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Cover picture

WRESTING THE JUNGLE'S SECRETS
(About 1886)

Scientific explorers opened vast new horizons for Pharmacy late in the 19th century. Sent in 1885 to Peru, Dr. Henry H. Rushy crossed South America amid incredible hardships. He returned with 45,000 botanical specimens, including Cocillana bark.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company.

George A. Bender, Director Robert A. Thom, Artist

Management of pre-eclampsia/eclampsia

Introduction

Hypertension in pregnancy is estimated to affect about 10 million women per year leading to death in 76 000 mothers, and approximately half a million babies worldwide [1]. In addition it is responsible for a large number of severe maternal and perinatal morbidities [2]. Hypertension in pregnancy is an important cause of direct maternal deaths in Sri Lanka [3].

Much is still to be learnt about their pathogenesis and the optimum management [4]. Based on available evidence however several clinical guidelines have been derived for management of this condition [3, 5, 6].

Diagnosis and classification of hypertensive disorders of pregnancy

Correct measurement of blood pressure (BP) is the first step in diagnosis of hypertensive disorders [7,8]. The steps to be followed are given in Panel 1.

Panel 1
Measurement of blood pressure in pregnancy

- Adequate rest before measuring blood pressure
- BP should be measured with the woman in the sitting position with the arm at the level of the heart
- An appropriately sized cuff (i.e., length of 1.5 times the circumference of the arm) should be used
- Initial inflation of the cuff 20-30 mmHg above the palpable systolic BP (SBP)
- Deflation at a rate of 2 mmHg per second
- Korotkoff phase V should be used to designate diastolic BP
- Recording BP to the nearest 2 mmHg

Hypertension in pregnancy should be defined as a SBP ≥ 140 mmHg and/or diastolic BP (DBP) ≥ 90 mmHg, based on the average of at least two measurements, taken at least 15 min apart, using the same arm [8]. Assessment of proteinuria is essential.

Diagnosis of hypertension in pregnancy should be followed by classification according to a standard system. The classification by International Society for the Study of Hypertension in Pregnancy (ISSHP) is given in Table 1 [9].

Table 1.
The revised (ISSHP) classification (2013) for hypertensive disorders in pregnancy

1. Chronic hypertension
2. Gestational hypertension
3. Pre-eclampsia – de novo or superimposed on chronic hypertension
4. White coat hypertension

Standard definitions exist for terminology to maintain the uniformity.

- **Chronic hypertension** is present at the booking visit or before 20 weeks. Any woman taking antihypertensive medications at booking are also included in this category. It can be primary or secondary in aetiology [5]
- **Gestational hypertension** is characterized by the new onset of hypertension after 20 weeks gestation [9].
- **Pre-eclampsia is hypertension** in pregnancy associated with recent onset of significant proteinuria (300 mg/l or 500 mg/ 24 hours or dipstick 2+ or more) [3]. It can however be super imposed on chronic hypertension as well.
- **Severe pre-eclampsia is defined as pre-eclampsia** with severe hypertension and/or with symptoms/ signs, and/or biochemical and/or haematological impairment which may indicate single or multiple organ decompensation [3].
- **Severe hypertension** is defined as SBP ≥ 160 mmHg and/or DBP ≥110 mmHg.

Symptoms of severe pre-eclampsia are severe headache, visual disturbance such as blurring or flashing before eyes, scotomas, epigastric or hypochondrial pain and nausea and vomiting. Clonus (3 beats or more), papilloedema, liver tenderness and oliguria (less than 400 ml per day or 0.5 mg/kg/hour over a 4 hour period can be considered as signs of severe pre-eclampsia. Platelet count falling to below 100 x 10^6/l, abnormal liver enzymes (ALT or AST rising to above 70 IU/l), HELLP syndrome (**H**aemolysis, **E**levated **L**iver Enzymes and **L**ow **P**latelets) are the haematological and biochemical features [3].

- **Eclampsia** is defined as the development of convulsions and/or unexplained coma during pregnancy or postpartum in patients with features of pre-eclampsia. However, hypertension and proteinuria can be absent in 16% and 14% of patients with eclampsia respectively [3].

