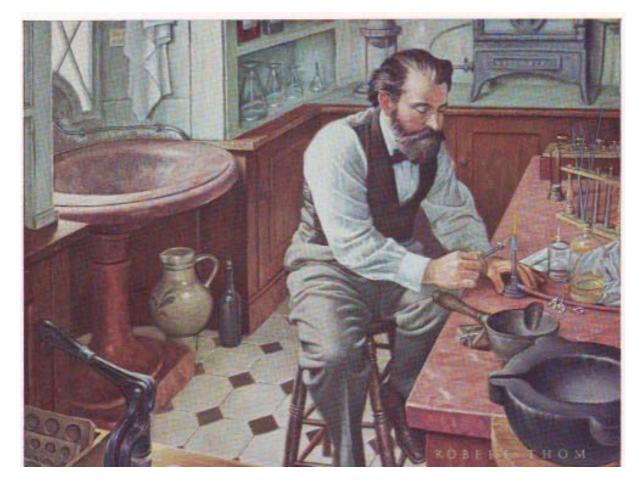


The Sri Lanka Prescriber



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The Sri Lanka **Prescriber**

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Cover picture

STANISLAS LIMOUSIN, PHARMACAL INVENTOR (About 1886)

The French retail pharmacist, Stanislas Limousin, introduced many devices to Pharmacy and Medicine. His greatest contributions were invention of glass ampoules; the medicine dropper; and apparatus for inhalation of oxygen.

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

George A. Bender, Director © 1957 Robert A. Thom, Artist

Prescribing for the elderly

Ours is a fast ageing population. The proportion of adults over the age of 60 years that was a little over 9% in year 2000, rose to over 13% by 2011, and is expected to rise to over 22% by 2031. Yet geriatrics is not a recognised medical speciality here in either State or private health care sectors. In our country, with a population of about 21 million there is not a single designated specialist geriatrician in clinical practice, whereas in the UK with a population of about 63 million in 2011 there were 1100 geriatrics specialists in active practice.

But geriatric specialist clinicians form only a small part of an ideal health care system. To make it both efficient and effective for older adults, developed countries employ a wide range of other health professionals such as specialist nurses, physiotherapists, occupational and speech therapists, and medical social workers in large numbers adequately trained to fulfill the health care needs of the elderly - but Sri Lanka has very few or none of them. Facilities for medium or long term institutional care of the elderly are utterly inadequate; most of the available few are shockingly filthy, and frequently frankly negligent or worse. It is in the context of this forlorn background that clinicians are called upon to protect the life and health of our elderly mothers, fathers and grand-parents. So let us resolve at least to do what we must to prescribe safely, in accordance with the best available evidence.

Age determined pharmacokinetic and pharmacodynamic changes

The absorption, distribution, metabolism and excretion (ADME processes) of many medicinal drugs are modified by ageing. In clinical practice the most important change is a decline of renal function with age, which reduces the glomerular filtration rate (GFR), and hence renal excretion of water soluble drugs and their metabolites [1]. These effects are particularly important for drugs with narrow ratios of the desired therapeutic effect to toxic effect such as digoxin, gentamicin and lithium.

Creatinine clearance is used as a surrogate for GFR. It is calculated from the serum creatinine using the Cockroft-Gault formula and reported as eGFR (estimated GFR), normalised to a body surface area (BSA) of 1.73m². Table 1 gives the staging of renal impairment in chronic kidney disease (CKD) based on the NICE guideline 73 (September 2008). Old people tend to have a reduced lean body mass, hence a reduced BSA, which influence both measured blood creatinine level and creatinine clearance.

Table 1. Degrees of renal impairment in relation to calculated eGFR (NICE guideline: 73)

Degree of impairment	eGFR ml/min/1.73 m²
Normal (stage 1)	>90*
Mild (stage 2)	60 - 89*
Moderate (stage 3)	30 - 59
Severe (stage 4)	15 - 29
Renal failure (stage 5)	< 15
(* with other evidence of	renal disease)

Other changes that may significantly affect drug pharmacokinetics in the elderly include reduction of liver parenchymal cell mass, hepatic blood flow, and gastrointestinal motility and absorptive capacity. Bioavailability of drugs that undergo hepatic first pass metabolism, especially the ones with a high hepatic extraction ratio, may be increased as a consequence of diminished hepatic functional capacity [2]. The reduction of total body water (TBW) in old people reduces the volume of distribution (VD) for water soluble drugs and metabolites, hence increases their blood levels. Others factors that often operate to diminish TBW and VD in the elderly include a reduced sensitivity to changes in plasma osmolality of the cranial osmoreceptor centre and consequently the thirst centre, coupled with polyuria as a result of diabetes or CKD.

Apart from pharmacokinetic issues, the elderly are more sensitive to the effects on the central nervous system of many drugs, for example benzodiazepines, antidepressants and antipsychotics.

