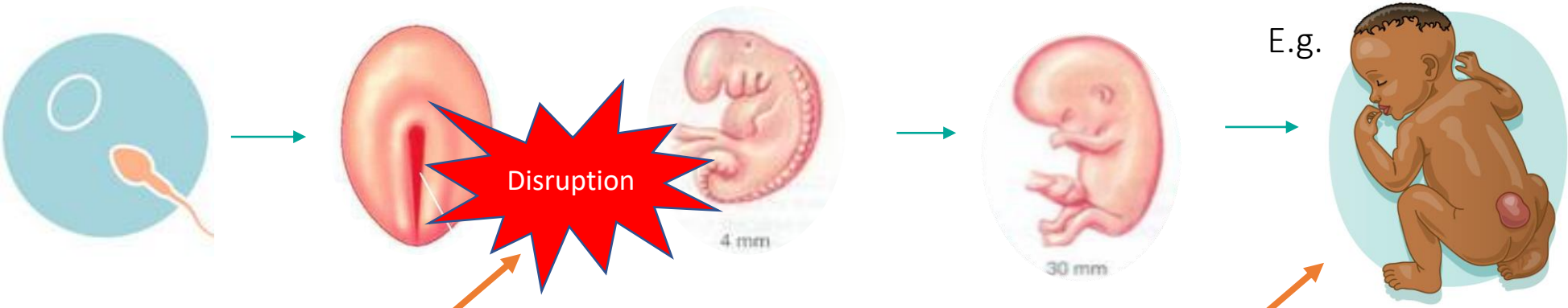
To understand teratogenic effects of medication, we need to consider how a baby is formed (embryology) and what happens if normal development is disrupted…

NORMAL FETAL DEVELOPMENT

Embryology involves cell division and differentiation in a programmed order, with recognised stages.

Specific organs develop at specific times.

ABNORMAL (DISRUPTED) FETAL DEVELOPMENT



Causes:
- Genetics
- Environment
- Genetics and environment
- Unknown……

Environment = external factors affecting the fetus e.g. Low folic acid levels in mother, teratogenic medication, maternal disease

Outcome examples:
- Miscarriage
- Intra-uterine death
- Decreased growth
- Congenital disorder
- Functional deficit / disability

TIMING OF EXPOSURE IS CRITICAL TO POTENTIAL IMPACT ON THE FETUS

Early gestation most sensitive to teratogenic effects, especially *structural* disorders (e.g. no ear)

Later gestation exposure can still cause *functional* problems (e.g. deafness)

Pre-embryonic period
Weeks 3 – 4

Embryonic period
Weeks 5 - 10

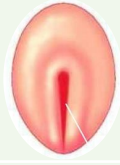
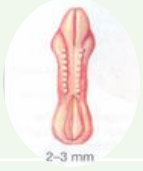
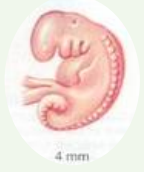
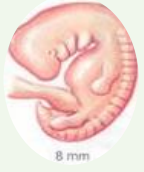
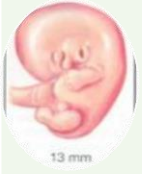
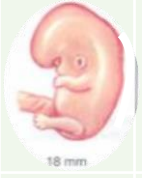
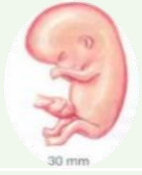
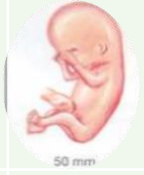
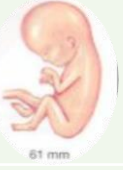
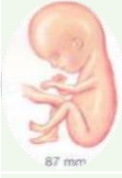
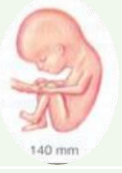
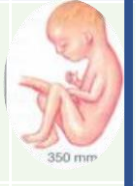
Fetal period
Weeks 11 – birth

Cell division

Tissue and organ formation

Gestational age

Growth and maturation

3	4	5	6	7	8	9	10	11	12	13-14	18	22-38	40
													
Cell division and Implantation	Neural tube starts to form	Neural tube closes; heart beats; arm buds form	Eye starts to form; leg buds form; brain enlarges	Webbed fingers; external ear forms	Webbed toes: bones start to harden, eyelids form	Fingers distinct; genitalia start to differentiate	Toes separate; palate closes	Face appears human; genitals appear male or female	Well-defined neck; genitalia complete	Blood cells and all major organs formed; hair appears	Organs mature; growth occurs	Growth