Management based on principles

1. Prevention if possible

In areas where dietary calcium intake is low, calcium supplementation during pregnancy (at a dose of 1.5 – 2.0 g elemental calcium/day) is recommended for the prevention of pre-eclampsia in all women, but especially those at high risk of developing pre-eclampsia [6]. For Sri Lankan women the recommended supplementation is 600 mg/day [3]. Low-dose acetylsalicylic acid (aspirin, 75 mg/day) is recommended for the prevention of pre-eclampsia in women with one high risk factor or two or more moderate risk factors (Panel 2). This should be initiated before 20 weeks of pregnancy [3,5,6].

Panel 2
Risk factors for hypertensive disorders in pregnancy

High risk factors

- Hypertensive disease during a previous pregnancy
- Chronic kidney disease
- Autoimmune disease such as systemic lupus erythematosus orantiphospholipid syndrome
- Type 1 or type 2 diabetes
- Chronic hypertension
- Multiple pregnancy

Moderate risk factors

- First pregnancy
- Age 40 years or older
- Pregnancy interval of more than 10 years
- Body mass index (BMI) of 35 kg/m² or more at first visit
- Family history of pre-eclampsia

2. Vigilant monitoring to identify hypertensive disorders

Blood pressure must be measured in every clinic visit by a Medical Officer and results recorded and plotted on a blood pressure chart. Proteinuria must be tested at every clinic visit [3].

3. Refining the diagnosis to classify accurately

The underlying condition in a mother with increased blood pressure could be diverse.

Relevant history and examination cannot be over emphasized. Urinalysis, renal function tests, AST, ALT and platelet count should always be performed as baseline investigations at first diagnosis. If chronic hypertension is diagnosed, renal imaging, endocrine assessments etc. may be indicated.

4. Be aware about the potential complications leading to maternal and perinatal morbidity and mortality

Healthcare workers should be aware of the potential complications. (Panel 3)

Panel 3
Maternal and perinatal complications of hypertensive disorders in pregnancy

Leading to maternal mortality and morbidity

- Severe hypertension
- Intra-cerebral haemorrhages secondary to severe hypertension (a main cause of maternal deaths)
- Eclampsia
- Placental abruption and severe antepartum hemorrhage
- Pulmonary oedema
- HELLP syndrome
- Disseminated intravascular coagulation
- Liver haemorrhages
- Acute renal failure
- Aortic dissection

Leading to perinatal mortality and morbidity

- Severe intrauterine hypoxia
  - ✓ Secondary to chronic hypoxia
  - ✓ Secondary to placental abruption
- Motor development delays in newborn

5. Evidence based measures to prevent complications

5.1 Severe hypertension and its associated complications – Prompt treatment of severe hypertension helps to avoid intra-cerebral haemorrhage. Hypertension should be treated if SBP ≥ 160 mmHg, or if DBP ≥ 110 mmHg, or if mean arterial pressure (MAP) ≥ 125 mmHg. Aim to maintain BP at around 130-140/90-100 mmHg.

Oral antihypertensive drugs may be used when the BP is <180/110 mmHg. The BP must be monitored every 15 minutes and intravenous (IV) antihypertensives added when the response is inadequate within 30 minutes.

A rapid fall in maternal blood pressure induced by antihypertensive treatment may impair placental bed perfusion causing fetal heart rate abnormalities, especially in growth restricted or compromised fetuses. After commencing antihypertensive therapy continuous CTG monitoring for 60 minutes is recommended [6].

A summary of antihypertensive treatment in severe hypertension is given in Panel 4 [3].

Panel 4
Drugs for severe hypertension

Labetalol

Oral
- BP<180/110 mm Hg - 200mg oral stat
- Repeated hourly up to 4 hours

Intravenous
- BP ≥ 180/110 mm Hg - 20 mg iv over two minutes.
- Record BP after 10 minutes.
- If BP ≥ 160 /110 mmHg - 40 mg iv over two minutes.
- Record BP after 10 minutes.
- If BP is still above 160/110 mmHg give hydralazine (see below)
- If BP is still above 160/110 mmHg start an iv infusion of labetalol, starting at 40 mg/hour, doubling dose at half- hourly intervals as required to a maximum of 160 mg/hour.