Polypharmacy

Polypharmacy in the elderly patient may be the result of inappropriate prescribing or rational therapeutic

intervention for multiple appropriate indications. Irrespective of the cause polypharmacy is linked to a number of negative outcomes including adverse drug reactions (ADRs), drug interactions, falls, hospital admissions, duration of hospital stay and mortality rate [3].

The incidence of negative outcomes of polypharmacy may be minimised by stopping drugs that are not providing the expected benefit, prescribing only clearly indicated new drugs, using simple drug regimens, reviewing prescribed medications regularly, and using only doses recommended for the elderly.

The Beers criteria for avoiding certain drugs in the elderly

Since the pharmacokinetics and pharmacodynamics of drugs change with ageing, an American consensus guideline referred to as the Beers criteria were developed and published in 1991. They have been last updated in 2003 [4], and provide a list of drugs regarded by an expert panel as especially likely to cause problems in the elderly. Some drugs included in the 2003 list are given in table 2.

Adverse drug reactions and side-effects

An adverse drug reaction (ADR) is defined as a harmful or seriously unpleasant reaction to an intended therapeutic, prophylactic or diagnostic dose of a medicinal drug that necessitates its withdrawal, dose reduction or prohibition from future use. A side-effect is a minor reaction that occurs with therapeutic doses, is predictable and usually dose related. Both ADRS and side-effects are commoner in the elderly than in young adults [3]. Since the elderly often have several medical problems requiring multiple medicinal drugs, the incidence of harmful drug-drug interactions is also higher in them.

Table 2. Some drugs from updated Beers criteria selected from the 2003 list [4], with concerns regarding use in elders

Drug	Concerns	Rating
Pentazocine	Narcotic analgesic, causing confusion hallucinations	High
NSAIDS, Aspirin	Exacerbation of peptic ulcers, haemorrhage; renal impairment	High
Indometacin	Highest incidence of CNS effects of all NSAIDs, exacerbation of peptic ulcer, haemorrhage	High
Meprobamate	Highly addictive and sedating; falls	High
Digoxin	Toxicity with decreased GFR and hypokalaemia	High
Glibenclamide	Prolonged hypoglycaemia	High
Amitriptyline	Strong anticholinergic action and sedation (Avoid tricyclic antidepressants)	High
Diazepam, Flurazepam	Long acting sedation, loss of balance, falls,	High
Promethazine, Chlorphenamine, Diphenhydramine etc	Anticholinergic actions, sedation. Prefer non-anticholiuergic antihistamines eg cetirizine	High
Nitrofurantoin	Potential renal impairment. Avoid in CKD. Safer alternatives available	High
G.I.T. antispasmodics: Propantheline Mebeverine	Highly anticholinergic, and uncertain effectiveness	

(*High = High risk of side-effects and/or ADRs)

Table 3. Some guidelines for good prescribing in elderly patients

- ✓ Consider non-pharamacological treatments such as counselling where appropriate (eg senile tremor, loss of taste or smell, memory failure without other signs of dementia, dizziness)
- ✓ Stop current drugs that are not indicated
- ✓ Prescribe an additional drug only when clearly indicated
- ✓ Prescribe the recommended dosages for the elderly
- ✓ Use simple regimens, using a few appropriate clearly indicated drugs
- ✓ Use once daily dosing and fixed dose combinations when possible
- ✓ Discuss the drugs and the regimen with the patient and care givers
- ✓ Review medication regularly

Good prescribing for older adults

Much has been written and spoken about this topic over the last 3 to 4 decades, and several studies from developed countries have reported slow but steady improvement of prescribing practices with continuing education of clinicians and nursing staff [5]. We do have numerous educational programs on various topics including good prescribing for practicing clinicians organised by many medical institutions and associations in Sri Lanka, but I am not aware of systematic and reliable studies of their outcomes or their outreach. The management of health problems of the elderly is too important a matter to be left to unplanned, uncoordinated and unsystematic approaches. Nor should educational programs about elderly health care rest predominately in the hands of the private sector whose primary objective is the marketing and sale of health care and health care products. The Ministry of Health is the appropriate and principal authority for continuing education of all health care professionals and other staff.

Consider the UK as an example. Although the proportion of its population over the age of 60 years is about 20%, this group receives about 60% of all prescriptions and accounts for over 52% of NHS drug costs [5]. I do not mean to say or imply therefore

that cost saving rather than benefits to patients is or should be the prime objective of good prescribing. Earlier on in this essay I have indicated the negative effects of polypharmacy on older patients and the health services as a whole. Table 3 lists some guidelines derived from several sources for good prescribing in older patients.