TERATOGENIC MEDICATION AND CONGENITAL DISORDERS

VERY IMPORTANT TO REMEMBER…

1. For *<u>any</u>* pregnancy there is a 2-3% *risk of a liveborn baby having a major congenital disorder*.

This is called "background risk"

3% affected 97% unaffected

2. Not every fetus exposed to a teratogen will be affected.

e.g. Lithium in first trimester - risk is around 6.5%

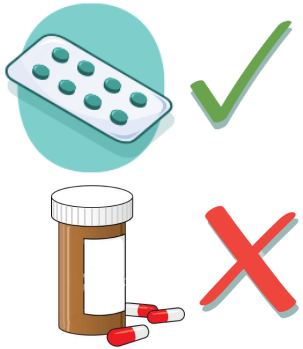
6% affected 94% unaffected

https://www.cdc.gov/ncbddd/birthdefects/data.html

UpToDate: lithium summary taken from 'Teratogenicity, pregnancy, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy

TERATOGENIC MEDICATIONS

- There is insufficient information about the safety of many medications in pregnancy because pregnant women are often excluded from drug research – but this is changing
- Some medicines are considered safer to use in pregnancy – refer to National/Provincial DOH guidelines
- Some medications are *well known* to be potentially teratogenic
- Certain medications taken at specific times in gestation can cause specific kinds of fetal abnormalities

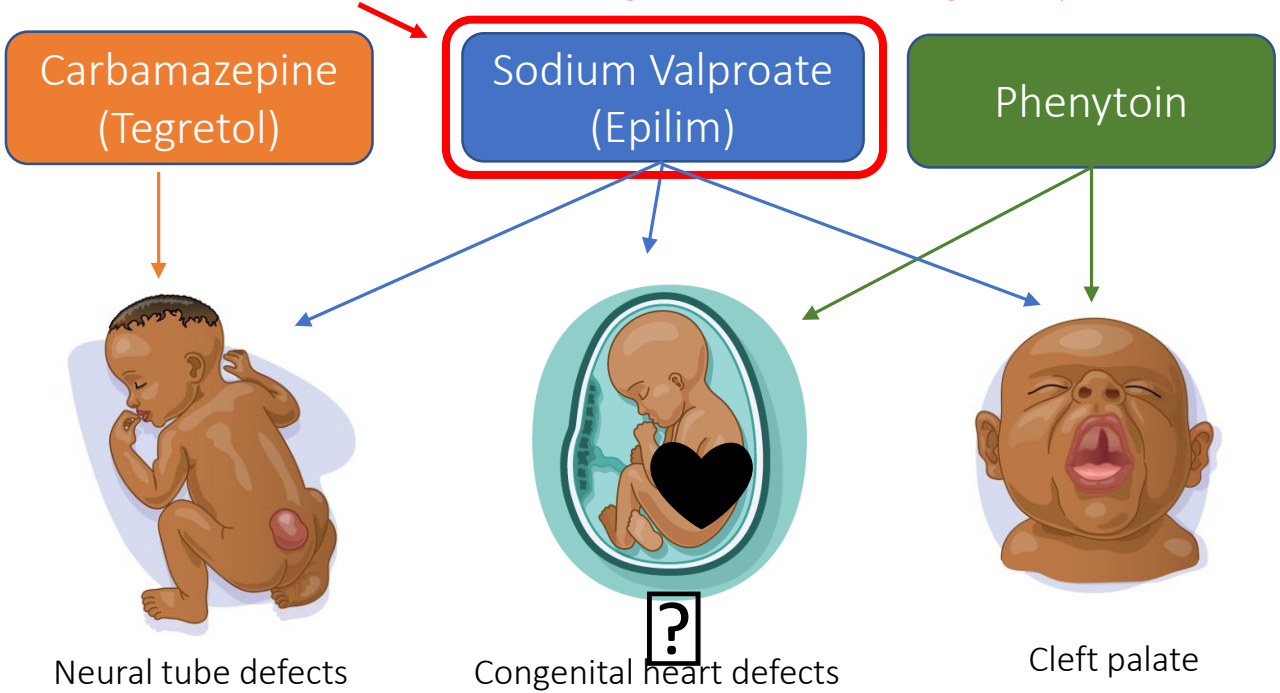


In the following slides on specific medications, the examples given are some more common effects, but the list is not exhaustive. Many other disorders can occur, including those not visible at birth, such as intellectual disability

ANTICONVULSANTS

What *possible* risks are there if these medications are used in pregnancy?

