

MoH

# Cardiovascular Guidelines

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NDTC

2012



MINISTRY OF HEALTH

# Standard Treatment Guidelines: Cardiovascular. 2<sup>nd</sup> Edition, 2012

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## Table of Contents

1. Medicines used in cardiovascular disease .....	7
1.1 <i>Beta-blockers</i> .....	7
1.2 Calcium channel blocking drugs (calcium blockers).....	8
1.3 Angiotensin converting enzyme inhibitors (ACEI) .....	9
1.4 Directly-acting vasodilators.....	9
1.5 Centrally-acting hypotensives .....	10
1.6 Diuretics .....	10
1.7 Anticoagulants, antiplatelet drugs and thrombolytics .....	11
1.8 <i>Lipid-lowering medicines</i> .....	13
1.9 Antiarrhythmics.....	13
1.10 Cardiovascular medicine interactions .....	14
2. Hypertension .....	14
2.1 <i>Definition</i> .....	15
2.2 <i>Types of hypertension</i> .....	15
2.3 <i>Management of hypertension</i> .....	15
2.4 Hypertensive emergency (urgent blood pressure reduction) .....	19
2.5 Hypertension in children .....	20
2.6 Isolated systolic hypertension in the elderly.....	21
2.7 <i>Blood pressure monitoring</i> .....	22
2.8 <i>Resistant hypertension</i> .....	22
2.9 Hypertension in pregnancy.....	22
3.1 <i>Prevention of cardiovascular disease</i> .....	26
3.2 <i>Principles of management</i> .....	27
3.3 Management of coronary pain syndromes.....	27
3. Heart failure.....	34
4.1 <i>Causes of heart failure</i> .....	34
4.2 <i>Precipitating factors of heart failure</i> .....	35
4.3 <i>General management of chronic heart failure</i> .....	35
4.4 <i>The role of beta-blockers in heart failure</i> .....	38
4.5 <i>Acute cardiogenic pulmonary oedema</i> .....	38
4.6 Diastolic Heart Failure.....	38
5 Cardiac arrhythmias .....	39
5.1 <i>Causes of cardiac arrhythmias</i> .....	39

5.2 Aims of treatment .....	40
5.3 Tachyarrhythmias.....	40
5.3.2 Ventricular arrhythmias.....	43
5.4 Bradyarrhythmias .....	46
6 Peripheral vascular disease (PVD) .....	48
6.1 Acute limb ischaemia .....	48
6.2 Chronic limb ischaemia .....	49
6.3 Intermittent claudication .....	50
7 Cerebrovascular disease .....	51
7.1 Risk factors.....	51
7.2 Transient ischaemic attack (TIA) .....	52
7.3 Completed stroke.....	53
7.4 Management of haemorrhagic stroke .....	54
7.5 Stroke related to subarachnoid haemorrhage .....	54
8 Non-hypertensive cardiovascular disease in pregnancy .....	54
8.1 Valvular heart disease.....	54
8.2 Antibiotic prophylaxis at delivery.....	55
8.3 Cardiac arrhythmias in pregnancy .....	56
Appendix .....	58



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# 1. Medicines used in cardiovascular disease

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## 1.1 Beta-blockers

- competitively block the adrenergic beta-receptors found at sympathetic nerve endings secreting adrenaline and noradrenaline.
- adverse effects - precipitation of asthma, mental depression, lethargy, and intermittent claudication.
- recent evidence supports the use of beta-blockade in **small doses** in stable chronic heart failure.
- abrupt withdrawal may result in exacerbation of angina, cardiac arrhythmias and occasionally, in a patient with pre-existing angina, myocardial infarction. **It is best to reduce doses slowly over a 7-10 day period if possible.**

### *Propranolol*

- blocks both beta-1 and beta-2 receptors.
- reduces cardiac rate, contractility and excitability.
- reduces the caliber of the bronchial tree.
- increases the resistance of peripheral limb arterioles and reduces the mobilisation of glucose from glycogen in response to hypoglycaemia.
- an older medicine which is not accorded first choice status in the following guideline
- main uses –thyrotoxicosis, essential tremor, prophylaxis in migraine, occasional use in anxiety states.

### *Atenolol, metoprolol*

- more selective for beta-1 receptors than propranolol. Despite these differences in selectivity, **beta-blockers should not be used in anyone with a history of, or currently with, asthma.**
- have the same action on the heart and blood pressure as other beta-blockers
- less likely to produce adverse effects on the peripheral vasculature, the bronchi and on the recovery from hypoglycaemia.
- largely excreted unchanged by the kidney
- doses may need to be reduced in patients with renal impairment.
- atenolol may be given once daily. Metoprolol requires twice daily dosing

## *Labetalol*

- has both beta- and alpha-blocking properties
- produces postural hypotension and failure of ejaculation as alpha-receptor-mediated effects.
- use is principally for urgent blood pressure reduction by the parenteral route.**

## 1.2 Calcium channel blocking drugs (calcium blockers)

- block calcium entry into cells of the cardiac conducting system, myocardial cells and the cells of vascular smooth muscle
- verapamil, nifedipine and diltiazem are in the Tuvalu (EML).

### *Verapamil*

- has greater selectivity for cardiac than for vascular calcium channels.
- main role is management of cardiac arrhythmias and angina.
- may cause bradycardia
- negative inotropic action can be harmful in heart failure.
- in overdose, verapamil produces bradycardia, reduction in cardiac output and occasionally electromechanical dissociation. **Massive** quantities of calcium salts may be required to reverse these effects.
- in therapeutic doses, verapamil causes constipation that can be corrected with oral or intravenous calcium.
- given together with beta-blocking drugs, may produce bradycardia and rarely heart block.

### *Nifedipine, felodipine*

- felodipine not available on Tuvalu EML
- greater action on vascular smooth muscle than on the heart
- main use management of hypertension and angina in which the cardiac afterload needs to be reduced
- dilator activity on peripheral arteries and arterioles produces reflex tachycardia and increases the cardiac output. This can lead to worsening of angina or even myocardial infarction in patients with critical stenosis of the coronary vessels. For this reason the **short-acting preparation of nifedipine is less safe than slow-release formulations.**
- despite indirect action to increase cardiac output, nifedipine and felodipine are negatively inotropic. In overdose, the **direct** cardiac effects predominate to produce bradycardia and reduction in cardiac output. This is treated in the same way as for verapamil and diltiazem.

### *Diltiazem*

- less negatively inotropic than verapamil
- has peripheral vasodilator effect
- available as both short-acting and slow-release preparation

### 1.3 Angiotensin converting enzyme inhibitors (ACEI)

- block conversion of angiotensin I to its active derivative angiotensin II- a vasoconstrictor which also stimulates secretion of aldosterone by the adrenal cortex.
- ACEI reduce constrictor tone in the blood vessels and reduce secretion of aldosterone.
- many ACEI on the market but little evidence for the clinical superiority of one over the rest. .
- enalapril can be taken once daily and its effects last over 24 hours in most patients with hypertension.
- major adverse effects- angioedema, cough (6-10%), worsening of renal function in patients with bilateral renal artery stenosis.
- promote potassium retention : electrolytes and renal function should be monitored when introducing them.
- the elderly, those dehydrated from intensive diuretic treatment or taking other hypotensive medication are at particular risk of “first dose hypotension”. ACEI should be introduced at a very low dose and increased gradually in these patients.
- potentially dangerous** renal interaction with non-steroidal anti-inflammatory medicines(NSAIM) in patients with some degree of renal impairment- may precipitate renal failure

**ACEI should not be used in pregnancy, obstructive valvular heart diseases and bilateral renal artery stenosis.**

#### **Angiotensin receptor blockers**

- this class of drug not available on Tuvalu EML
- block the action of angiotensin at vascular receptors
- provide no additional benefit in blood pressure control but do not interfere with bradykinin metabolism
- possibly through this lack of action on bradykinin, do not produce cough
- are useful in the approx.6% of patients on ACEI who develop persistent cough
- candesartan, losartan are some of the medicine of this group

### 1.4 Directly-acting vasodilators

#### ***Hydrallazine***

- directly-acting vasodilator used to treat hypertension and heart failure.
- given intravenously in urgent cases – especially pregnancy.
- produces reflex tachycardia, flushing and headache which can be reduced beta-blocking drugs used in combination.
- principal place is in the urgent reduction of blood pressure- especially in pregnancy.

#### ***Nitrates***

The Tuvalu EML contains glyceryl trinitrate (sublingual tablet 600 micrograms) and isosorbide dinitrate (an orally available formulation that has a comparatively low and variable bioavailability) -both act as precursors for nitric oxide, the endothelium's intrinsic vasodilator that is not produced as effectively in diseased arteries.

- major drawback to nitrate treatment is the emergence of tolerance.

- nitrate-free periods help to reduce the development of tolerance.

- glyceryl trinitrate deteriorates in storage particularly in glass bottles and is likely to have very little effect after three months' storage in this way.

- nitrates must not be used concomitantly with sildenafil ("Viagra") as it potentiates their action to produce significant hypotension, which, rarely, has been fatal in patients with critically narrowed cerebral or coronary arteries.

## 1.5 Centrally-acting hypotensives

- alpha-methyldopa is the only medicine in this category available in Tuvalu

- effective orally and reduces peripheral resistance and blunts cardiac sympathetic response.

- major place is the management of pregnancy-related hypertension where its efficacy and safety have not been matched by other medicines-not recommended for the non-pregnant.

- adverse effects -mental depression, impotence, and rarely, autoimmune haemolytic anaemia and hepatotoxicity.

## 1.6 Diuretics

### *Frusemide*

- a potent "loop" diuretic of particular value in the treatment of heart failure.

- duration of action 3-4 hours and may be given orally or, for a quick response, intravenously.

### *Hydrochlorothiazide and bendrofluazide*

- Bendrofluazide is not available in Tuvalu

- less potent diuretics used in hypertension and as "add-on" treatment in heart failure.