References

- Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics; basic principles and practical applications. *British Journal* of Clinical Pharmacology 2003; 57: 6-14.
- 2. Milton JC, Hill-Smith I, Jackson SHD. Prescribing for older people. *British Medical Journal* 2008; **236**: 606-9.
- 3. Frazier SC. Health outcomes and polypharmacy in elderly individuals. *Journal of Gerontology Nursing* 2005; **31**: 4-11.
- 4. Fick DM, Cooper JW, Wade WE, *et al* Updating the Beers criteria for potentially inappropriate medication use in older adults. *Archives of Internal Medicine* 2003; **163**: 2716-24.
- 5. Franklin BD, O'Grady K, Donyal P, et al. The impact of a closed-loop electronic prescribing and administration system on prescribing errors, administration errors and staff time: a before-and-after study. Quality and Safety in Health Care 2007; 16: 279-84.

Professor Colvin Goonaratna, MBBS, FRCP (Lond and Edin), PhD, FCCP. *Co-editor, Sri Lanka Prescriber; Chair, Sri Lanka Clinical Trials Registry*. Email <si7np5e@gmail.com> I have no competing interests with regard to my designations or this article.

How to communicate instructions on taking medicines to your hearing disabled patient

Introduction

One may be born with a hearing disability (congenital deafness) or develop a hearing disability after birth (acquired deafness). Hearing community and especially health professionals consider deafness as a pathological condition. However, congenitally deaf individuals identify themselves as a separate ethnic group or a community called the 'Deaf community' and consider deafness as a different experience rather than a disability. Hence they use a capital "D" in "Deaf" to imply that they are from a different community.

They use sign language to communicate and share habits, traditions and beliefs which are common to them but socially and culturally different from others. In interacting with hearing disabled people, health professionals should understand their thinking and respect their ideas so as not to embarrass them and hurt their feelings.

Hearing disabled individuals need to take medicines for both communicable and non-communicable diseases, acute and chronic. Some become pregnant and may need to take medicine during pregnancy. Some are parents and need to administer medicines to their children. In short, they need medicine just as much as people with good hearing.

Communication barrier makes using medicines difficult

Hearing disabled people face difficulties in using medicines due to communication difficulties with doctors and pharmacists.

- 1. They have difficulty communicating their health problems to doctors.
- 2. They may not understand the questions asked by doctors during the medical consultation.
- 3. They may not understand the instructions given by the doctor or pharmacist on how to take the medicines.
- 4. They may find it difficult to clarify any queries they have on taking medicines.
- 5. They may find it difficult to remember instructions given by health providers regarding medicines.

These communication barriers hinder safe and effective medicine use among this community, cause dissatisfaction and frustration and poor compliance to treatment. Hence doctors and other health professionals looking after their health needs should have the knowledge and skills to communicate medicinal instructions and information effectively to this special group.

During a study done in Sri Lanka it was found that hearing disabled patients frequently felt left out from the discussion during medical consultations. Most of the time doctors conveyed the necessary information only to the interpreter or relative accompanying the patient, ignoring the patient completely. Health professionals should pay attention to this finding and try to develop communication skills to rectify this deficiency.

How to improve communication with your hearing disabled patient

The following are some suggestions to improve the interpersonal communication with the patient.

- 1. The doctor should be seated so that his face is not in the dark and the patient can see the expressions on his face well. Especially if you are going to use a lip reading method with your patient this is very important.
- 2. You should welcome the patient with a friendly gesture such as gently touching his shoulder or shaking his hand.
- 3. Look at the patient even when you are providing instructions and information on using the medicines to a relative or a sign language interpreter. Do not communicate with the interpreter ignoring the patient.
- 4. You should smile and maintain eye contact with your patient as much as possible throughout the consultation.

Communication methods

The following are some useful ways to communicate with hearing disabled patients. Different patients have different preferences and abilities to use these

methods. You should select one or a combination of methods suitable for you and your patient based on mutual preference and ability to use these methods.

- 1. Sign language
- 2. Lip reading
- 3. Written information
- 4. Pictograms and visual sequence maps

Using sign language

Sign language is the first language of many hearing disabled patients. However, sign language differs from country to country, different parts of the same country, as well as individual households. Further-more, conveying certain medical concepts, instructions and information using sign language is difficult. Most doctors and pharmacists do not know sign language and need to rely on sign language interpreters to communicate with the patient. Professional sign language interpreters are generally not available at healthcare settings and the doctor needs to rely on relatives accompanying the patient to help with the sign language. Yet the accuracy of the communication is in doubt, as it and depends on the relative's ability to understand the instructions given by the doctor and to convey it to the patient.

Lip reading

Only some hearing disabled patients are able to lip read. The ability to communicate medicinal instructions via lip reading depends on the skill of the doctor in using the lips to formulate words that give meaning to the patient, and also the patient's skill and experience in lip reading. You should not exaggerate your lip movements or speak at a very slow pace. Avoid speaking too loudly since it may appear unfriendly to your patient, may result in loss of privacy, and breach of confidentiality. Two local studies have shown that most patients are unable to lip read to receive instructions accurately and that they did not prefer lip reading.

Written instructions

You may believe that giving written instructions is an effective way of communicating with the hearing disabled patients. However the ability to understand written information is poor in the majority of deaf people since their first language is sign language, and

any other language is a foreign or a second language to them. So most of them are not able to read prescription labels, medicine labels or patient information leaflets given to the general public to access necessary information on administering medicines.