Which of these has the highest risk of teratogenicity?



…and many other potential problems, including neurological

- Do not discontinue prescribed medication abruptly on diagnosis of pregnancy.
  Why not?
  New onset seizures could be detrimental for the client and fetus.
- Refer for further management, including screening for teratogenic effects on fetus.
- Ideally consultation before falling pregnant to consider changing medication.

ANTICOAGULANTS

Which of these is safer to use in pregnancy?

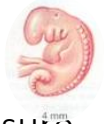
Heparin

- Heparin does not cross the placenta and has no teratogenic effects.

Warfarin

First trimester exposure

- increased rate of miscarriage
- warfarin embryopathy syndrome (can cause nasal hypoplasia, limb abnormalities)



Late gestation exposure

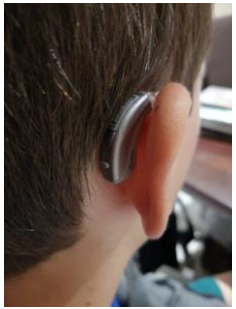
- CNS abnormalities due to bleeding

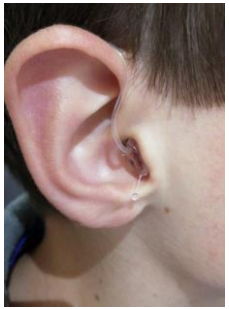
- Warfarin needs to be changed to heparin during specific stages of pregnancy
- Do not stop warfarin abruptly when a pregnancy is diagnosed – refer urgently for specialist review; arrange for ultrasound to screen for teratogenic fetal effects
- Ideally review of medication before falling pregnant

ANTIBIOTICS

What *possible* risks are there if these medications are used in pregnancy?

Aminoglycosides E.g. Amikacin	Tetracycline	Fluoroquinolones E.g. Ciprofloxacin
Can cause deafness and inner ear damage	Can cause permanent damage to teeth and bones	Can cause joint abnormalities in animal studies





PSYCHOTROPIC AGENTS

What *possible* risks are there if this medication is used in pregnancy?

Lithium

First trimester exposure can cause cardiac anomalies

Lithium is also not recommended while breastfeeding

CHEMOTHERAPY

Chemotherapy

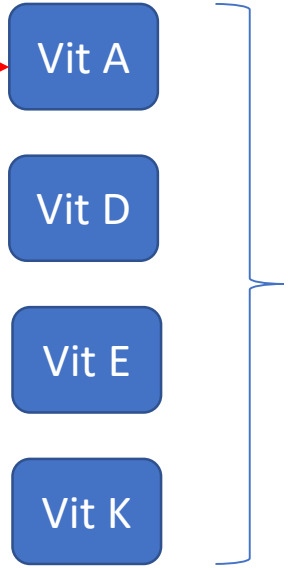
Can cause:
- organ malformations
- growth restriction
- increased risk of stillbirth

- Some agents are contraindicated during all stages of pregnancy
  E.g. Methotrexate
- Other agents may be used in certain trimesters without adverse effects
- Breastfeeding not advised while receiving chemotherapy until more safety information is available

NUTRIENTS

Some nutrients may be fetal toxic in high doses

E.g. Very high dose vitamin A in the first trimester can produce malformations



- These vitamins are fat soluble
- Not excreted if taken in excess
- May have adverse effects for mother and/or baby.

VACCINES

Which of these vaccines can be given in pregnancy?