- adverse effects of frusemide and thiazides -hypokalaemia, elevation of serum uric acid (sometimes presenting as gout), impairment of glucose tolerance, and rarely, ototoxicity.

- thiazides may increase serum calcium.

- parenteral diuretics may occasionally be needed in heart failure or high dose oral preparations such as frusemide 500 mg daily, or twice a day, in renal failure.

### *Spirolactone*

- competitive inhibitor of aldosterone at the distal renal tubule.

- promotes sodium loss and potassium retention.
- used with thiazide or loop diuretics, enhances sodium loss and helps prevent hypokalaemia.
- in low doses (25 mg daily) is of value when added to conventional treatment in congestive heart failure.
- causes hyperkalaemia in renal impairment.
- anti-androgen activity can cause painful gynaecomastia in men and irregular or postmenopausal vaginal bleeding in women.

## 1.7 Anticoagulants, antiplatelet drugs and thrombolytics

### ***Heparin (unfractionated, UFH) and enoxaparin (low molecular weight-LMW- heparin)***

- heparin acts by binding to antithrombin. This inactivates thrombin and activated factor X (Xa), diminishes their procoagulant effect and tips the balance of the clotting cascade towards anticoagulation.
  - action of UFH is dose-dependent and is measured by the activated partial thromboplastin time (APTT). The unmodified APTT is less than 50 seconds and the therapeutic range lies between 60 and 85 seconds.
  - effects are readily reversed in emergency by the intravenous use of protamine sulphate.
  - may be administered by the intravenous or subcutaneous routes.
- Low molecular weight –LMW-heparins selectively inhibit Factor Xa activity. Their effect is only partially reversed by protamine.
- a major but rare adverse effect is heparin-induced thrombocytopenia and thrombosis syndrome (HITTS). This is an autoimmune process that results in low platelet counts, paradoxical thrombosis from platelet deposition and a tendency to bleed.

### ***Warfarin***

- an oral anticoagulant that antagonises Vitamin K-mediated final steps in the synthesis of clotting factors II, VII, IX and X in the liver.
  - inhibits the synthesis of proteins C and S that normally maintain an anticoagulant effect. As protein C has a short half-life in the plasma and falls early after starting warfarin, this may lead to a hypercoagulable state in the first 24-48 hours.
  - therefore recommended to maintain heparin treatment for the first 48 hours after introducing warfarin until the inhibition of the procoagulant factors outweighs the effects on protein C.
- therapy is monitored by the international normalised ratio (INR).
  - bleeding is the major risk from overdosage.
  - major risk for ineffective dose is the failure to treat the thrombotic disease adequately.

Medicines that may enhance the anticoagulant effect of warfarin include:

- amiodarone
- chloramphenicol
- ciprofloxacin
- cotrimoxazole
- doxycycline
- erythromycin
- ketoconazole
- metronidazole
- miconazole
- simvastatin
- tetracycline

Aspirin, and non-steroidal anti-inflammatories may enhance the risk of bleeding when on warfarin..

Medicines that may reduce the effect of warfarin include:

- barbiturates
- carbamazepine
- nutritional supplements providing vitamin K
- phenytoin
- rifampicin

-vitamin K antagonises the action of the anticoagulant directly..

-bleeding from warfarin can be treated with Vitamin K (takes from 2-3 hours to reverse) or more rapidly with fresh frozen plasma or whole blood transfusion.

### ***Aspirin***

-technically not an anticoagulant but given for antiplatelet action.

-effect of a single 300 mg (one standard tablet) dose can still be detected in the patient's blood up to 10-14 days later.

-prophylactic aspirin should be discontinued for about two weeks prior to surgery (substituting heparin if necessary)..

### ***Streptokinase***

- acts by binding to plasminogen and this activates uncomplexed plasminogen to plasmin, the endogenous fibrinolytic substance. Fibrin is lysed and generates fibrin degradation products that appear in blood and urine.

-antibodies to streptokinase appear after its use but may also be caused by exposure to streptococcal antigens.

-can cause allergic, hypotensive and even anaphylactic reactions.

## 1.8 Lipid-lowering medicines

- can produce substantial survival benefit in patients after a myocardial infarction or diabetics with high cardiovascular risk--regardless of the lipid level.

Simvastatin is available in the Tuvalu EML taken once daily (restricted to NDTC recommendations)

-onset of action is over 4-6 weeks

- blood lipids should not be re-measured until six weeks have elapsed.

-main side effects are muscle pain accompanied by elevation of serum creatine kinase rarely progressing to rhabdomyolysis. These changes are reversible on discontinuing the drug.

## 1.9 Antiarrhythmics

### ***Atropine***

-an anticholinergic compound used to reverse symptomatic bradycardia.

-antagonises the action of acetylcholine at many different sites and it may produce dry mouth and impairment of accommodation leading to visual blurring.

### ***Digoxin***

-slows heart rate by depressing conduction through the bundle of His by slowing atrioventricular conduction and by enhancing vagal activity.

-strengthens cardiac contraction and is also a mild diuretic.

-has a slow distribution time after both oral and intravenous administration and takes 4-6 hours to express its action. It is therefore of little extra benefit to give the drug parenterally.

-hypokalaemia potentiates its effect and may predispose to toxicity.

-adverse effects include, sequentially, bradycardia, ventricular ectopic beats, bigeminy, ventricular tachycardia and, if no action is taken, ventricular fibrillation and death. The systemic features of toxicity are anorexia, nausea, vomiting and xanthopsia (yellow vision).

-has a half-life of 24-36 hours in patients with normal renal function.

-excreted almost entirely through the kidney and toxicity is more likely in renal failure and in the elderly.

### ***Lignocaine***

-a Class I antiarrhythmic that blocks inward sodium movement in excitable tissues and can also be used as a local anaesthetic.

-has a short half-life of around two hours and is metabolised in the liver to produce two pharmacologically active metabolites that may cause central nervous system toxicity if excessive doses of lignocaine are given.

- toxicity includes visual disturbances, paraesthesiae and convulsions.

-cleared through the liver and accumulates if hepatic blood flow is reduced as in congestive cardiac failure.

### *Amiodarone*

- second-line antiarrhythmic medicine used particularly for ventricular arrhythmias not responding to other treatments
- very long half-life
- high rate of adverse effects including hypo and hyperthyroidism, pulmonary fibrosis and neuropathy
- should be reserved as a secondary agent in serious disease.
- interacts with warfarin to increase its plasma concentration and effect.

## 1.10 Cardiovascular medicine interactions

Many interactions are possible in the management of cardiovascular diseases. Some of the more important ones are described below.

The action of digoxin is potentiated by diuretics through potassium depletion.

The negative inotropic action of verapamil is potentiated by beta-blocking drugs.

The negative chronotropic effect of verapamil is potentiated by beta-blocking drugs.

There is reduced metabolism of lignocaine with concomitant use of beta-blockers due to reduction in liver blood flow.

The effect of warfarin is decreased with concomitant use of barbiturates, carbamazepine, phenytoin and rifampicin. These all increase metabolism of warfarin.

The effect of warfarin is increased with the concomitant use of amiodarone, chloramphenicol, ciprofloxacin, cotrimoxazole, doxycycline, erythromycin, ketoconazole, metronidazole, simvastatin and tetracycline. These inhibit the metabolism of warfarin.

Plasma concentrations of digoxin are increased with concomitant use of verapamil.

The combination of ACEI and NSAIDs may precipitate renal failure in patients with even mild compromise of renal circulation

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## 2. Hypertension

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Hypertension is very common in the Tuvalu and is the single biggest risk factor for stroke and may also lead to left ventricular and congestive heart failure, chronic renal failure and retinopathy. The importance of hypertension is increased in the presence of other cardiovascular risk factors such as smoking, diabetes mellitus, raised total or low-density lipoprotein (LDL) cholesterol or a family history of premature cardiovascular disease. Therefore, treatment should be more vigorous in the presence of multiple risk factors.

Adequate treatment of hypertension substantially reduces the risk of stroke as well as of heart failure, renal failure and, to a lesser extent, myocardial infarction.

## 2.1 Definition

The World Health Organization (WHO) defines hypertension as blood pressure (BP) greater than 140/90 mm Hg. For many patients, especially diabetics with high blood pressure there is evidence of extra benefit if 130/85 can be achieved.

**Mild hypertension is defined as BP of 141-159/91-99 mm Hg; moderate hypertension, BP of 160-179/100-109 mm Hg; and severe as BP of 180/110 mm Hg.**

Not less than two readings should be made at least 30 minutes apart, and preferably on separate occasions, before deciding if a patient has sustained hypertension or not. The appropriate cuff size should be used depending on the arm circumference of the patient. There is usually no urgency to reduce mild or moderate hypertension, unless indicated. Severe hypertension with or without symptoms and any evidence of target organ damage should be treated promptly.

## 2.2 Types of hypertension

More than 90-95 percent of patients with hypertension are of the **primary** or essential type, often with a positive family history. Usually, these patients do not need comprehensive investigations but, whenever possible, urinalysis, blood urea, electrolytes and creatinine are desirable.

For **secondary** hypertension, careful history and examination will provide clues to underlying causes that are worth investigating further. Secondary hypertension is suspected in the following:

- patients less than 40 years old with significant hypertension and no family history of hypertension
- patients with severe hypertension
- patients whose blood pressure is difficult to control despite good drug compliance
- patients with signs and symptoms suggestive of secondary cause
- patients with accelerated hypertension (with retinal haemorrhages/exudates with or without papilloedema)

Chronic renal disease is the commonest underlying cause for secondary hypertension. The other causes include: renal artery stenosis, phaeochromocytoma, Cushing's disease, primary aldosteronism (Conn's syndrome), coarctation of the aorta, and pregnancy-induced hypertension. Occasionally, hypertension is caused by medications such as

corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or oral contraceptives or excessive ingestion of liquorice.

## 2.3 Management of hypertension

The decision to treat hypertension should be based on patient's **overall cardiovascular risk** rather than the level of blood pressure alone.