Using pictograms and visual sequence maps

Hearing disabled people are used to receiving information and instructions via pictograms as these are used in their educational programs at school, and they can readily grasp information conveyed via pictograms. When pictograms are aligned in a sequence to convey a series of instructions (visual sequence map) they can comprehend them well. So pictograms and visual sequence maps can be used effectively to convey medicinal instructions to them.

The following are selected examples of pictograms developed and validated in a recent study in Sri Lanka to convey medicinal instructions to hearing disabled individuals. These pictograms were comprehended by more than 80% of the participants and have been accepted as valid according to guidelines on validating pictograms.

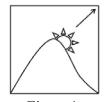






Figure 1.

Figure 2.

Figure 3.

Meanings conveyed by Figures 1, 2, and 3 respectively are *morning*, *mid day* and *night*.







Figure 4.

Figure 5.

Figure 6.

Meanings conveyed by Figure 4, 5, and 6 are respectively, *a meal, take two capsules*, and take *two tablets*.

Using the developed pictograms, simple visual concept maps were developed to convey medicine administering methods as depicted in figures 7 and 8.



Figure 7.

In the morning, take two capsules after meals

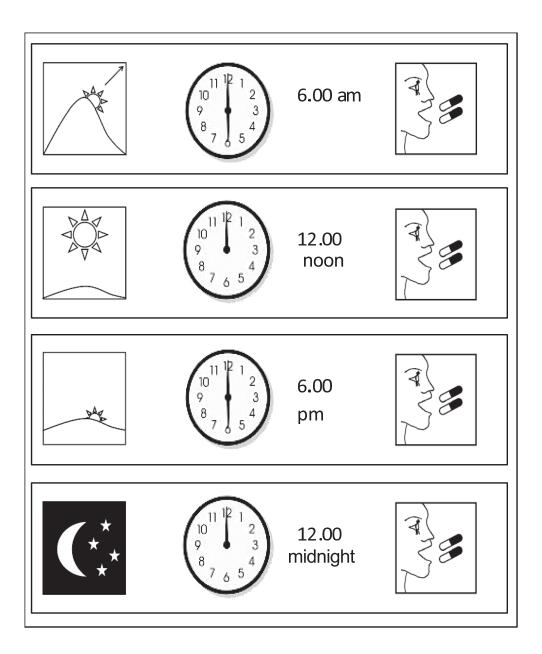


Figure 8. Instructions conveyed; take 2 capsules at 6 o'clock in the morning, noon, at six o'clock in the evening and at midnight.

Examples of how pictograms can be modified to depict different drug regimes.

• Figure 9: Instruction being conveyed: Take two capsules after breakfast; at noon take no medicine; at night take one capsule after dinner.

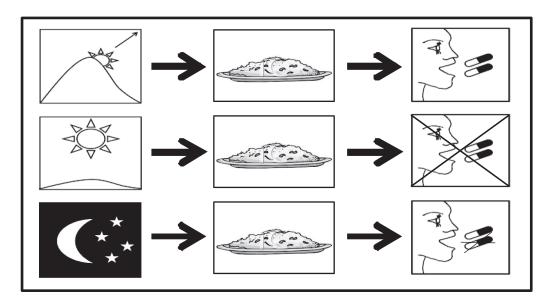


Figure 9.

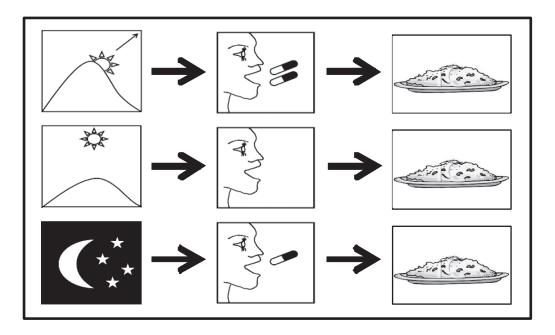


Figure 10.

Figure 10: Instruction being conveyed: *Take two capsules before breakfast, at noon take no medicine, at night take one capsule before dinner*. Method of modification: applying correction fluid to delete unwanted items.

Conclusions

Communication difficulties with doctors and difficulties in understanding a written language are major limitations that hinder medicine use by the deaf and mute. There is a risk of developing negative attitudes and dissatisfaction in them regarding medicine use because of these limitations. Health professionals and policy makers should be aware of and sensitive to these limitations to promote safe and effective medicine use in these patients.

Way forward

Official sign language interpreters should be made available at healthcare settings frequented by hearing impaired patients to enable efficient communication. Pictograms and visual sequence maps should be used by doctors to improve communication with them during the medical consultation. Medicine labels using pictorial methods described above should be used at pharmacies to enable these patients to understand and remember the instructions on using medicines better.