Hydralazine
- 5 - 10 mg IV bolus over two minutes.
- Must be accompanied by a fluid bolus of 5ml/kg of 0.9% sodium chloride or Ringer-lactate solution over 30 min, started at the same time as iv hydralazine, except in the presence of pulmonary oedema.
- Record BP at 15 minute intervals.
- Repeat boluses of 5 - 10 mg iv after a 15 minute interval.
- Maximum dose is 20 mg.
- If inadequate response, give labetalol bolus doses.
- If no lasting effect with above boluses, consider an infusion of hydralazine 2.0 mg/hour increasing by 0.5 mg/hour as required (2-20 mg/hour usually required).*

Oral nifedipine
- Where BP< 180/110 mm Hg, in asymptomatic patients.
- Give 10 mg orally.
- Repeat at 20 minute intervals up to a maximum of 40 mg.
- If there is no response proceed to intravenous labetalol or hydralazine.*

*Watch for wide pulse pressure

Where these measures fail, the mother must be moved to a high-dependency area or an intensive care unit.

If BP is controlled by the above, continue monitoring the BP at 15-minute intervals for 1 hour and at 30-minute intervals thereafter.

5.2 Eclampsia – Magnesium sulfate is recommended for the prevention of eclampsia in women with severe pre-eclampsia in preference to other anti convulsants. The capacity for clinical surveillance of women and administration of calcium gluconate are essential in managing these patients. When these facilities are unavailable administering a loading dose alone is still acceptable than not administering magnesium sulphate at all. Magnesium sulphate is effective in the prevention of eclampsia in mild pre-eclampsia as well as in the treatment of severe pre-eclampsia. To obtain effective results the number of cases of mild pre-eclampsia that should be treated is high [6].

The protocol for administration of magnesium sulphate is given in the Panel 5.

Panel 5
Protocol for administering magnesium sulphate

Give loading dose of 4 g iv over 10 minutes irrespective of the knowledge of renal functional status. There are two methods for intravenous administration.
- Diluted to a total volume of 20 ml with 0.9% sodium chloride solution, given via an infusion pump or 'manually'.
- Diluted to a total volume of 80 ml with 0.9% sodium chloride solution via a burette.

Immediately after the loading dose, start infusion of 1 g iv per hour. Continue this infusion for at least 24 hours after delivery.

Where there are difficulties with intravenous access, magnesium sulphate 5 g with 1 ml of 2% lignocaine in the same syringe may be administered intramuscularly into each buttock.

If intramuscular magnesium sulphate is continued as maintenance therapy, give 5 g to alternate buttocks 4 hourly, with 1ml of 2% lignocaine in the same syringe.

Monitoring to ensure
- Hourly urine output of 30 ml per hour
- Respiratory rate >16/ minute
- Oxygen saturation >90%
- Presence of patellar reflexes.

If the above signs of toxicity appear, the antidote is calcium gluconate, 1 g intravenously (10 ml of 10% solution), given over 10 minutes.

5.3 Pulmonary oedema – Accurate recording of fluid balance is essential. Restrict total fluid intake to 80 ml per hour [3, 6]. The volumes of all drugs administered must be taken into account.

6. Monitoring the mother and the fetus to identify occurrence of above complications

Continued monitoring of blood pressure is essential to identify development of complications. Mild to moderate hypertension can be monitored on an outpatient basis. Severe hypertension is an indication for inpatient monitoring.

Education of the mothers in the milder stages, on the symptoms of impending eclampsia is an essential requirement.

7. Rational management of complications

7.1 Severe hypertension – Management of severe hypertension was discussed in the section of prevention of complications.

7.2 Eclampsia – The steps to be followed are given in Panel 6 [3].

Panel 6
Management of eclampsia

During the seizure

- Turn the patient to a side and support in that position.
- Suck out secretions from the mouth.
- Administer oxygen via a face mask.
- Most eclamptic seizures resolve spontaneously.

As soon as possible following a seizure

- Establish intravenous access.
- Obtain blood for full blood count, liver transaminases, blood urea, electrolytes and blood for cross-match.
- Start magnesium sulphate.
- Treat blood pressure.
- Insert an indwelling catheter.
- Monitor respiratory rate, urine output, reflexes, SpO2.
- Arrange intensive care.
- Establish a plan of management with involvement of multi-disciplinary team.

A second convulsion could be treated with 2 g of magnesium sulphate. Convulsion resistant to magnesium sulphate is an indication for cerebral imaging with paralysis and ventilation.