***Non-pharmacological***

This is the first line of management for mild to moderate hypertension unless the patient has the following:

- multiple cardiovascular risk factors
- diabetes
- renal impairment
- past history of cardiovascular event
- target organ damage

Non-pharmacological measures that have been shown to be effective in clinical trials include:

- weight reduction in obese subjects
- reduction in alcohol intake
- smoking cessation
- regular physical activity
- moderate reduction in dietary sodium intake

Please Note:

- Cholesterol machine should now be available to all outer islands
- Blood pressure should also be available and working

<b>Steps and their characteristics</b>	<b>Treatment</b>	<b>Target</b>
<b>Step 1:</b> Mild to moderate hypertension with no risk factors	Lifestyle modification (exercise, diet and loose weight)	Blood pressure at around 120mmHg and definitely below 140/90mmHg
<b>Step 2:</b> Failure of step 1 after 3-8 implementation plus one risk factor, or deterioration of hypertension	Lifestyle modification and <i>Start an antihypertensive such as either hydrochlorothiazide 25 -50mg 'o' daily OR enalapril 12.5mg bd OR atenolol 25mg 'o' daily</i>	Blood pressure control within 1 to 3 months. Aim at 120/80 and definitely below 140/90mmHg

<b>Step 3:</b> Failure of step two after 1-3 months	Lifestyle modification. <i>If a thiazide was initiated, increase the dose or ADD an ACEInhibitor or -blocker OR a calcium channel blocker.</i> Beware of diabetics when one should not use a -blocker and a thiazide together. Titrate doses to effect of blood pressure	Blood pressure control within 1-3 months to be around 120/80 and definitely below 140/90mmHg
<b>Step 4:</b> Failure of step 3	Refer to specifications below	

### *Pharmacological*

#### **Tablet 3: Step wise treatment of hypertension**

If non-pharmacological measures do not reduce blood pressure to normal (<140/90 mm Hg) after 6-8 weeks in mild to moderate hypertension, pharmacological treatment should be added.

Recent trials have shown that thiazides, beta-blockers, ACEI and calcium channel blockers can all be effective when used as first line drugs. Thiazides are as effective as other classes but are more cost-effective.

Ideally, target levels of blood pressure should be achieved using one medicine and once daily dosing to enhance patient compliance. This is often not possible in practice and combination treatment is commonly required.

If there are no specific contraindications (e.g. asthma for beta-blockers; gout for thiazides; diabetes is a relative, but not absolute, contraindication for thiazides), single agent treatment may be started with:

 **If there are no specific contraindications (eg. Asthma for beta-blockers; gout for thiazides; diabetes is relative, but not absolute contraindication for thiazides),**

<b>SINGLE AGENT TREATMENT may be started with:</b>			
<b>Drug</b>	<b>Dose</b>	<b>Duration</b>	<b>Daily</b>
<b>Bendrofluazide</b>	2.5mg Orally	OD (Twice	Once
<b>Or</b>			
<b>Atenolol</b>	25mg – 100mg Orally	As a single dose	SINGLE DOSE
<b>OR</b>			
<b>Metoprolol</b>	25mg – 50mg Orally	BD (Twice daily)	TWICE
<b>Nb. Doses of bendrofluazide greater than 5mg produce little extra hypotensive effects but increase the risk of high plasma uric acid or low serum potassium level.</b>			
<b>⚡ If a combination of medicines is required to achieve blood pressure control, give (each point is a separate regimen)</b>			
<b>First Point</b>			
<b>Atenolol</b>	25 – 100mg Orally	OD (daily)	DAILY
<b>Or</b>			
<b>Metoprolol</b>	25 – 50mg Orally	BD (Twice daily)	TWICE
<b>With</b>			
<b>Bendrofluazide</b>	2.5 – 5mg Orally	OD (daily)	DAILY
<b>Second Point</b>			
<b>Atenolol</b>	25 – 100mg Orally	As a single dose	Single dose
<b>Or</b>			
<b>Metoprolol</b>	25 – 50mg	BD (Twice daily)	TWICE
<b>With</b>			
<b>Nifedipine</b>	20-40mg Orally	BD (TWICE daily)	Twice
<b>Third Point</b>			
<b>Nifedipine</b>	20-40mg Orally	BD (Twice daily)	Twice
<b>With</b>			
<b>Enalapril</b>	2.5 – 40mg Orally	OD (Once daily)	Once
<b>Fourth Point</b>			
<b>Enalapril</b>	2.5 – 40mg Orally	OD (Once daily)	Once
<b>With</b>			
<b>Benzdrofluazide</b>	2.5 – 5mg Orally	OD (Once daily)	Once

Hydralazine should rarely be used on its own. It produces headache, reflex tachycardia (both prevented by beta-blockade) and fluid retention (prevented or treated by a thiazide diuretic).

The angiotensin converting enzyme inhibitors (ACEI) can be used as monotherapy or in combination. They should be considered as the medicines of first choice in the management of hypertension in the following conditions:

- complicated by heart failure
- requiring treatment after a myocardial infarction
- associated with left ventricular systolic dysfunction

- occurring in diabetic patients.

If an ACEI is indicated give :-

- *Enalapril 2.5-40 mg orally daily and monitor blood pressure over 4 hours. Some patients are very sensitive to ACEIs*

If the dose of enalapril is above 20 mg daily, it can be given in divided doses but the daily total should not exceed 40 mg.

**Methyldopa should not be used as first-line treatment in non-pregnant hypertensives** as it may produce mental depression, impotence in males and rarely autoimmune haemolytic anaemia. It is occasionally useful where response to other agents is inadequate or other antihypertensive drugs are not available.

## 2.4 Hypertensive emergency (urgent blood pressure reduction)

**This is seldom needed** but may be required in hypertensive encephalopathy, acute hypertensive heart failure, acute myocardial infarction, dissecting aneurysm and phaeochromocytoma. Patients with these conditions should be admitted to hospital and monitored. The aim is to reduce blood pressure within 60-90 minutes.

While the blood pressure may respond to oral agents (as above), initial parenteral treatment may be needed:

- *Hydrallazine 5 mg bolus intravenously (IV) over 5-10 minutes and repeated every 20 minutes up to a maximum of 20 mg followed by intravenous infusion of hydrallazine (see Appendix).*

OR

- *Labetalol (100 mg per 20 ml); initial dose of 20-40 mg given intravenously over 1-2 minutes and repeated at intervals of 5-10 minutes until 200 mg have been given. Alternatively, labetalol may be given as a continuous intravenous infusion at a rate of 2 mg per minute (see Appendix).*

After initial stabilisation, the patient should be changed to oral treatment for maintenance.

The practice of opening a nifedipine 10 mg capsule and giving it sublingually is **not supported** as emergency treatment. It delivers an uncertain dose and most of the effect occurs as a result of absorption of the swallowed drug. **On occasions, in older patients, unexpectedly rapid falls in blood pressure have resulted in stroke or myocardial infarction.**

## 2.5 Hypertension in children

### *Definition*

Hypertension in children is defined statistically as systolic/diastolic blood pressure levels greater than 95<sup>th</sup> percentile for age, gender and height. Below are normal blood pressure readings at various ages

**Table 4. Normal blood pressure in children**

Age (years)	Systolic blood pressure (95 percentile)	Diastolic blood pressure (95 percentile)
Neonate	95	70
0-5	115	75
6-10	120	80
11-15	135	85

### *Etiology*

Hypertension in the paediatric age group is uncommon. Renal parenchymal disease, renovascular disease and coarctation of the aorta account for 90 percent of all hypertension in children. Essential hypertension is **rare** before 10 years of age.

#### **2.13.2 Non-pharmacological management**

Non-pharmacological interventions are used initially for management of essential hypertension in children. These include:

- weight reduction
- low salt diet
- physical activity

### *Pharmacological management*

#### **a. Asymptomatic hypertension**

Refer for investigation for underlying causes of hypertension.

#### **b. Symptomatic hypertension**

Symptomatic hypertension requires immediate treatment.

In the Pacific region, post-streptococcal glomerulonephritis (haematuria and oedema and proteinuria) is one of the most common cause of hypertension requiring treatment in children. It appears to be rare in the Tuvalu.

Give:

- *Frusemide 1-2 mg per kg intravenously 8-12 hourly*

If blood pressure is not controlled, ADD

- *Nifedipine 0.25-0.5 mg per kg orally (up to a maximum of 10 mg) every 4-8 hours*

In severe cases, ADD

- *Enalapril 0.1 mg per kg orally daily increasing up to 0.5 mg per kg daily over two weeks*

In cases where urgent reduction of blood pressure is necessary:

If the patient is conscious and not vomiting:

*Nifedipine 5 mg (for patients <2 years) and 10 mg (for patients >2 years) crushed and swallowed with water or given by orogastric tube. Repeat dose every 20 minutes to achieve BP control.*

If level of consciousness is impaired or patient is vomiting:

- *Hydrallazine 0.1-0.2 mg per kg intravenously or intramuscularly (IM) stat then 4-6 micrograms per kg per minute by intravenous infusion*

OR

- *Labetalol 0.2 mg per kg intravenous push over 2 minutes. If no response in 5-10 minutes, increase to 0.4 mg per kg up to a maximum of 60 mg.”*

## 2.6 Isolated systolic hypertension in the elderly

Systolic blood pressure rises (systolic BP of >160 mm Hg and diastolic BP of <90 mm Hg) with age in most, but not in all patients. Recent trials show that reducing isolated systolic hypertension at all ages reduces risk of stroke and heart failure.

- Hydrochlorothiazide 12.5-25 mg orally daily OR bendrofluazide 2.5 mg orally daily

And, if necessary ADD

*Atenolol 25-100 mg orally daily OR metoprolol 25-50 mg orally twice daily*

AND/OR

*Nifedipine Retard 20-40 mg orally twice daily*

Always start with low doses and increase them slowly in the elderly patient. Target systolic pressure is 160 mm Hg or below which can be achieved gradually over several weeks.