Suggested reading

- 1. Munoz-Baell IM, Ruiz MT. Empowering the deaf. Let the deaf be deaf. *Journal of Epidemiology and Community Health* 2000; **54**: 40-4.
- 2. Luke WANV, Weeraratne CL, Maduranga BBS, Madugalle SSB. Limitations to effective use of medicine among deaf students and strategies adopted by themselves to overcome the limitations, 5th Singapore PHOM and 4th Asian Regional HTA Conference, 19 and 20 August 2010.
- 3. Dealing with Hearing-impaired Patients. [Doctor] Patient.co.uk. [http://www.patient.co.uk/doctor/dealing-with-hearing-impaired-patients] (Last accessed 16th May, 2013)
- 4. Chong-hee Lieu C, Sadler GR, Fullerton JT, *et al.* Communication strategies for nurses interacting with patients who are deaf. *Dermatology Nursing* 2007; **19**: 541-44; 549-55.
- Desmon P, Weeraratne CL. Communicating medicine instructions to hearing disabled consumers. Berlin: Lambert Academic Publishing: 2012.
- 6. Tijus C, Barcenilla J, de Lavalette BC, Meunier J. The design, understanding and usage of pictograms, *Studies in Writing* 2007; **21**: 17-32.

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Hypertensive disorders of pregnancy

Summary

Hypertensive disorders of pregnancy are common and represent a spectrum of disease ranging from chronic and gestational hypertension to eclampsia. They are associated with increased risk of both adverse maternal and fetal outcomes.

Drug treatment is generally reserved for moderate or severe hypertension. Preeclampsia-eclampsia can be life-threatening and requires urgent investigation and intervention. There are limited data about the safety of many hypertensive drugs in pregnancy. ACE inhibitors and angiotensin receptor blockers should be avoided.

Women who have had any hypertensive disorder in pregnancy have an increased cardiovascular risk. They require long-term follow-up.

Key words: antihypertensives, breastfeeding, preeclampsia

(Aust Prescr 2012;35:47-50)

Introduction

Hypertensive disorders affect 10–22% of pregnancies and have been classified into four conditions, reflecting potential differences in aetiology and pregnancy outcomes:^{1,2}

- chronic hypertension
- gestational hypertension
- pre-eclampsia-eclampsia
- pre-eclampsia superimposed on chronic hypertension.

The incidence of these disorders is not entirely clear, but pre-eclampsia is thought to affect 5–8% of pregnancies. Chronic hypertension accounts for approximately 20% of the cases of high blood pressure seen in pregnancy.^{1,3}

Chronic hypertension

Chronic hypertension is diagnosed when hypertension is confirmed before pregnancy or before 20 weeks gestation (blood pressure >140 mmHg systolic and/ or >90 mmHg diastolic).³ However, chronic hypertension is frequently diagnosed when high blood pressure fails to resolve post-partum. Women with chronic hypertension require careful monitoring during pregnancy as they have an increased risk of adverse events, including superimposed pre-eclampsia,

placental abruption, fetal growth restriction, premature delivery and stillbirth.³

Pre-pregnancy counselling and management of chronic hypertension is essential. Some commonly prescribed antihypertensive drugs are contraindicated or best avoided before conception and during pregnancy (Table 1). These include ACE inhibitors, angiotensin receptor antagonists, diuretics and most beta blockers.^{3,4}

Where indicated, it is advisable to look for secondary causes of hypertension before conception, as normal physiological changes in pregnancy can make many of these screening tests difficult to interpret. If this is not possible, with the exception of phaeochromocytoma, further investigation is often best deferred until the postpartum period. In all cases, preconception assessment for proteinuria (with urine protein: creatinine ratio) is recommended as a baseline measurement.

Treatment

With the exception of acute, severe hypertension, treatment with antihypertensive drugs during pregnancy remains controversial. In many cases, the physiological fall in blood pressure that occurs during the first trimester leads to normalisation without the need for medication. There is no direct evidence that continued treatment of chronic hypertension leads to a reduction in the risk of adverse pregnancy events.³

Table 1. Antihypertensive drugs to avoid in pregnancy and preconception

Antihypertensive	Advice	Potential adverse events
ACE inhibitors	Contraindicated	Teratogenic in first trimester. Fetal renal dysfunction, oligohydramnios and skull hypoplasia in second and third trimesters.
Angiotensin receptor blockers	Contraindicated	Teratogenic in first trimester. Fetal renal dysfunction and oligohydramnios in second and third trimester.
Diuretics	Avoid	Fetal electrolyte disturbances, reduction in maternal blood volume.
Beta blockers (except labetalol and oxprenolol)	Avoid	Fetal bradycardia, long-term use of atenolol associated with fetal growth restriction.
Calcium channel antagonist (except nifedipine)	Avoid	Maternal hypotension and fetal hypoxia.