For settings where it is not possible to administer the full magnesium sulfate regimen, the use of magnesium sulfate loading dose followed by immediate transfer to a higher level healthcare facility is recommended for women with eclampsia [6]. The patient should ideally be accompanied by a doctor and emergency drugs and equipment (e.g. Ambu bag) must be available [3].

7.3 Pulmonary oedema is treated on its own merits with diuretics, strict fluid balance and central venous pressure monitoring.

7.4 HELLP syndrome Attention should be paid to management of liver failure, coagulation and maintenance of haemoglobin. The use of corticosteroids for the specific purpose of treating women with HELLP syndrome is not recommended [6].

7.5 Placental abruption and severe antepartum haemorrhage is an indication for delivery.

7.6 Renal failure should be managed with close attention to fluid balance and dialysis if required.

7.7 Disseminated intravascular coagulation Correction of coagulopathy should be carried out in conjunction with a haematologist and immediate delivery should be considered.

7.8 Fetal hypoxia Definitive management is delivery of the baby. The urgency for delivery depends on the maturity of the fetus and the severity of hypoxia.

8. Delivery of the baby at a gestation where risks to the mother and baby of continuation of pregnancy outweigh the risks of delivery

Recommendations are summarized in Panel 7.

Panel 7
Recomendations for delivery in hypertensive disorders in pregnancy

- Eclampsia
  - ✓ Is an indication for immediate delivery after stabilizing the mother. There is no place for prolongation of the pregnancy in these women, unless under rare exceptional circumstances [3].
- Severe pre-eclampsia
  - ✓ At a gestational age when the fetus is not viable or unlikely to achieve viability within one or two weeks induction of labour is recommended.
  - ✓ With a viable fetus and before 34 weeks of gestation a policy of expectant manage-ment **is** recommended, provided the above complications are absent and can be monitored.

(Continued)

Panel 7
(Continued)

- ✓ With a viable fetus and between 34 and 36+6 weeks of gestation a policy of expectant management **may be** recommended, provided that the above complications are absent and can be monitored.
- ✓ At term early delivery is recommended.

- Mild pre-eclampsia or mild gestational hypertension at term.
  - ✓ Induction of labour is recommended.
- Chronic hypertension and gestational hypertension without complications.
  - ✓ Delivery can be safely achieved close to term.

Only known cure for the severe pre-eclampsia is delivery of the baby [6]. Ergometrine should not be used during the third stage.

9. Postpartum management of the mother and management of the newborn

Magnesium sulphate if started should be continued for 24 hours after the delivery or after the last fit, whichever is later [3].

In women treated with antihypertensive drugs antenatally, continued antihypertensive treatment postpartum is recommended [6]. Monitoring for signs of maternal organ dysfunction should be continued.

The maximum increase in BP usually occurs towards the end of the first postpartum week when, in most settings, women have already been discharged from the hospital. Thus careful monitoring by the healthcare staff during field visits is essential [6].

10. Long term follow-up and contraception

Life-long cardiovascular impact of pre-eclampsia with the potential for premature death in women are now recognized. Postpartum screening on cardiovascular risk factors and subsequent treatment in women with a history of gestational hypertension or pre-eclampsia is likely to be cost-effective.
Prescription of appropriate contraception based on Medical Eligibility Criteria is an essential component.

In the event of another pregnancy being considered pre-conceptional assessment is recommended.

Conclusions

Hypertensive disorders in pregnancy have multiple organ pathologies, leading to diverse presentations. Management remains a challenge, and should be based on individual case manifestations.

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Drugs in breastfeeding

Summary

Most commonly used drugs are relatively safe for breastfed babies. The dose received via milk is generally small and much less than the known safe doses of the same drug given directly to neonates and infants.

Drugs contraindicated during breastfeeding include anticancer drugs, lithium, oral retinoids, amiodarone and gold salts.

An understanding of the principles underlying the transfer into breast milk is important, as is an awareness of the potential adverse effects on the infant.

Discussion with the mother about the possibility of either negative product information or ill-informed advice from others will reduce the confusion and anxiety that may be generated.

Good resources about medicines and breastfeeding are available and include state-based medicines information services.