## *2.7 Blood pressure monitoring*

Once patients have been stabilised on regular treatment they should normally be reviewed at 2-3 monthly intervals. Serum creatinine and electrolytes need to be measured within the first 6-8 weeks of stable treatment and thereafter annually .

## *2.8 Resistant hypertension*

Consider :

- non-compliance with treatment (almost certainly the commonest cause)
- failure to detect a primary cause especially renal artery stenosis or primary
- hyperaldosteronism
- ingestion of substances interacting with the antihypertensive treatment, e.g. NSAIDs, steroids, liquorice
- ingestion of a large sodium load or consumption of a large amount of alcohol

## *2.9 Hypertension in pregnancy*

Hypertension less than 20 weeks of pregnancy is due to either:

- chronic hypertension or
- chronic hypertension with superimposed pre-eclampsia

After 20 weeks of pregnancy, hypertension can be due to:

- pregnancy- induced hypertension (PIH) – hypertension without proteinuria
- mild pre-eclampsia
- severe pre-eclampsia
- eclampsia

### ***Mild pre-eclampsia***

Mild pre-eclampsia is defined as hypertension that occurs after 20 weeks of pregnancy and

characterized by the following:

- two readings of diastolic blood pressure of 90-110 mm Hg taken at least four hours apart
- PLUS
- proteinuria 2+ and
- no signs or symptoms of severe disease (see below)

It is recommended that patient be admitted if:

- BP 150/100 mm Hg on two occasions
- there are symptoms of severe disease (see below) and
- there is concern about foetal well being
- follow-up and accessibility of obstetric care is a concern

Mild pre-eclampsia does not usually require treatment. However, if the BP is >160/100 mm Hg,

- *Methyldopa 250-500 mg orally two-three times a day*

AND, if necessary, ADD

- *Hydrallazine 25 mg three orally times daily*

It is recommended that BP should be maintained at 130-140/80-90 mm Hg.

### ***Severe pre-eclampsia (see also the Obstetric and Gynaecology Guidelines)***

Severe pre-eclampsia is defined as hypertension that occurs after 20 weeks of pregnancy and characterized by the following:

- diastolic BP >110 mm Hg
- proteinuria 3+
- epigastric tenderness, headache, visual changes, hyperreflexia, pulmonary oedema,
- oliguria and/or convulsions

Severe pre-eclampsia needs urgent referral and transfer to the hospital.

In the hospital, the management of severe eclampsia includes the following:

If the diastolic BP >110 mm Hg

*Labetalol (100 mg per 20 ml); initial dose of 20-40 mg given intravenously over 1-2*

*minutes and repeated at intervals of 5-10 minutes until 200 mg have been given. Alternatively, labetalol may be given as a continuous intravenous infusion at a rate of 2 mg per minute (see Appendix). Note, Labetolol not available in Tuvalu EML.*

After initial stabilisation, the patient should be changed to oral treatment for maintenance.

OR

*Hydrallazine 5 intravenously as a bolus dose*

Start intravenous fluids, e.g. 500 ml plasma expander over one hour.

Maintain strict fluid balance chart.

Monitor BP, pulse and respiration regularly.

Insert indwelling catheter and maintain urine output at >30 ml/hr.

For maintenance of blood pressure:

- *Nifedipine 10-20 mg orally as required to a maximum of 60 mg daily to keep diastolic BP <110 mm Hg*

OR

- *Hydrallazine by slow intravenous infusion, 50 mg in 100 ml of dextrose saline in a chamber titrated in order to keep diastolic BP <110 mm Hg*

**It is not necessary to reduce BP to normal levels, rather it is more important to maintain BP at “safe” level of diastolic BP of <110 mm Hg. The definitive treatment for pre-eclamptic toxemia (PET) is delivery of the baby. This should be undertaken as soon as it is practicable, preferably in a referral hospital.**

**Prevention of recurrent seizures in eclampsia / prevention of seizures in pre-eclampsia.**

If convulsion occurs or is imminent, administer magnesium sulphate as described below.

If infusion pump is available:

*Magnesium sulphate 4 grams as loading dose (diluted in 100 ml of dextrose 5% to be infused slowly over 20 minutes). This is to be followed by maintenance dose of magnesium sulfate (12.5 grams in 100 ml of dextrose 5%) to be infused at 1 gram per hour (see Appendix).*

Magnesium sulphate	50%, 2 ml (1 g) ampoule; 10 ml (5 g) ampoule	<p>Loading dose: Magnesium sulfate 50%, 4 g (8.0 ml) diluted in 100 ml of dextrose 5%.</p> <p>Maintenance dose: Magnesium sulfate 50% (25 ml) in 100 ml dextrose 40%.</p>	<p>Loading dose: Use infusion pump and run at 300 ml/hr and set total volume at 108 ml.</p> <p>Maintenance dose: Infuse at 1 g/hr. Set infusion pump to run at 10 ml/hr and set total volume at 125 ml.</p>
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Monitor the patient by checking deep tendon reflexes and respiratory rate. Both are depressed if the magnesium serum levels become too high. If respiration rate falls to 12/min or below **immediately** reduce the rate of infusion if the intravenous route is being used. If an antidote is needed use calcium gluconate by IV infusion

If infusion pump is not available:

give: *magnesium sulphate 4 Gm. IV over 5-15 minutes followed by*

**EITHER** *IV infusion 1 Gm/hour for at least 24 hours after the last seizure*

**OR**

*magnesium sulphate deep IM injection 5 Gm into each buttock, then 5 Gm. every 4 hours into alternate buttocks for at least 24 hours after the last seizure*

Use no greater than 20% concentration of magnesium sulphate for IV injection

Use 50% magnesium sulphate for IM injection .Mix each 5 Gm. magnesium sulphate solution with 1 mL of 2% lignocaine for IM injections.

Monitor patient as above

After delivery of the baby (24-48 hours) when the patient's condition is stable, blood pressure can be maintained with either:

- *Methyldopa 250-500 mg orally two-three times daily*

OR

- *Nifedipine 20-40 mg orally twice daily*

OR

- *Hydrallazine 25-50 mg orally three times daily.*

## **Ischaemic heart disease**

Major risk factors for coronary atherosclerosis are: positive family history (premature mortality due to coronary artery disease in first degree relatives), smoking, sedentary lifestyle, obesity, diabetes, hypertension and hyperlipidaemia. The high prevalence of diabetes in the Tuvalu is likely to lead to further increase in coronary artery disease in the future.

Others aggravating factors include anaemia, arrhythmias, thyrotoxicosis and valvular heart disease.

Treating the presenting syndrome and ignoring the associated risk factors is a poor and inadequate approach to the patient with coronary artery disease.

### *3.1 Prevention of cardiovascular disease*

Major non-modifiable risk factors are age, gender and family history.

These with the modifiable risk factors (i.e. smoking, diabetes mellitus, dyslipidaemia and hypertension) account for most cases of cardiovascular disease.

**Risk factors should be assessed in any appraisal of a patient with coronary artery (or any other arterial) disease.**

#### *Primary prevention*

Strategies that are beneficial include:

- smoking cessation
- treatment of hyperlipidaemia
- treatment of hypertension
- good control of diabetes mellitus
- Physical activities

A balanced and appropriate diet exerts a protective effect. Patients should be helped to achieve ideal body weight (body mass index between 20 and 25 kg/m<sup>2</sup>) and should reduce dietary saturated fat and added salt. There is evidence that at least two serves of fish a week provide benefit.

Physical activity may not be an independent protective factor but may have an impact on obesity, cardiorespiratory fitness and elevated blood pressure.

The major risks associated with lipids are elevated LDL cholesterol and reduced HDL cholesterol. There can be little doubt about the need to treat elevated LDL cholesterol in patients with familial hypercholesterolaemia and a poor family prognosis. However, debate currently centers on the appropriate cut off point for starting lipid lowering treatment in the population at large.

Guidelines and studies on which to base them are lacking for most developing countries.

## *Secondary prevention*

It is not too late to improve the natural history of cardiovascular disease even after it is clinically apparent as angina, claudication, transient ischaemic attacks or occlusive events.

**Modification of modifiable risk factors together with the near routine use of aspirin, beta-blockers, statins and, in most cases ACEIs, is supported by good quality clinical trials showing improved survival after myocardial infarct.**

### *3.2 Principles of management*

The principles of management of ischaemic heart disease are:

- patient education
- modification of risk factors
- identification and management of precipitating factors
- drug therapy
- consideration for coronary revascularization

### *3.3 Management of coronary pain syndromes*

Pain attributable to coronary artery obstruction occurs in each of the three coronary pain syndromes-**stable angina, unstable angina and myocardial infarction. However, there are patients who are asymptomatic but have evidence of myocardial ischaemia.**

#### *3.3.1 Stable angina*

Angina pectoris is pain, usually felt in the central chest, which may radiate to the neck, both arms and occasionally, the back that occurs during exercise or emotional stress and is rapidly relieved by rest. Angina is stable if, for at least one month, it has been brought on by the same amount of exertion and is not accompanied by pain at rest – unless caused by emotional stress.

#### **a. Pharmacotherapy i.**

#### **Acute attack**

- *Glyceryl trinitrate 300-600 micrograms sublingually*

Repeat every 5 minutes if pain persists up to a maximum of three tablets. If pain persists, check that tablets are active (a tingling sensation if put on the tongue). If no response and tablets are of good quality, treat as for unstable angina. Patients should sit or lie down when first using glyceryl trinitrate because of the possibility of symptomatic hypotension. Glyceryl trinitrate should not be exposed to light.

## **ii. Subsequent treatment**

Patients should be on aspirin and will usually require further treatment to improve exercise tolerance. Initially, use

- *Aspirin 100-150 mg orally daily*

AND

- *Atenolol orally 50-100 mg daily*

OR

- *Metoprolol 25-50 mg. orally twice daily*

The other medicine that can be considered in uncontrolled angina include:

- *Isosorbide dinitrate 10-40 mg orally three times daily*

(To prevent the development of nitrate tolerance, there should be an interval of eight hours between the night dose and the first dose the next day.)