Benefits appear to be confined to reducing severe hypertension (≥170/110 mmHg), however most centres start or continue antihypertensive drugs when blood pressure exceeds 160 mmHg systolic and/or 100 mmHg diastolic on more than one occasion.³ Table 2 outlines the antihypertensive drugs most commonly used in pregnancy.^{3,4}

Blood pressure reduction to 140–160 mmHg systolic and 90–100 mmHg diastolic are acceptable treatment goals. Stricter blood pressure control may be associated with fetal growth restriction, presumed to be related to relative placental hypoperfusion. Importantly, women need to be carefully monitored for any signs of pre-eclampsia which may include worsening hypertension and new or worsening proteinuria (see Box). Repeated assessment of fetal wellbeing and growth is appropriate, although given that there are no guidelines, the frequency of monitoring is usually at the discretion of the woman's treating obstetrician.

Box

Features of pre-eclampsia

Hypertension with onset after 20 weeks gestation

Renal manifestations

Significant proteinuria Serum creatinine >90 micromol/L (or renal failure) Oliguria

Haematological manifestations

Disseminated intravascular coagulation Thrombocytopenia Haemolysis

Hepatic manifestations

Raised serum transaminases Severe right upper quadrant or epigastric pain

Neurological manifestations

Eclamptic seizure Hyperreflexia with sustained clonus Severe headache Persistent visual disturbances Stroke

Pulmonary oedema

Fetal growth restriction

Placental abruption

Gestational hypertension

Gestational hypertension is defined as:

- new onset of hypertension after 20 weeks gestation
- no other features to suggest pre-eclampsia (see Box)
- normalisation of blood pressure within three months postpartum.

Gestational hypertension is associated with adverse pregnancy outcomes. These are more common if it presents earlier in the pregnancy, if it progresses to pre-eclampsia or if hypertension is severe (≥170/110 mmHg).³

Although rare, phaeochromocytoma can initially present in pregnancy. It can be fatal. Investigation is needed if there are any other features to suggest a phaeochromocytoma (for example paroxysmal hypertension, episodic headache and sweating), or if the onset of hypertension occurs early in the pregnancy or is severe. Plasma or urinary metanephrines (catecholamine metabolites) tend not to be affected by the physiological changes of pregnancy and are useful as screening investigations.⁵

The benefits of treating mild to moderate hypertension are limited to the prevention of severe hypertension and appear to have no effect on the potential for adverse pregnancy outcomes. The indications for treatment with antihypertensive drugs, goals of therapy and the choice of drug are similar to the treatment of chronic hypertension in pregnancy (Table 2). Up to 25% of women who develop hypertension in pregnancy will eventually be diagnosed with pre-eclampsia, even if no other manifestations are present initially. Regular monitoring of blood pressure, and investigation for proteinuria and other features of preeclampsia (up to once or twice per week) is reasonable.³

By definition, gestational hypertension should resolve within three months postpartum and the patient can generally be weaned off antihypertensive drugs within weeks. If hypertension has not resolved within three months, an alternative diagnosis – for example chronic (essential or potentially secondary) hypertension – needs to be considered. There is a risk of recurrence in subsequent pregnancies so increased monitoring will be required.

Table 2. Relatively safe antihypertensive drugs in pregnancy

Antihypertensive	Class	Starting Dose	Maximum Dose	Important adverse effects
Labetalol	Beta blocker	100–200 mg twice a day	400 mg three times a day	Bradycardia, bronchospasm, transient scalp tingling
Oxprenolol	Beta blocker	40–80 mg twice daily	80–160 mg twice daily	Bradycardia, bronchospasm
Nifedipine	Calcium channel antagonist	10 mg twice a day, 30 mg daily controlled release	20–40 mg twice a day, 120 mg daily controlled release	Severe headache, peripheral oedema
Methyldopa	Centrally-acting	250 mg twice a day	500 mg four times a day	Sedation, light-headedness, dry mouth, nasal congestion, haemolytic anaemia, depression
Hydralazine	Vasodilator	25 mg twice a day	50–200 mg total daily dose	Flushing, headache, lupus-like syndrome
Prazosin	Alpha blocker	0.5 mg twice a day	3 mg total daily dose	Postural hypotension

Pre-eclampsia, eclampsia and superimposed pre-eclampsia

The aetiology of pre-eclampsia is unclear although a combination of maternal and placental factors are likely to contribute. Abnormal placental formation, resulting in aberrant angiogenic factor production and systemic endothelial dysfunction, as well as genetic and immunological factors, are thought to play a role. Risk factors include nulliparity, age less than 18 or more than 40 years, a past history of pre-eclampsia and maternal medical comorbidities (hypertension, diabetes mellitus, renal disease, obesity, antiphospholipid antibodies or other thrombophilia and connective tissue disease).6 Pre-eclampsia is associated with fetal growth restriction, preterm delivery, placental abruption and perinatal death.7 Severe preeclampsia has the potential for progression to eclampsia, multi-organ failure, severe haemorrhage and rarely maternal mortality.