Introduction

Although the National Health and Medical Research Council recommends exclusive breastfeeding for around six months, continued alongside complementary food until a minimum of 12 months, current breastfeeding statistics show Australia falling well below these recommendations. While 96% of women start breastfeeding, exclusive breastfeeding rates drop off to 39% of babies at three months and 15% at five months.[1] Faced with these statistics, it is important to be able to give accurate advice on the safety of drugs so that breastfeeding is promoted whenever possible.

Most drugs are not of concern in breastfeeding.[2-4] In addition, most lactating women take few medicines, and then only occasionally. Further, even though virtually all drugs are transferred into breast milk to some extent, the amount of drug is usually small and unlikely to cause an adverse effect on the baby. Considering the number of drugs available, relatively few known adverse effects occur in babies and it is generally not necessary to suspend breastfeeding because of the mother's medication. This concept is not new. It was suggested over 100 years ago that '… it is possible to show that drugs … when given to a mother, rarely affect the milk injuriously, and almost never the babe to a marked degree'.[5]

Although the number of drugs available now is much greater, the same approach can apply. If ongoing medication use is necessary, only a few drugs warrant the cessation of breastfeeding (see Table). However, given the vulnerability of infants, vigilance is required.

What affects the concentration of a drug in milk?

It is important to be aware of how drugs transfer into breast milk and what factors can influence this.

Table **Examples of drugs contraindicated in breastfeeding**

Drug	Comment
Amiodarone	Long half-life, iodine-containing molecule, and may affect thyroid function in infant
Antineoplastics	Leukopenia, bone marrow suppression
Gold salts	Rash, nephritis, haematological abnormalities
Iodine	High doses (>150 micrograms daily) lead to risk of infant hypothyroidism
Lithium	Breastfeeding only feasible with rigorous monitoring
Radiopharmaceuticals	Contact obstetric information service
Retinoids (oral)	Potential for serious adverse effects

Maternal plasma concentration

Passive diffusion is the primary pathway by which drugs enter milk. There is a good concordance between the time-course of maternal plasma-drug concentration and milk-drug concentration. Maternal plasma concentration is also affected by the drug's distribution into different tissues. A high volume of distribution (as for sertraline) will contribute to a lower maternal plasma concentration and a subsequent lower concentration in milk.

Maternal plasma protein binding

Transfer into breast milk is also influenced by the extent to which the drug is bound by maternal plasma proteins. Free unbound drug diffuses readily while highly protein-bound drugs like ibuprofen or warfarin (both 99% protein bound) are unable to diffuse in significant amounts.[6] Sertraline is highly protein bound (98%) so overall it will be minimally transferred to the breastfed baby.[6] By comparison, venlafaxine has much lower protein binding and so more of the drug will be present in milk.[6]

Size of the drug molecule

Most drug molecules, including alcohol, nicotine and caffeine, are small enough to enter milk. Exceptions are drugs with high molecular weights such as heparins and insulin.

Degree of ionisation

Drugs cross membranes in an un-ionised form. Milk is generally slightly more acidic (pH 7.2) than the mother's plasma (pH 7.4) so it attracts weak organic bases such as oxycodone and codeine.[7] Such drugs become ionised and 'trapped' in the milk. Conversely, weak organic acids such as penicillin tend to be ionised and held in maternal plasma.

Lipid solubility

In addition to the passive diffusion into the aqueous phase, lipid-soluble drugs such as citalopram[8] may have co-secretion by dissolution in the fat droplets of milk.[2] In practical terms, this may not be of concern. It would not be an indication to change therapy if citalopram has been effective, but infant drowsiness should be monitored. Although the fat content of the milk varies according to infant age and phase of the feed, this is unlikely to impact on the choice of drug therapy.

Maternal pharmacogenomics

A growing understanding of the influence of pharmacogenomics is well exemplified with codeine which is variably metabolised to morphine by the cytochrome P450 (CYP) 2D6 enzyme. The ultra-rapid metaboliser phenotype occurs in up to 10% of Western Europeans and up to 30% of North Africans. Repeated codeine doses in these women produce significant amounts of morphine. Rapid transfer from maternal plasma to the milk may result in central nervous system depression and potentially infant death.[9] Codeine should be avoided during breastfeeding[10] and alternative analgesia is recommended, such as paracetamol or ibuprofen.

What influences the risk of adverse effects on the baby?

If the baby is exposed to a drug in milk, several factors determine if there is an effect.