Live vaccines ✗

E.g. Polio, rubella, yellow fever

Should not be given in pregnancy

Non-live vaccines ✓

E.g. Tetanus, rabies, injectable flu, hepatitis B

Considered suitable to give in pregnancy

OTHER

ACE inhibitors

- Exposure in 2nd and 3rd trimester can cause impaired renal function in fetus resulting in abnormalities due to oligohydramnios (reduced amniotic fluid volume)
  e.g. - growth restriction
  - under-developed lungs

May be used for early TOPs, which may fail

Misoprostol

- 1st and 2nd trimester exposures can cause limb defects

Used for acne

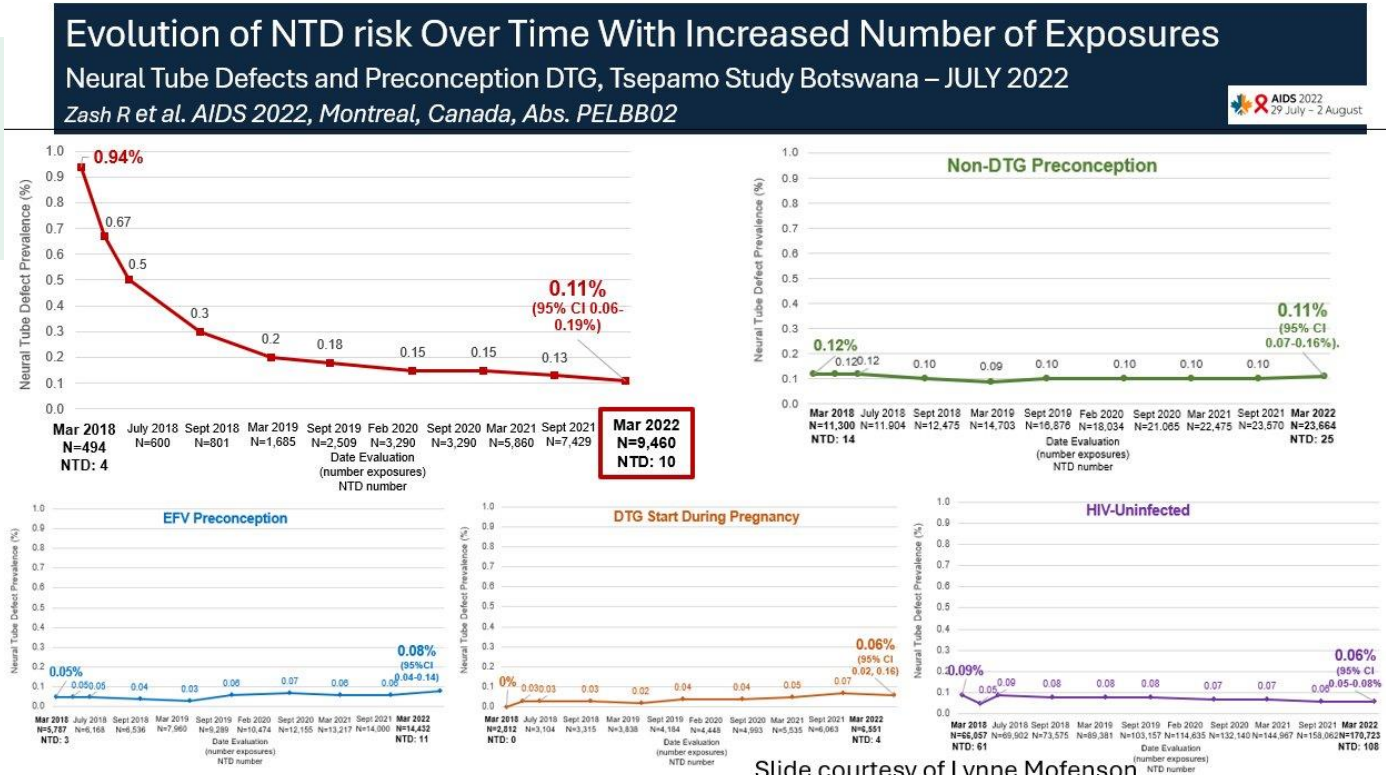
Isotretinoin (e.g. Roaccutane)

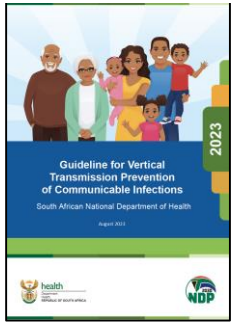
- Highly teratogenic
- Females should be on *highly effective* contraception when using retinoids, and for 1 month after discontinuation
- Can cause congenital malformations of skull, face, eyes, limbs, CNS, cardiac

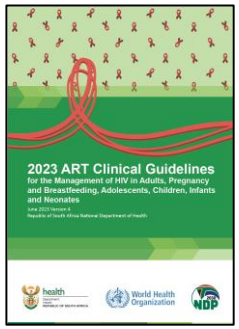
DOLUTEGRAVIR

- "Evolving evidence has found there to be no significant difference in neural tube defect (NTD) prevalence between Dolutegravir-and Efavirenz-exposure at conception."