Pre-eclampsia is a disorder with many manifestations.

New onset hypertension after 20 weeks gestation and proteinuria are the most common presenting features. A urine dipstick for proteinuria can be a useful screening test, but is confounded by high false positive and false negative rates. If there is any uncertainty, assessment of the urine protein:creatinine ratio is advised. Peripheral oedema is no longer considered a diagnostic feature of pre-eclampsia as it is neither a sensitive nor specific sign. Other clinical manifestations are outlined in the Box, with their presence suggesting severe pre-eclampsia.

The presence of severe pre-eclampsia mandates urgent review. A multidisciplinary team approach (obstetrician, midwife, neonatologist, anaesthetist and physician) is often required. Delivery is the only definitive management for pre-eclampsia. The timing of delivery is dependent on the gestational age and well-being of the fetus and the severity of the pre-eclampsia. The pregnancy is rarely allowed to go to term. Management of pre-eclampsia before 32 weeks

gestation should occur in specialist centres with sufficient expertise and experience. Severe hypertension may require parenteral antihypertensive drugs (such as hydralazine), which should only be given in a suitably monitored environment (birth suite or high dependency unit). Intravenous magnesium sulfate is given for the prevention of eclampsia in severe cases.⁸

Although pre-eclampsia progressively worsens while the pregnancy continues, outpatient management may be considered in selected cases. The antihypertensive drugs used in pre-eclampsia are the same as those used to treat chronic and gestational hypertension (Table 2).³ The treatment goals for blood pressure control are also the same (140–160 mmHg systolic and 90–100 mmHg diastolic). Although widely advised in the past, there is little evidence to support bed rest. Given the potential for venous thromboembolism from immobilisation, bed rest is generally only advised with severe, uncontrolled hypertension.⁹

Postpartum management and secondary prevention

Most of the manifestations of pre-eclampsia resolve within the first few days or weeks postpartum. The features of pre-eclampsia, including hypertension, may worsen before they improve. Rarely the first manifestations occur postpartum. Frequent review of blood pressure during this period is essential, for example once to twice weekly. Antihypertensive doses are reduced or ceased when the blood pressure falls to less than 140/90 mmHg. Home blood pressure monitoring with an automated device can be helpful to avoid hypotension. This is a common occurrence, as the features of pre-eclampsia and therefore antihypertensive requirements can recede precipitously. Like gestational hypertension, if the blood pressure does not normalise within three months consider an alternative diagnosis. It is also important to confirm that proteinuria has resolved.

Pre-eclampsia can recur in subsequent pregnancies with the most prominent risk factors being previous severe or early onset pre-eclampsia or chronic hypertension. The use of low-dose aspirin has been shown to be safe and beneficial in decreasing this risk in women with a moderate to high risk of pre-eclampsia. Aspirin is therefore generally advised in subsequent pregnancies. It is started at the end of

the first trimester and can be safely continued until the third trimester, with most centres ceasing therapy at 37 weeks gestation. Calcium supplements (1.5 g/day) may be of benefit, particularly in women at risk for low dietary calcium intake. The administration of vitamin C and E supplements has not been shown to be beneficial and may be harmful.³

Antihypertensive drugs postpartum

The choice of antihypertensive drugs depends on whether breastfeeding is attempted. When the woman wishes to breastfeed, consideration must be given to potential transfer of the drug into breast milk. Most drugs safely used in pregnancy are excreted in low amounts into breast milk and are compatible with breastfeeding. Table 3 shows antihypertensive drugs to use or avoid during lactation.⁴ Should there be no desire to breastfeed and adequate contraception is used, the choice of antihypertensive drug is the same as for any other non-pregnant patient.

Long-term follow-up

Pre-eclampsia and gestational hypertension appear to be associated with an increased long-term risk of cardiovascular disease, including hypertension, ischaemic heart disease, stroke and venous thromboembolism. ¹⁰ There may also be a small increased risk of chronic renal failure and thyroid dysfunction after pre-eclampsia. ^{11,12} Annual assessments of blood pressure and at least five-yearly assessments for other cardiovascular risk factors are advisable. ³ Thyroid and renal function should also be measured intermittently.

Conclusion

Pregnancies affected by hypertensive disorders require careful monitoring due to the increased risks of adverse pregnancy outcomes. New onset hypertension in pregnancy warrants consideration of preeclampsia. Antihypertensive drugs for all forms of hypertensive disorder of pregnancy tend to be reserved for persistent or severe hypertension. Many standard antihypertensive drugs are contraindicated in pregnancy and lactation. In women at moderate to high risk for recurrent pre-eclampsia, prophylaxis with low-dose aspirin and calcium supplements in subsequent pregnancies may be of benefit. Long-term follow-up, particularly in regard to cardiovascular risk, is important in women with a history of hypertensive disorders in pregnancy.