Timing of the dose

Feeding the baby just before the mother takes a drug results in the baby receiving the lowest possible drug concentration. However, this principle clearly does not apply for drugs with a long half-life, such as diazepam. For these drugs, there should be an even more rigorous assessment of whether they are needed.

Toxicity

Premature babies and neonates have a lower capacity to metabolise and excrete drugs.[2] In addition, for babies who may already have been exposed to a drug in utero just before delivery, further exposure via breast milk will augment the existing drug concentration.

The Table lists drugs that are contraindicated in breastfeeding. Some drugs are inappropriately regarded as unsafe. Metronidazole, despite unfounded fears of carcinogenicity and mutagenicity, is safe in breastfeeding for short-term use.[11] However, anecdotally, its bitter taste in milk may lead to fussiness in the feeding infant. Valproate is regarded as safe, especially in monotherapy when the risk of infant sedation is low.[11] Monitoring the infant for liver and platelet changes may be advisable.[12]

The immunosuppressant azathioprine is excreted into breast milk as an active metabolite 6-mercaptopurine. Cautious use is advised in lactating women, and monitoring of the infant for signs of immunosuppression and other toxicity is recommended.[6,11,12]

Oral bioavailability

The drug's presence in breast milk does not necessarily lead to significant exposure for the baby. The infant gut may degrade or destroy a drug, for example omeprazole (for which the standard formulation is enteric-coated). Gentamicin is given intravenously to the mother. As it is poorly absorbed orally by the baby, drug concentrations will not be reflected in infant plasma.

Volume of breast milk

The amount of milk a baby receives varies. The estimated intake by an exclusively breastfed baby is 150 mL/kg/day. However, if the breast is being offered only as a comfort to an older baby, for example at night, the volume ingested is likely to be small.

Relative infant dose

The relative infant dose is the dose received via breast milk (mg/kg/day) relative to the mother's dose (mg/kg/day). It is expressed as a percentage. A relative dose of 10% or above is the notional level of concern,[6] but this is rare. An example is lithium,[6,12] which is generally contraindicated in breast-feeding.[13]

Age of infant

A review found that most adverse effects of drugs in breast milk occurred in newborns under two months and rarely in those older than six months.[14] An infant's metabolism and excretion capacity at birth is only a third of what it is at 7-8 months.[15]

Drugs used to stimulate milk production

Domperidone and metoclopramide are galactogogues and have both been used off-label to stimulate prolactin and enhance milk supply. However, these drugs do not have high evidence of efficacy for this indication.[11,16] Also, there are concerns about the overuse of domperidone given that it may be prescribed on discharge from obstetric hospitals and used long term, sometimes at high doses. Non-pharmacological approaches to boost milk supply, such as correct advice, support and more frequent breastfeeding, are preferable.

Practice points for prescribing in breastfeeding

- If a drug is needed, prescribe it at the lowest effective dose. Temporarily suspend breast-feeding (and express milk) for potentially toxic drugs, such as cytotoxics and radiopharmaceuticals (see Table). Reinstatement of a drug will be determined by its half-life. It may not be possible to continue breastfeeding if lengthy treatment with a toxic drug is needed.
- Select alternative routes or products to minimise systemic exposure in the mother. For example, choose a poorly absorbed fibre laxative over a stimulant laxative.
- Choose drugs with a relatively short half-life, such as sertraline rather than fluoxetine, to minimise drug exposure in milk.
- Advise the mother to feed the infant before taking her medicine so that the drug concentration in milk will be at its lowest. Reassure her that the drug will return to her bloodstream from the milk as her blood concentration falls and will not 'store' in the milk until the next feed. This advice does not apply to drugs with a long half-life. The need for these drugs should be reassessed, especially in the neonatal period.

Advice on social drugs

Advise mothers to delay a glass of alcohol until after a feed and wait for two hours before the next feed to minimise infant exposure. Nicotine replacement therapy is not an absolute contraindication to breastfeeding and is preferable to smoking, although short-acting forms should be selected. Smoking, including passive smoking, has been associated with sudden infant death syndrome. High maternal intake of caffeine is associated with irritability and poor sleep patterns in the infant.

Breastfeeding in the context of illicit drug use is likely to be problematic. A follow-up study of one-year-old breastfed infants of mothers who used cannabis found some impairment in motor development, although the researchers found it difficult to determine whether in utero exposure was a greater influence.[17] Women should be encouraged to stop using cannabis and avoid exposure of the baby to second-hand smoke.