- "Tenofovir/Lamivudine/ Dolutegravir is the *preferred first-line regimen* in all WOCP, *regardless of her intentions to conceive, her pregnancy status, or whether she is using contraception or not*."







Please refer to DOH guidelines for full details

OVER-THE-COUNTER MEDICATION

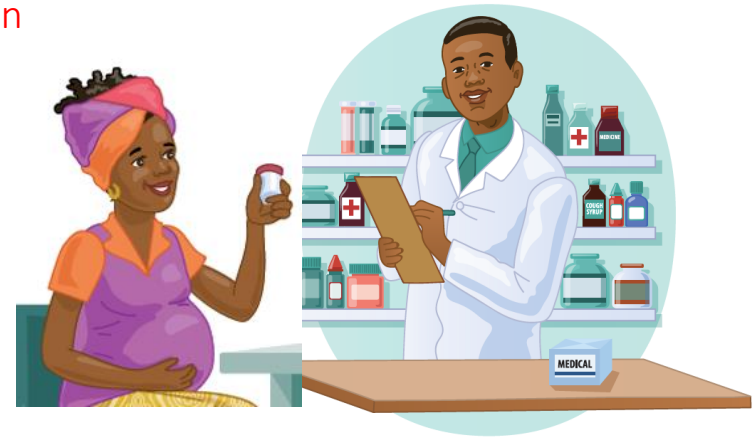
Is over-the-counter medication safe to use in pregnancy?

- Over-the-counter (OTC) medication is available without a prescription
- This does NOT mean that it is safe in pregnancy
- Some OTC medications are not established as being safe
- Some OTC medications can be harmful

E.g. Non-steroidal anti-inflammatories (NSAIDS) should not be taken especially in the last 3 months of pregnancy – can cause reduced amniotic fluid and other problems.

Pregnant women should always ask a health care professional before taking *any* OTCs

e.g. Brufen



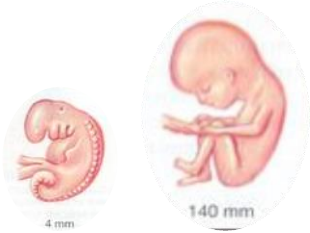
FACTORS THAT INCREASE RISK WITH TERATOGEN EXPOSURE

Response to teratogens is individualized and influenced by multiple factors:

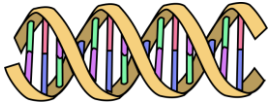
- Dose and duration

- Route of exposure

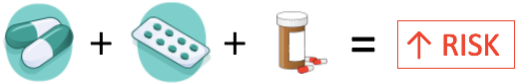
- Timing of exposure (critical period of organ development and susceptibility)



- Genetics: some fetuses are more genetically susceptible than others

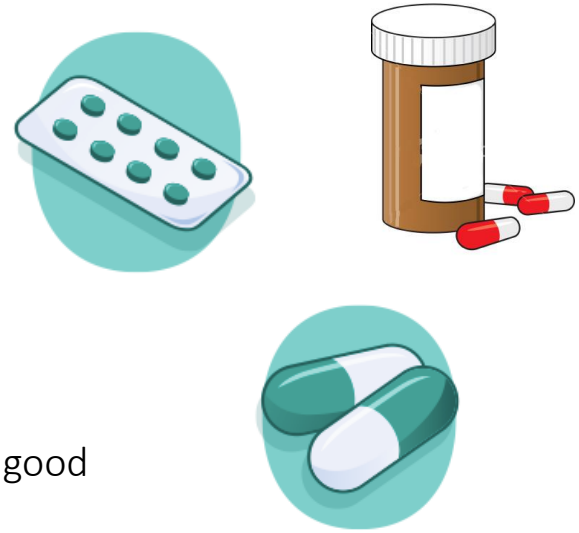


- Concurrent exposures (multiple drugs) or illnesses during pregnancy



IF MEDICATIONS NEED TO BE PRESCRIBED…

- Use lowest effective dose
- Single rather than multiple drug regimes
- Shortest effective duration
- Choose medication that has been widely used in pregnancy, with good safety track record (Refer to national/provincial DOH guidelines)