OR

- *Verapamil 40-120 mg orally 2-3 times daily*

OR

- *Nifedipine 20-40 mg orally twice daily<sup>5</sup>*

**The combination of a beta-blocker and verapamil is contraindicated. iii.**

## **Use of glyceryl trinitrate as prophylaxis**

Nitrates may be used prophylactically for any form of physical or emotional stress.

- *Glyceryl trinitrate 300-600 micrograms sublingually*

#### **iv. Refractory stable angina**

Occasionally, patients will not respond to preventive treatment even if a combination of beta-blocker, calcium channel blocker (nifedipine) and nitrates is prescribed.

If pain persists despite addressing the modifiable risk factors and optimum drug therapy, it is recommended that if possible, the patient be referred for further cardiac assessment .

### ***Unstable angina***

Characterised by anginal pain which is severe, of recent onset, or which has recently become abruptly worse. Angina occurring at rest or following recent myocardial infarction is also classified as unstable angina.

All patients diagnosed to be suffering from unstable angina should be referred for admission

The most important distinction to make is between unstable angina and an acute myocardial infarction. The factors favouring an acute myocardial infarction include pain of more than 15-20 minutes duration; pain not responsive to nitrates or requiring narcotics; systemic features such as pallor, sweating, vomiting and hypotension. If any or all of these are present, admit to hospital or health. An electrocardiogram (ECG) is critically important in making the diagnosis.

The aim of treatment in unstable angina is to relieve the pain and to modify the environment around the “active” plaque to reduce the likelihood of coronary artery occlusion. However, it should be borne in mind that chest pain might be secondary to other serious conditions like acute myocardial infarction, pericarditis, aortic dissection and pulmonary embolism.

For initial treatment:

- Oxygen therapy
- *Aspirin 150-300 mg orally stat*

AND

- *Morphine 2.5-10 mg intravenously as needed*

AND

- *Atenolol 50-100 mg orally daily*

OR

- *Metoprolol 25-50 mg orally twice daily*

If pain persists and if the patient's hemodynamic status allows, ADD:

- *Nifedipine 20-40 mg orally twice daily*

AND, if required, ADD

- *Isosorbide dinitrate 10-40 mg orally three times daily*

If pain still persists, heparin should be given , in addition, as follows:

- *Heparin 5,000 units by bolus dose intravenously followed by 1,000 units per hour by intravenous infusion*

*OR*

calculated as 400units/kg over a 24 hour period divided into 24 equal doses, following the initial bolus dose of 5,000 units

Subsequent doses should be adjusted to keep the APTT (activated partial thromboplastin time) between 60 and 85 seconds. The APTT should be measured 6- hourly until stable, then daily.

Heparin will normally be required for at least three days and possibly longer depending on clinical response.

If symptoms persist despite all of the above treatment, cardiological intervention, if available, is required with a view to further investigation and revascularisation.

### ***Myocardial infarction***

Complete occlusion of a coronary artery leads to the death of the cardiac muscle it supplies. Occlusion of a large, proximal vessel may cause myocardial ischaemia of such an extent that the patient dies rapidly of pump failure. Alternatively, a ventricular arrhythmia (tachycardia, fibrillation) may reduce cardiac output to such a drastic extent that, if the abnormal rhythm cannot be reversed, death is most likely.

Severity of pain by itself is a poor indicator of the extent of myocardial damage especially in a diabetic patient. Poor cerebral function, peripheral circulatory signs such as pallor, sweating and hypotension combined with extensive ECG changes with or without arrhythmias point to a large infarct.

The aims of immediate management are to:

- relieve pain
- achieve coronary reperfusion and minimise infarct size

- prevent and treat complications
- allay the patient's anxiety

All patients with suspected myocardial infarction should be admitted to hospital and preferably to a unit where cardiac monitoring can be performed.

**a. Immediate management**

Unless the patient is very anxious, routine use of a sedative (e.g. diazepam) is not recommended.

**i. Pain relief**

*Morphine 2.5-10 mg intravenously with repeat doses as necessary*  
AND

*Glyceryl trinitrate 600 micrograms sublingually with a repeat dose in 5 minutes if no response*

Glyceryl trinitrate should not be given if patient hypotensive.

**ii. Limiting infarct size**

*Aspirin 300 mg chewed or dissolved before swallowing*

*Oxygen 4-6 L per minute by mask*

*Thrombolytic therapy – streptokinase if available.*

*Use only under the supervision of a specialist physician.*

The indications for thrombolytic therapy includes chest pain that has developed within the previous 12 hours with either ST-segment elevation myocardial infarction (STEMI) or development of new left bundle branch block (LBBB) or both.

**Streptokinase**

- 1.5 million International Units (IU) by intravenous infusion over 30-60 minutes. If blood pressure falls as a result of the infusion, reduce the rate or stop briefly and restart at half the previous rate.

Streptokinase induces antibody formation that makes it unsuitable for use in subsequent episodes of coronary occlusion. It may also produce allergic symptoms (i.e. bronchospasm, angio-oedema, urticaria, flushing and musculo- skeletal pain).

The contraindications to thrombolytic therapy are shown in Table 1.

Patients most likely to benefit from thrombolytic treatment are those presenting within

6 hours..with large anterior infarcts especially if complicated by heart failure. Those presenting after 24 hours have less chance of benefit and increased risk of cardiac rupture.

For mild or moderate allergic reactions to streptokinase:

- *Promethazine 25 mg intravenously*

OR

- *Hydrocortisone 100 mg intravenously*

**Table 5. Contraindications to thrombolytic therapy**

<b>Absolute contraindications</b>	<b>Relative contraindication</b>
Active internal bleeding	Previous peptic ulcer disease
Recent surgery, biopsy or trauma	Warfarin therapy
Prior cardiopulmonary resuscitation	Liver disease
Known bleeding disease (haemophilia, platelet disorders)	Previous streptokinase therapy within the last four years.
Recent or disabling stroke	Previous hypersensitivity to streptokinase
Neurosurgery within 6 months	Heavy perivaginal bleeding
A previous intracranial bleed	Diabetic proliferative retinopathy
Severe uncontrolled hypertension (a blood pressure greater than 180/110 mmHg during presentation)	Pregnancy
Aortic dissection	
Coma	
Oesophageal varices	

Severe allergic reactions should be treated as for anaphylaxis.

- *Adrenaline 1 in 1,000 solution, 0.5- 1 ml ( 0.5-1 mg) intravenously over 5 minutes*

If response is poor, increase dose to:

- *Adrenaline 1 in 1,000 solution 2 to 5 ml ( 2-5 mg) intravenously over 5 minutes*

AND ADD

- *Promethazine 25 mg intravenously*

OR

- *Hydrocortisone 100 mg intravenously*

**b. Management in the post-infarct period i.**

**Beta-blockers**

- *Atenolol 25-100 mg orally daily*

OR

- *Metoprolol 25-50 mg orally twice daily*

The benefit persists long-term and beta-blockade should be continued indefinitely.

**ii. Angiotensin converting enzyme inhibitors (ACEI)**

- *Enalapril 5-40 mg orally daily*

Outcome is improved after myocardial infarction with these agents. ACEIs should be started 24-48 hours after the acute episode in patients with a previous myocardial infarct, diabetes mellitus, hypertension, anterior infarct or evidence of persisting left ventricular dysfunction. Persistent hypotension and/or renal dysfunction are the only major contraindications.

**iii. Antiplatelet agent**

*Aspirin 150-300 mg orally daily*

**iv. “Statin” (hydroxymethylglutaryl CoA reductase inhibitor)**

Recent large-scale trials have demonstrated a substantial role for statins in the secondary prevention of coronary thrombosis and myocardial infarction, **independent of lipid level.**

A combination of lifestyle modification, and ongoing treatment with aspirin, beta blockade, a statin, and, in many cases, ACEIs has been justified by clinical trials of adequate size and duration.

The administration and supervision of this potentially complex regimen is best organised through a cardiac rehabilitation program for the first few months after the myocardial infarction. Extensive patient education is required during this period

**c. On discharge**

At the time of discharge, a cardiac rehabilitation program is recommended. The program should include the following:

- continuing medication, as above
- patient education
- modification of risk factors
- avoidance of precipitating factors
- dietary management
- resumption of work, driving and sexual activity
- advice on air travel
- further investigations, e.g. stress test, echocardiography, and coronary angiography with a view to possible intervention if indicated

### 3. Heart failure

Heart failure occurs when the heart is unable to pump adequate blood to meet the metabolic demands of the tissues. It is a syndrome and not a disease in itself.

Heart failure is the result of a **primary underlying cause** and this should always be looked for and, if possible, treated in the course of investigation and management. More often, the heart failure is in a compensated state and symptoms develop due to one or many precipitating factors. Identification and management of these precipitating factors are very important. Hence, in the treatment of heart failure it is vital to address both the **underlying etiology** and **the precipitating factors**.