Finding information and advice

If unsure, seek advice on the use of a drug during breastfeeding. There are a number of different information sources available.

Drug information services

State-based obstetric drug information services provide detailed advice on the use of drugs during lactation and should be able to advise about past clinical experience with the drug (see Box).

LactMed

LactMed[11] is a freely accessible, well-resourced and peer-reviewed online database that can be downloaded as an app for mobile devices. It is updated to keep pace with new information, including published studies and drug approvals. It also incorporates information on complementary treatments.

Australian Medicines Handbook

The Australian Medicines Handbook (AMH)[16] also provides information on prescribing during lactation. It includes advice about drugs that may suppress lactation and those that are contraindicated or should be used with caution. However, lack of evidence of harm does not mean that a drug is safe.

The Women's Pregnancy and Breastfeeding Medicines Guide

The Women's Pregnancy and Breastfeeding Medicines Guide, originally published in book format, is now available as an online subscription.[12] The online version is constantly updated, providing evidence-based recom-mendations on the use of medicines during pregnancy and breastfeeding.

Product information

Be aware that the drug's product information sometimes contains advice that is contrary to recommended treatment.[18] An example is the treatment of mastitis with cephalexin: 'Alternative feeding arrangements for the infant should be considered'. Explanation should be given to the mother (and, if appropriate, her partner) that, while taking any antibiotic for mastitis, it is recommended to breastfeed more frequently and perhaps also express milk, to prevent stasis in the milk ducts and to maintain supply.

Conclusion

Most commonly used drugs are relatively safe for breastfed babies. The dose received via milk is generally small and much less than the known safe doses of the drugs used in neonates and infants. Further, most lactating women take few medications and often only occasionally. For women on chronic medications, most can be reassured, but some drugs will be contraindicated and others not yet adequately studied. Good resources are available, including state-based drugs and medicines information services.

Box **Obstetric drug information services in Australia**

Australian Capital Territory	Medicines Information Service Canberra Hospital and Health Service Phone: 02 6244 3333
New South Wales	MotherSafe Royal Hospital for Women Phone: 02 9382 6539 Toll free (NSW): 1800 647 848
Northern Territory	Northern Territory Drug Information Centre Royal Darwin Hospital Phone: 08 8922 8424
Queensland	For health professionals: Queensland Medicines Advice and Information Service (QMAIS) Royal Brisbane and Women's Hospital Phone: 07 3646 7599 or 07 3646 7098
South Australia	SA Pharmacy Obstetric and Paediatric Medicines Information Service Women's and Children's Hospital Phone: 08 8161 7222
Tasmania	No drug information centre currently available
Victoria	Medicines Information Services Pharmacy Department, Royal Women's Hospital Phone: 03 8345 3190 Medicines Information Centre Monash Health Phone: 03 9594 2361
Western Australia	Drugs in Pregnancy and Breastfeeding Information Service King Edward Memorial Hospital Phone: 08 9340 2723

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FURTHER READING

Alcohol

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Veiby G, Engelsen BA, Gilhus NE. Early child development and exposure to antiepileptic drugs prenatally and through breastfeeding: a prospective cohort study on children of women with epilepsy. JAMA Neurol 2013;70:1367-74.

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MEETINGS

1. **Eighteenth Annual Conference of the Society for Emergency Medicine India, EMCON 2016, Madurai, Tamil Nadu, India 10 – 13 November 2016**
   Information: Narendra Nath Jena, Organizing Chairman, EMCON 2016; *www.emcon2016madurai.in*

2. **Fifth Geriatric Medicine Conference, Atlanta, USA 14 – 16 November 2016**
   Information: Kelly Susan, Geriatric Medicine 2016, 2360 Corporate Circle. Suite 400, Henderson, NV 89074-7722, USA.

3. **The Fortieth All India Cell Biology Conference and International Symposium on Functional Genomics and Epigenomics, Gwalior, Madhya Pradesh, India 17 – 19 November 2016**
   Information: P.K. Tiwari, Organizing Secretary; I.K. Patro, Convener; *xlaicbc20l6@gmail.com*

4. **International Conference on Integrative Medicine and Nutrition, Atlanta, USA 28 – 29 November 2016**
   Information: Conference Secretariat, 2360 Corporate Circle, Suite 400 Henderson, NV 89074-7722, USA.