INTRODUCTION TO SHARED DECISION-MAKING

Clients are more likely to adhere to the treatment plan if:

- ✓ They are part of the decision-making process
- ✓ They understand the importance of the treatment they are taking
- ✓ Their concerns or doubts about the treatment are addressed

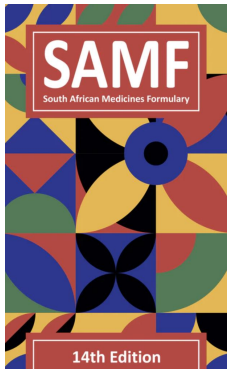
STEPS FOR SAFER PRESCRIBING – SHARED DECISION-MAKING

1. Gather information

HCP gathers all information before discussion

- Maternal disease
- Fetal gestation
- Medication options and risks

Find out information if you don't know



2. Shared decision-making

HCP shares information

- Reason for treatment
- Treatment options
- Benefits and risks of each option

Client gives input about her preferences and concerns

HCP addresses client's concerns

Make decision together on disease management

3. Shared monitoring

Review together at follow up

- Is the medicine working?
- Any side effects?
- Adherence?
- Monitor fetal development

This approach acknowledges that the client brings expertise too…

MANAGEMENT OF CLIENTS AT RISK FOR TERATOGENICITY

Primary healthcare facility

E.g.
- Change anti-hypertensives to methyldopa for uncomplicated chronic hypertensive patients

OR

Refer

E.g.
- Chronic medication that needs to be assessed and possibly changed by specialist, such as anti-epileptics or warfarin
- Client on a potential teratogenic medication, for medication review, counselling and fetal monitoring

MANAGEMENT OF CLIENTS AT RISK FOR TERATOGENICITY

What to do if you discover that your client is taking a potentially teratogenic medication?

- Always remain calm and reassuring (most babies will be unaffected)
- As the healthcare professional, be aware of your own anxiety and how it impacts on the way you communicate with your client
- Obtain and record an accurate history of exposures
- Assess and record gestational age at exposure
- Advise the client to continue with the chronic medication until review by the specia avoid maternal health deterioration
- Arrange an urgent assessment by a specialist. Write a thorough referral letter.

"You are taking (or have taken) a medication that can sometimes cause problems for the baby. ***The majority of babies are not affected*** but I will refer you to a doctor/ specialist for a full assessment."