#### 4.1 Causes of heart failure

The common causes of heart failure are:

- ischaemic heart disease (see relevant section)
- valvular heart disease remains a common and important cause of heart failure in Tuvalu
- hypertension is a treatable cause that is also common
- hyperthyroidism – cardiac manifestation might be the only presentation of this condition
- cardiomyopathy that can occur from several different causes

The less common causes of heart failure are:

- congenital heart disease
- infective endocarditis
- myocarditis
- cor pulmonale

- pericardial diseases

#### 4.2 *Precipitating factors of heart failure*

. These include:

- poor compliance with medication
- excess dietary salt
- fluid excess
- other medicines – NSAIDs, steroids, antidepressants, verapamil
- arrhythmias – tachyarrhythmias or bradyarrhythmias (most commonly atrial fibrillation)
- intercurrent infections particularly respiratory infections
- acute myocardial infarction
- infective endocarditis
- anaemia
- hyperthyroidism
- uncontrolled hypertension
- physical overexertion
- pregnancy

#### 4.3 *General management of chronic heart failure*

The principles of management are:

- non-pharmacological treatment
- pharmacological treatment
- treatment of underlying etiology
- treatment of precipitating factors
- other general measures

##### ***Non-pharmacological***

- weight reduction
- salt restriction – ideally, no added salt is advised
- water restriction – this is not necessary unless there is dilutional hyponatraemia; in this situation, reduction to no lower than 1.5 liter per day is recommended

##### ***Pharmacological***

The aims of treatment are to improve the prognosis and to relieve and control the symptoms and signs of heart failure. The commonly used medicines in the treatment of heart failure include:

- diuretics – frusemide, spironolactone, thiazides
- angiotensin converting enzyme inhibitors – unless contraindicated, virtually all

patients with heart failure should be on ACEI

- digoxin
- beta-blockers – carvedilol, very low dose metoprolol and bisoprolol have been proven in clinical trials to be effective in heart failure (these drugs or dose-forms are not current in the Tuvalu EML)
- isosorbide dinitrate
- hydrallazine

**a. Mild to moderate heart failure**

Treatment is commenced with diuretics and ACEI added to potentiate the response.

- *Frusemide 40-80 mg orally daily*
- *Enalapril 2.5 mg daily followed by gradual increments to a maximum of 20 mg daily*

Hypotension can result after the first dose in the elderly, patients who are already dehydrated from previous diuretic therapy, in the presence of pre-existing hyponatraemia, and concurrent treatment with other anti-hypertensives.

If heart failure is not controlled by these, ADD

*Digoxin 0.0625-0.5 mg orally daily according to age and renal function.*

Digoxin is recommended if the patient is in atrial fibrillation and the ventricular rate is not controlled.

If ACEI cannot be used in patients with heart failure because of angioedema, worsening renal function or intractable cough, alternative treatments to reduce cardiac “after-load” include:

*Hydrallazine 25-50 mg orally two-three times daily*

PLUS

*Isosorbide dinitrate 10-20 mg three times a day*

**b. Severe heart failure**

If despite the above treatment the heart failure worsens or fails to respond, hospitalization is recommended. Treatment in the hospital includes:

- *Frusemide up to a maximum of 1 gram daily in divided doses*

Absorption of oral diuretics is often impaired in severe heart failure and frusemide starting with 80 mg IV BD is advised. Patients having significant renal impairment will require higher doses of frusemide.

PLUS

- *Enalapril orally as above*

PLUS

- *Spironolactone 25-50 mg orally daily*

PLUS

- *Digoxin 0.0625-0.5 mg orally daily according to age and renal function*

If these treatments are inadequate, the following can occasionally be required:

- *Hydrochlorothiazide 25-50 mg orally daily*

OR

- *Hydrallazine 25-50 mg orally three times daily*

PLUS

- *Isosorbide dinitrate 10-20 mg orally three times daily*

Furosemide and hydrochlorothiazide act at different sites in the nephron and will supplement each other's action if used together.

### ***4.3.3 Treatment of underlying etiology and precipitating factors***

In all cases, the underlying etiology and precipitating factors must be treated.

### ***4.3.4 General measures***

The general measures in the treatment of chronic heart failure may include:

- bed rest
- oxygen therapy
- regular weight monitoring
- patient education
- therapeutic aspiration of fluids from serous cavities
- heparin 5,000 units subcutaneously BD till patient is mobilized as prophylaxis for
- deep vein thrombosis (DVT)

#### 4.4 *The role of beta-blockers in heart failure*

Beta-blockers are used to counteract the effect of the activated sympathetic nervous system in heart failure.

Studies have shown that beta-blockers are useful in all stages of heart failure from various causes except in decompensated heart failure. The beneficial effects include improvement in survival, reduction in all cause mortality and hospitalization rate, and improvement of ejection fraction and functional class.

It is recommended that beta-blockers should be started in small doses and increments made to maximum tolerable dose.

The drugs and dose forms that have shown efficacy in clinical trials are not currently in use in Tuvalu. If and when they are introduced their use should be restricted to **specialist physicians** and the medicines should only be started under hospital in-patient conditions.

#### 4.5 *Acute cardiogenic pulmonary oedema*

Immediate treatment should include:

- bed rest
- maintain airway
- administer oxygen 4-6 L per minute by mask
- furosemide 40-80 mg IV repeated in 30 minutes if needed
- morphine 5-10 mg IV
- salbutamol nebulizer 2.5-5 mg 4-hourly, if there is evidence of bronchospasm (e.g. wheezing)
- sublingual glyceryl trinitrate if patient is not hypotensive
- other treatments that may be required when there is significant hypotension:
  - dopamine infusion if patient is hypotensive (refer to Appendix)
- ventilatory support if required

The underlying etiology and precipitating factors must be treated and the general measures discussed above have to be followed.

#### 4.6 **Diastolic Heart Failure**

Patients with classical signs and symptoms of heart failure but normal cardiac (left ventricular) ejection fraction on investigation may have:

- fluid overload (or renal failure producing the same picture)

- a mechanical cause for the heart failure such as severe mitral regurgitation
- principally diastolic heart failure resulting in poor diastolic filling and correspondingly poor forward perfusion

The main causes of this relatively uncommon form of heart failure include:

- pericardial disease
- myocardial hypertrophy with fibrosis (e.g. long-standing hypertension)
- atrial fibrillation and any other causes of poor diastolic filling
- infiltrative diseases (e.g. amyloidosis, sarcoidosis, haemochromatosis)

The importance of diastolic heart failure and its recognition lie in the fact that patients with this condition are **very sensitive** to the effects of diuretics and vasodilators both of which can precipitate severe reductions in cardiac output and in blood pressure.

In a case of suspected diastolic heart failure referral to a specialist physician is required.

## 5 Cardiac arrhythmias

Cardiac arrhythmias range from trivial ectopic beats to the life-threatening ventricular fibrillation. Whether or not an arrhythmia requires intervention depends largely on its capacity to make a **significant impact on cardiac output**.

In a patient whose myocardial function is already impaired (e.g. by a large infarct) a change from normal sinus rhythm to atrial fibrillation with a ventricular rate of 140 beats per minute may be sufficient to cause heart failure. By contrast, a young person with a normal myocardium may sustain a supraventricular tachycardia at the same rate for days without any evidence of cardiac decompensation.

### 5.1 Causes of cardiac arrhythmias

The common and/or important causes of arrhythmias are:

- ischaemic heart disease
- valvular heart disease
- cardiomyopathy
- hypoxia
- electrolyte disturbance- hypokalaemia, hyperkalaemia, hypocalcaemia, hypomagnesaemia
- endocrine – hyperthyroidism, phaeochromocytoma
- medicines– digoxin, tricyclic antidepressants
- congenital conduction abnormalities

## 5.2 Aims of treatment

In general, there are four aims in the treatment of cardiac arrhythmias:

- return the heart to normal sinus rhythm, if possible
- control the heart rate
- treat any associated risks (e.g. anticoagulant therapy in atrial fibrillation)
- treat the underlying cause

**Most arrhythmias are benign and injudicious use of antiarrhythmic drugs can be harmful as many of them are proarrhythmic on their own.**

## 5.3 Tachyarrhythmias

### 5.3.1 Atrial

#### a. Sinus tachycardia

This implies a persistent heart rate over 100 per minute in a resting patient.

It usually has an underlying cause such as anxiety, thyroid overactivity or systemic illness. The first approach should be to identify and treat the underlying cause.

**If no obvious underlying cause is apparent, treatment is generally not needed.**

#### b. Atrial premature complexes

Treatment is seldom required. If patient is symptomatic,

- *Atenolol 25-100 mg orally daily*

OR

- *Metoprolol 25-50mg orally twice daily*

#### c. Paroxysmal supraventricular tachycardia (PSVT)

This occurs intermittently and sometimes can be converted to sinus rhythm by carotid sinus massage (may be hazardous in elderly patients), by the Valsalva manoeuvre or by holding ice cold water in the mouth or immersing the face briefly in cold water. If these are ineffective,

Give, with ECG monitoring,

- *Adenosine 3mg (in 1 mL)IV. over 5-10 seconds.*

*This may produce transient hypotension and a feeling of chest constriction. Patients*

*should be warned this may happen*

*If no response, after 2 minutes,*

- *give Adenosine 6 mg IV over 5-10 seconds.*

*This can be increased by one further increment to 12 mg iv if needed after a further 2 minutes.*

**OR**

provided the QRS complex is not broad (wider than 0.12 seconds)\* and blood pressure monitoring is in place

- *Verapamil 5 mg intravenously slowly; repeat if needed up to 15 mg*

If not available,

*Digoxin 0.25-0.50 mg orally stat,  
repeat same dose orally six hours later,  
followed by 0.25 mg orally six hours after the second dose, and  
followed by 0.25 mg orally six hours after the third dose and  
continue at 0.25 orally mg daily.*

The maintenance digoxin dose should be adjusted depending on the patient's renal function and serum potassium level.

**\*Verapamil must NEVER be given to a patient with a wide-complex undiagnosed tachycardia – QRS > 0.12 seconds. If there is any possibility that the rhythm is a ventricular tachycardia treat as such.**

**d. Prophylaxis for paroxysmal supraventricular tachycardia (PSVT)**

A few patients may require prophylaxis if attacks are frequent.

- *Atenolol 25-100 mg orally daily*

**OR**

- *Metoprolol 25-50 mg orally twice daily*

**e. Atrial flutter and fibrillation (AF)**

Atrial flutter usually presents with a 2:1 atrioventricular block and a completely regular rate of around 150 beats per minute. Atrial fibrillation presents with a similar rate which is

however quite irregular.