5. **Sixty-fourth National Conference of Anatomical Society of India, Jodhpur, Rajasthan, India 28 November – 1 December 2016**
   Information: Conference Secretariat, All India Institute of Medical Sciences, Basni Industrial Area, Phase 2, Jodhpur 342005, Rajasthan; *secretariat@ natcon64.in*

6. **Twenty-third World Congress of the Association of Social Psychiatry, New Delhi, India 30 November – 4 December 2016**
   Information: Rakesh K. Chadds, Conference Secretariat, Department of Psychiatry, Government Medical College, D-Block, Level 5, Chandigarh 160030; *secretariat@wasp20l6.com; www.wasp2016.com*

7. **Third International Conference on Birth Defects (ICED 2016) and Third National Conference of the Society of Indian Academy of Medical Genetics (SIAMG), New Delhi, India 7 – 10 December 2016**
   Information: Madhulika Kabra, Organizing Chairperson, Division of Genetics, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110029; *www.iamg.in*

8. **Fifth International Conference of Physical Therapy, New Delhi, India 8 – 12 December 2016**
   Information: Arushi Kaul Saraf, Physiotherapy Unit, Department of Anaesthesiology, Pain Medicine and Critical Care, All India Institute of Medical Sciences, AB8, 8th Floor, Main Building, New Delhi 110029; *incptaiims2016@gmail.com; www.incptaiims.org*

9. **Sixty-first Annual National Conference of the Indian Orthopaedic Association – IOACON 2016, Kochi, Kerala, India 12 – 17 December 2016**
   Information: Tajan P.J., Organizing Secretary, IOACON 2016, 41/1057, Vrindavan Colony, Robinson Road, Palakkad 678001, Kerala; *ioacon20l6@gmail.com*

10. **Sixty-fifth Annual Conference of the Neurological Society of India, Chennal, Tamil Nadu, India 15 – 18 December 2016**
    Information: K. Sridhar, Organizing Secretary, NSICON 2016; *secretary@ nsicon2016.com*

11. **Second International Public Health Management Development Program (IPHMDP), Chandigarh, India 16 – 20 December 2016**
    Information: Programme Director, Harlem Kaur Arora, School of Public Health, PGIMER, Chandigarh; *iphmdp@gmail.com*

12. **Twenty-Second AIPNA–ICP International CME 2017, Kolkata, West Bengal, India 27 – 29 January, 2017**
    Information: Deepak K. Mishra, Organizing Secretary; *deepak.mishra@tmckolkata.com; www.tmckolkata.com* (News Section); *www.pathoindidcom; WWW.iapm.org.in*

13. **International CME in Pathology, Histopathology and Cytopathology, Goa, India 2 – 4 February 2017**
    Information: Conference Secretariat, R.G.W. Pinto, 3, Sunshine Building, Near Geeta Bakery, Benard Guedes Road, Panaji 403001, Goa; *wisemanpinto@gmail.com*

Answers to self-assessment questions

Question 1

- Hypocalcaemia with hyperphosphataemia in a person with no evidence of renal disease and normal ALP (no osteomalacia) suggests hypoparathyroidism. The causes of hypoparathyroidism include: Familial (autosomal dominant or recessive, rare), autoimmune (rare), surgical (thyroidectomy, parathyroidectomy), and DiGeorge's syndrome.

- Read up causes of hypocalcaemia.

Question 2

These data are consistent with chronic renal disease (CKD). The marked hyperphosphataemia, normocytic normochromic anaemia and the raised ALP (osteomalacia) are all suggestive of CKD. Compensatory secondary hyperparathyroidism in the early stages of CKD raises serum calcium to normal or near normal levels, and later raises it to levels above normal range, which is referred to as tertiary hyperparathyroidism. At this stage, the parathyroids are enlarged and autonomous i.e. no longer responsive to serum ionized calcium levels.

Question 2

The blood gases indicate acute respiratory alkalosis. It would be wise to have the serum electrolytes and a measure of salicylates in blood.

Professor Colvin Goonaratna FRCP, PhD, FCCP, Hon DSc

(I have no conflicts of interests regarding these questions and answers)

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