Table 3. Antihypertensive drugs during breastfeeding

Class	Drugs considered safe	Avoid – Potentially harmful, no or limited data
Beta blockers	Propranolol, metoprolol, labetalol	Avoid atenolol, no data for other beta blockers
Calcium channel antagonists	Nifedipine	More limited data for diltiazem and verapamil – may be safe; avoid other calcium channel blockers
ACE inhibitors	Captopril, enalapril	Other ACE inhibitors
Angiotensin receptor blockers	None	No data
Thiazide diuretics	None	Limited data
Other	Methyldopa, hydralazine	Limited data for prazosin, consider alternatives

References

- ACOG Committee on Obstetric Practice. Clinical management guidelines for obstetriciangynecologists. Diagnosis and management of preeclampsia and eclampsia. ACOG practice bulletin. 2002;33:1-9. http://mail.ny.acog.org/website/ SMIPodcast/DiagnosisMgt.pdf [cited 2012 Mar 6]
- Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). Hypertens Pregnancy 2001;20:IX-XIV.
- 3. Lowe SA, Brown MA, Dekker GA, Gatt S, McLintock CK, McMahon LP, et al. Guidelines for the management of hypertensive disorders of pregnancy 2008. Aust N Z J Obstet Gynaecol 2009;49:242-6.
- Australian Medicines Handbook. Adelaide: AMH; 2010.
- Sarathi V, Lila AR, Bandgar TR, Menon PS, Shah NS. Pheochromocytoma and pregnancy: a rare but dangerous combination. Endocr Pract 2010;16:300-9.
- Milne F, Redman C, Walker J, Baker P, Bradley J, Cooper C, et al. The pre-eclampsia community guideline (PRECOG): how to screen for and detect onset of pre-eclampsia in the community. BMJ 2005;330:576-80.

- 7. Heard AR, Dekker GA, Chan A, Jacobs DJ, Vreeburg SA, Priest KR. Hypertension during pregnancy in South Australia, part 1: pregnancy outcomes. Aust N Z J Obstet Gynaecol 2004;44:404-9.
- 8. Sibai BM. Magnesium sulfate prophylaxis in preeclampsia: evidence from randomized trials. Clin Obstet Gynecol 2005;48:478-88.
- 9. Meher S, Abalos E, Carroli G. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database Syst Rev 2005;19:CD003514.
- Bellamy L, Casas JP, Hingorani AD, Williams DJ. Preeclampsia and risk of cardiovascular disease and cancer in later life: systematic review and metaanalysis. BMJ 2007;335:974.
- 11. Vikse BE, Irgens LM, Leivestad T, Skjaerven R, Iversen BM. Preeclampsia and the risk of end-stage renal disease. N Engl J Med 2008;359:800-9.
- Levine RJ, Vatten LJ, Horowitz GL, Qian C, Romundstad PR, Yu KF, et al. Pre-eclampsia, soluble fms-like tyrosine kinase 1, and the risk of reduced thyroid function: nested case-control and population based study. BMJ 2009;339:b4336.

Further reading

Nelson-Piercy C. Handbook of Obstetric Medicine. 4th ed. London: Royal College of Obstetricians and Gynaecologists; 2010.

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Self-assessment questions

(Select the *best* response in each question)

- 1. The commonest pathogenic organism causing community acquired bacterial meningitis is
 - (a) Streptococcus pneumoniae
 - (b) Staphylococcus aureus
 - (c) Pseudomonas aeruginosa
 - (d) Listeria monocytogenes
 - (e) Haemophilus influenzae
- 2. In community acquired bacterial meningitis empirical antibiotic therapy is best started
 - (a) immediately after clinical diagnosis, before drawing blood for culture and biochemistry
 - (b) immediately after clinical diagnosis **and** drawing blood for culture and biochemistry, but before lumbar puncture
 - (c) after completing drawing blood for culture and biochemistry, and completing lumbar puncture for CSF
 - (d) only after the urgent CSF report of low blood glucose, or raised neutrophils ± Gram stain positivity is available
 - (e) After CSF is sent for analysis and after brain imaging
- 3. Which of the following combination therapeutic regimens for acne is known to cause benign intracranial hypertension (hence absolutely contraindicated)?
 - (a) oral contraceptive with an oral anti-androgen, **plus** benzyl peroxide gel for topical application
 - (b) oral contraceptive with an oral anti-androgen, **plus** topical tretinoin once daily
 - (c) oral erythromycin 250 mg bd, **plus** topical tretinoin once daily
 - (d) oral doxycycline 50 100 mg daily, **plus** topical tretinoin once daily
 - (e) oral doxycycline 50 100 mg daily (or oral minocycline 50 100 mg daily), **plus** oral isotretinoin

Answers to self-assessment questions

Question 1. Correct response is a

Question 2. Correct response is b

Question 3. Correct response is e

All the correct responses are simply matters of fact selected from 2 articles in September 2012 issue of the *SLP*, so explanations are unnecessary.

Professor Colvin Goonaratna, MBBS, FRCP, PhD, Hon DSc Competing interests: none.

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