**i. Control ventricular rate**

This is only required if the ventricular rate is >100 per minute. The urgency to control the rate depends on the pre-existing ventricular rate and the state of the cardiac function –e.g. adequate or in heart failure. For many patients especially the elderly rate control is best achieved and maintained with digoxin

*Digoxin 0.5-1.0 mg orally, followed by 0.25-0.5 mg every 4-6 hours up to a maximum of 1.5-2.0 mg in the first 24 hours.*

Maintenance treatment thereafter will require digoxin 0.0625-0.5 mg daily depending on age, renal function and plasma digoxin level, if available. The intravenous route is rarely necessary because oral digitalization is just as effective.

**OR**

Control rate with beta-blockade

- *Atenolol 25-100 mg orally daily*

**OR**

- *Metoprolol 25-50 mg orally twice daily*

If beta-blockers are contraindicated,

*Verapamil 40-80 mg orally three times daily*

**ii. Treatment of underlying cause**

Whenever possible, the underlying cause should be identified and treated (e.g. hypokalaemia, thyrotoxicosis).

**iii. Anticoagulant therapy**

Unless contraindicated and impractical (i.e. poor patient compliance, difficulty in monitoring), anticoagulant therapy should be considered in **every** patient with chronic AF to prevent thromboembolic events. If warfarin cannot be used for one reason or another, aspirin can be used as alternative but is not as effective as warfarin. The risk of thromboembolism increases in patients with previous thromboembolism,

mitral valve disease, heart failure, hypertension and in older patients – especially women over the age of 75 years.

#### **iv. Cardioversion**

This should only be attempted where facilities are adequate and **experienced** staff are available.

It is appropriate to try to restore sinus rhythm if the patient has only been in atrial fibrillation for a few hours. Anticoagulation with intravenous unfractionated heparin (5000units iv. followed by hourly 1000units/hour) or enoxaparin (1mg/kg subcut.twice daily: reduce dose if creatinine is raised or calculated creatinine clearance<30mL/min) should be initiated before cardioversion even if the arrhythmia has existed for as short a time as a few hours, as thrombus may already have started to form in the fibrillating atrium. Restoration of sinus rhythm may save the patient from long-term anticoagulation- although heparin should be continued for 2-4 days after successful conversion as “stunned” atria may develop after the conversion and clot may begin to develop.

It is never appropriate to attempt cardioversion in a patient with AF of long, or unknown, duration without prior full anticoagulation. The risk to the patient of thrombo-embolism is greater than that of continuing AF with a well-controlled ventricular rate

After successful cardioversion, rhythm may be maintained with amiodarone 200-400mg orally three times each day for one week, 200-400mg twice daily for a further week and then a maintenance dose of 100-200mg daily as continuing treatment.

### *5.3.2 Ventricular arrhythmias*

#### **a. Premature ventricular ectopics including bigeminy**

These are benign unless patients have underlying heart disease. If no obvious cause is found, the following measures are advisable:

- reduce coffee and tea intake
- stop smoking
- reduce alcohol intake

Drug treatment is not normally required but in symptomatic cases beta-blockade may be of value.

- *Atenolol 25-100 mg orally daily*

*OR*

- *Metoprolol 25-50mg orally twice daily*

**b. Ventricular tachycardia (VT)**

**i. Non-sustained ventricular tachycardia**

In hospitals where ECG monitoring is possible, treat only prolonged episodes that cause cardiovascular haemodynamic instability.

*Lignocaine 2% , 50-100 mg intravenously over 1-2 minutes followed by 4 mg per minute intravenous infusion for a maximum of one hour then 1-2 mg per minute by intravenous infusion for 24 hours (see Appendix).*

**ii. Sustained ventricular tachycardia**

**(a) With haemodynamic stability**

Treatment is the same as for non-sustained ventricular tachycardia.

**(b) With haemodynamic instability (“pulseless VT”)**

The treatment for this condition is immediate intervention by defibrillation. Maintenance of sinus rhythm after electrocardioversion requires drug therapy:

- *Lignocaine 50-100 mg intravenously over 1-2 minutes followed by 4 mg per minute intravenous infusion for a maximum of one hour then 1-2 mg per minute by intravenous infusion for 24 hours (see Appendix).*

If long-term oral drug treatment is required to maintain sinus rhythm:

- *Atenolol 25-100 mg orally daily*
- OR
- *Metoprolol 25-50 mg orally twice daily*

In difficult cases, sotalol can be considered but it is not currently available in Tuvalu. Oral amiodarone may be an alternative but the drug is also not available in Tuvalu.

**c. Torsades de pointes**

This is a rare, polymorphic ventricular tachycardia in which the QRS axis is constantly shifting (turning, “torsade”). Patients usually have a prolonged QTc (greater than 0.45 seconds) on the ECG. The rhythm is particularly prone to occur as a result of drug therapy including treatment with tricyclic antidepressants, phenothiazines, erythromycin and ketoconazole. Any medicine suspected of causing the arrhythmia should be stopped immediately.

Patients should be managed in hospital with ECG monitoring. No consensus exists about the most effective treatment. If the arrhythmia is associated with cardiovascular collapse, treat as for “pulseless VT”-see above  
If patient is stable, give –

- *Lignocaine 75-100 mg intravenously over 1-2 minutes followed by 4 mg per minute for a maximum of one hour. Maintenance infusion thereafter of 1-2 mg per minute by intravenous infusion (see Appendix).*

Alternatively,

- *Magnesium sulphate 50%, 2 g intravenously over 10-15 minutes followed, if necessary, by 0.5-0.75 g per hour by intravenous infusion for 12-24 hours*

**Do not use amiodarone in this arrhythmia**

d. **Ventricular fibrillation** (see under cardiac arrest, below)

e. **Ventricular asystole**  
Institute CPR.

- *Adrenaline 1mg (1 ml of a 1:1,000 solution) intravenously and repeat at 5 minute intervals until the return of spontaneous circulation is achieved*
- *Atropine 3 mg intravenously with a saline flush of 20 ml*

f. **“Pulseless” ventricular activity**

Treatment is as for ventricular asystole with the addition of the need to exclude potentially reversible causes such as:

- hypoxia
- hypovolaemia
- hypothermia or hyperthermia
- hypokalaemia or hyperkalaemia and metabolic disorders
- cardiac tamponade

- tension pneumothorax
- toxins, poisons, medicines
- thrombosis – pulmonary or coronary

### 5.3.3 Cardiac arrest

This is due to ventricular tachycardia, fibrillation, asystole or “pulseless” ventricular activity.

**On the assumption that no immediate ECG diagnosis can be made of the underlying rhythm, immediately:**

- Institute and continue cardio-pulmonary resuscitation (CPR).
- Defibrillate at 200 joules and, if no response, twice more at 360 joules (for children: 4 joules per kg).
- Secure airway and ventilate at maximum oxygen percentage achievable.
- Obtain an ECG tracing while maintaining CPR.
- Give adrenaline 1 mg (1 ml of a 1:1,000) as an intravenous bolus followed by 20ml saline flush.
- Repeat defibrillation at 360 joules three times in succession.
- Repeat intravenous adrenaline. If venous access cannot be obtained in order to administer adrenaline, give adrenaline 5mg (5 ml of a 1:1,000 solution) diluted to 10 ml of normal saline through the endotracheal tube.
- Repeat defibrillation at 360 joules on three successive occasions.

If no response has been achieved at this point, the chances of recovery are slight. Acidosis will certainly have occurred and may be treated with:

- *Sodium bicarbonate 8.4% (1 mmol per ml) 1 mmol per kg intravenously over 5-15 minutes*

Sodium bicarbonate is also indicated in cases where arrhythmia is secondary to hyperkalaemia.

Control of rhythm may be attempted with:

- *Lignocaine 1%, 75-100 mg intravenously over 1-2 minutes followed by 4 mg per minute for the next hour and decreasing to a maintenance dose of 1-2 mg per minute thereafter (see Appendix).*

However, the mainstay of management remains effective CPR followed by urgent defibrillation. The primary drug in emergency treatment is adrenaline.

## 5.4 Bradyarrhythmias

### **5.4.1 Sinus bradycardia**

Treat only if symptomatic. Exclude hypothyroidism, pituitary failure and medicines (e.g. beta-blockers, digoxin, and verapamil).

If intervention is required:

- *Atropine 0.6-1.8 mg intravenously and repeat as needed*

### **5.4.2 Atrioventricular block**

Medicines (digoxin, beta-blockers or verapamil) may be the cause and should be withheld if this appears to be the case.

#### **a. First degree AV block**

There is prolonged PR interval on ECG. This requires no treatment.

#### **b. Second degree AV block**

There are two types.

##### **i. Wenckebach phenomenon (Mobitz type I)**

In this type of AV block, there is successive prolongation of the PR interval followed by a dropped beat and the whole cycle repeats.

##### **ii. Mobitz type II**

There is a fixed ratio between the atrial and ventricular contractions in this type of arrhythmia, e.g. 2:1 or 3:1.

Generally, both types of AV block do not require treatment. Rarely, pacing may be required in Mobitz type II AV block.

#### **c. Third degree heart block**

This may be an acute and potentially spontaneously reversible complication of, for example, an acute **anterior or inferior** myocardial infarction. In centres where cardiac pacing is possible, this is the treatment of choice.

If pacing is not available give

- *Isoprenaline 20 micrograms intravenously, repeat according to clinical response and*

*follow with an infusion of 1-4 micrograms per minute or occasionally higher in patients who have been on beta-blockers (see Appendix).*

There is anecdotal evidence for the efficacy of salbutamol and theophylline in maintaining response if the block has responded to isoprenaline.

**The treatment of choice for chronic heart block is permanent cardiac pacing.**

## *6 Peripheral vascular disease (PVD)*

Atherosclerotic disease of the limb vessels is part of the overall spectrum of atheromatous disease. Risk factor modification is as much a strategy in managing PVD as in the prevention of coronary artery disease and stroke.