CLIENT EDUCATION

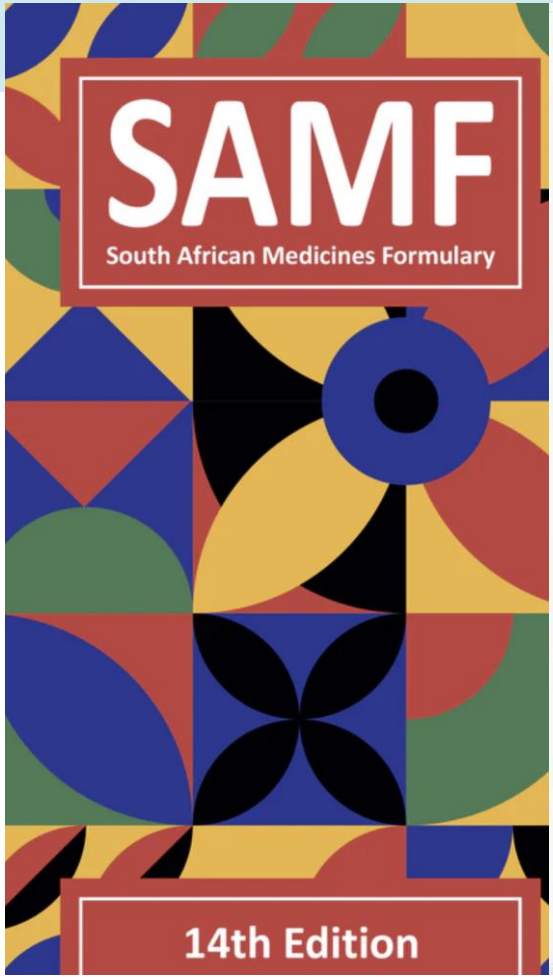
KEY MESSAGES FOR CLIENTS

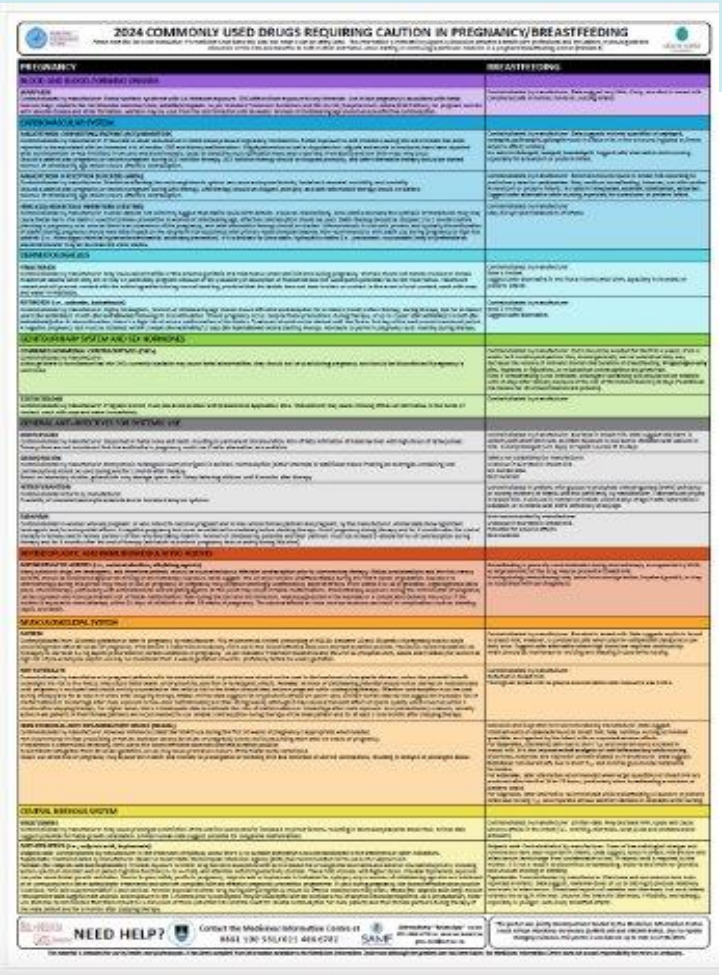
Do not stop any chronic medication when you find out you are pregnant. Discuss it with your HCP first.

Ask your HCP about safety in pregnancy before taking OTC medications or herbal remedies

Bring your medication boxes/packets to your ANC appointments

RESOURCES


SAMF
South African Medicines Formulary
14th Edition


2024 COMMONLY USED DRUGS REQUIRING CAUTION IN PREGNANCY/BREASTFEEDING
PREGNANCY
BREASTFEEDING
NEED HELP?


Division of Clinical Pharmacology, University of Cape Town
MEDICINES INFORMATION CENTRE
FREE SERVICE TO HEALTH CARE WORKERS FOR ANY MEDICINE- OR TREATMENT-RELATED QUERIES
Back: Anri Uys, Vivian Raath, Samantha Hare, Ewan Tommy; Front: Jackie Jones, Briony Chisholm, Annoesjka Swart
0800 212 506 / 021 406 6829
SMS/Whatsapp/"Please call me": 071 840 1572
Email: pha-mic@uct.ac.za
www.mic.uct.ac.za
Monday - Friday 08:30 - 16:30

RESOURCES

Online resources:

E.g. UK Teratology Information Service (for HCPs): http://www.uktis.org/html/maternal_exposure.html

UK Teratology Information Service (Patient PILs): https://www.medicinesinpregnancy.org/

CDC guidelines: https://www.cdc.gov/pregnancy/meds/treatingfortwo/treatment-guidelines.html

FDA guidelines: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/index-drug-specific-information

Other: https://mothertobaby.org/fact-sheets/


ubomi buhle
Life is beautiful
Understanding Birth Outcomes from Mothers and Infants
Building Healthcare by Linking Exposures

Thank you!