### *6.1 Acute limb ischaemia*

The signs and symptoms of this condition are:

- pain
- paresthaesiae
- paralysis
- pulseless
- pallor

#### *6.1.1 Causes*

The common causes of acute limb ischaemia are:

- embolization from the heart
- thromboembolism from a large atheromatous vessels or an aneurysm
- *in situ* thrombosis of a diseased vessel
- use and abuse of ergot derivatives for migraine

**This is an emergency. Urgent investigation and surgical consultation are required.**

The limb should be protected using a bed cage and heel pad but should not be elevated.

#### *6.1.2 Medicines*

- *Morphine 2.5-5 mg intravenously as required to control pain*

AND

- *Heparin sodium 5,000 units intravenously as a loading dose followed by 1,000 units per hour by intravenous infusion, and thereafter adjusted according to the APTT.*

If viability of the limb is restored:

- *Warfarin for 3-6 months aiming at an INR of 2.0 to 3.0*

There should be efforts to determine and treat the cause of the thromboembolic event. Depending on the cause, (e.g. atrial fibrillation), warfarin might need to be taken for an indefinite period.

Following a local thrombus rather than an embolic event:

- *Aspirin 150-300 mg orally, daily, which may be preferable to warfarin.*

All cases must be assessed by the surgical team as there may be a place for embolectomy.

## **6.2 Chronic limb ischaemia**

The gradual loss of circulation caused by atheroma and local thrombosis may present with resting ischaemic pain often worsening, over a few weeks (and needing increasing amounts of analgesic), to ulceration and gangrene of the feet and toes.

The aims of management are:

- pain relief
- improvement and preservation of circulation
- treatment of sepsis
- modification of risk factors

### **6.2.1 Pain relief**

Pain is often very severe and may require:

- *Morphine 2.5-10 mg intravenously repeated 4-hourly or more often until pain is controlled.*

### **6.2.2 Improvement and preservation of the circulation**

- Surgical intervention will normally be required. Early consultation should be requested.
- Elevate the head of the bed.
- Reduce antihypertensive medication, if possible, to permit a high normal blood pressure

- Withdraw any beta-blocking medicines, including eye drops.
- Sympathectomy may provide some symptomatic relief but will not improve ultimate outcome.
- Anticoagulation.

### 6.2.3 Treatment of sepsis

Patients should be assessed at a hospital. Outer islands should refer all cases to on call doctor. Organisms are commonly of several sorts but anaerobes will be present. It is recommended that culture of specimens from the ischaemic limb be taken prior to empirical antibiotic treatment:

- *Metronidazole 400 mg orally 8-hourly*

*PLUS*

- *Cloxacillin 500 mg orally 6-hourly*

In patients hypersensitive to penicillin, erythromycin or chloramphenicol can be used. The antibiotic may need to be modified once the culture results are available.

If the patient is not receiving heparin intravenously as treatment, this drug should be used prophylactically:

- *Heparin sodium 5,000-7,500 units subcutaneously every 12 hours*

### 6.2.4 Modification of risk factors

All modifiable risk factors listed under the section on Ischaemic Heart Disease should be addressed

**Smoking is a major preventable risk.**

## 6.3 Intermittent claudication

Intermittent claudication refers to pain felt in the legs on exertion that is relieved by rest (as differentiated from spinal claudication where the pain persist even with rest). Most patients do not suffer loss of a limb as a result of this disease. Life expectation is dictated primarily by co-existing atheroma elsewhere - especially in the coronary circulation.

The single most important management strategy is **modification of risk factors**. The other modalities of treatment are:

- A graded exercise program, e.g. walking 50-60 minutes per day can extend

claudication distance

- *Aspirin 150-300 mg orally daily*

## 6.4 Raynaud's phenomenon

Episodic blanching of the fingers, especially on exposure to the cold, is commonly benign but may be a symptom of an underlying connective tissue disease. Again, there should be efforts in identifying and treating the underlying cause.

The first line drug therapy is:

- Nifedipine SR 20-40mg orally twice daily

If not successful in relieving symptoms and frequency of the attacks:

- Glyceryl trinitrate 2% ointment 0.5cm applied at the base of the affected fingers. (GTN 2% ointment is not available in our EML).

## 7 Cerebrovascular disease

Cerebrovascular disease is common. However our ability to treat stroke and reverse neurological damage once it has occurred is strictly limited. This makes it all the more important to institute **primary prevention** in the hope of reducing stroke incidence in the community.

### 7.1 *Risk factors*

The risk of stroke doubles with each succeeding decade above 20 years (although the absolute risk of stroke at 20 is very low). The major modifiable risk factors are:

#### 7.1.1 *Hypertension*

Stroke risk increases linearly with initial height of blood pressure. Effective treatment of all forms of hypertension **reduces** stroke risk. Isolated systolic hypertension, common in the elderly and once thought to be benign, also constitutes a stroke risk.

#### 7.1.2 *Smoking*

Smoking is clearly identified as a major risk factor for cerebrovascular disease, as it is for peripheral vascular and coronary artery disease.

### 7.1.3 *Diabetes mellitus*

While tight control of blood sugar has been shown to delay the progression of retinopathy and nephropathy, this evidence is not so strong for the occurrence of cerebrovascular disease.

### 7.1.4 *Dyslipidaemias*

Association exists between high low-density lipoprotein (LDL) cholesterol and stroke. While evidence exists for the protective effect of lowering lipids for coronary artery disease, similar evidence is not available for cerebrovascular disease. It seems reasonable to modify dyslipidaemia as part of risk factor management.

### 7.1.5 *Pre-existing cardiovascular disease*

Asymptomatic carotid artery stenosis increases stroke risk.

Atrial fibrillation with or without valvular disease of the heart disease or valve prosthesis is a major risk factor. Treatment with aspirin or warfarin reduces stroke substantially.

### 7.1.6 *Medicines*

Excessive alcohol consumption is a modifiable risk factor for stroke.

Oral contraceptives (irrespective of oestrogen dose) in women over 35 years of age who also smoke are a documented risk for cerebrovascular disease even though the absolute risk of stroke in this age group is low.

**If patient has multiple risk factors:**

*Aspirin 150-300 mg orally daily*

## 7.2 Transient ischaemic attack (TIA)

A TIA is an episode of neurological impairment of sudden onset with a duration of less than 24 hours unassociated with symptoms of migraine. Common primary causes are emboli from a cardiac source or from major atheromatous extracranial vessels – especially the carotid arteries.

The risk of stroke after a TIA is 5-7 percent per year and as high as 10-18 percent per year for patients with greater than 70 percent carotid stenosis on the relevant side.

The medical management in the **absence** of a source for embolism involves anti-platelet

therapy:

- *Aspirin 150-300 mg orally daily*

If the TIA is due to a demonstrable cardiac cause and no evidence of cerebral hemorrhage by CT scan, warfarin may be commenced immediately. .

## 7.3 Completed stroke

### 7.3.1 *Diagnosis*

. Clinical diagnosis unsupported by brain imaging has been shown to be less reliable than was earlier thought. This is important if causes with specific therapy are to be detected and treated early.

The two most important categories that have therapeutic importance are **thromboembolic disease** and **haemorrhage**.

### 7.3.2 *Management of ischaemic stroke*

The aims of management are:

- to reverse ischaemia
- to protect brain cells from the effects of ischaemia
- to rehabilitate the patient
- to introduce vigorous secondary prevention

#### **a. Reversing ischaemia**

The use of streptokinase has shown little or no benefit and the risk of bleeding is high. Other forms of thrombolytic therapy are not an option in Tuvalu yet but are being trialled overseas.

#### **b. Protecting cells from ischaemic injury**

Brain cells die not only from ischaemia itself but also from the local release of excitotoxic molecules in response to the ischaemia. Therefore, adequate hydration and oxygenation is important. In ischaemic stroke, it is advisable not to be aggressive to lower the blood pressure (i.e. maintain diastolic BP at 100-110 mm Hg) rapidly during the first ten days. However, in hemorrhagic stroke, BP of less than 140/90 is advisable.

#### **c. Rehabilitation**

Rehabilitation should be commenced as soon as urgent diagnostic and therapeutic measures have been taken. Therefore, referral to a physiotherapist and eventually, if

possible, to a rehabilitation unit is recommended.

#### **d. Secondary prevention**

There is clear evidence that modifying risk factors after a completed stroke confers benefit.

### 7.4 Management of haemorrhagic stroke

The underlying cause of hemorrhagic stroke should be identified and treated accordingly (i.e. control blood pressure in hypertensive intracerebral bleed). Without imaging it is not possible to make a certain diagnosis.

### 7.5 Stroke related to subarachnoid haemorrhage

Many patients with subarachnoid haemorrhage have a primary cause potentially amenable to intervention – in particular aneurysm. Vasospasm in this condition may produce reversible neurological deficits which can persist and even lead to death. Vasospasm manifests as an altered conscious state or increased neurological defect.

## 8 Non-hypertensive cardiovascular disease in pregnancy

The ideal time to evaluate a woman with cardiovascular disease is before she becomes pregnant. This allows time to make or confirm the diagnosis and make a management plan.

Enormous changes occur in the cardiovascular system in normal pregnancy. Vasodilatation occurs very early. Cardiac output increases by up to 40 percent at 20 weeks, yet the impact of vasodilatation is so great that blood pressure continues to fall to its minimum at mid-term and only slowly returns to normal as term approaches. Blood volume increases slowly in response to vasodilation and reaches its maximum in the final trimester after 30 weeks.

All these changes are normally reversed within 5-7 days of delivery.

These changes put demands on a normal cardiovascular system and can lead to heart failure if, for example, severe valvular disease is present.

### 8.1 *Valvular heart disease*

Mitral stenosis is the most important valvular lesion to be encountered in pregnancy. It may present with pulmonary oedema or sudden onset of atrial fibrillation.

The same treatment principles apply as in the non-pregnant patient (see section on heart

failure).

Although diuretics are not recommended in the treatment of pregnancy-related hypertension, in pulmonary oedema or congestive heart failure they should be used and are safe. Digoxin may also be given if indicated.

**Angiotensin converting enzyme inhibitors should not be used in pregnancy.**

Vasodilatation (“cardiac unloading”), if required, is best achieved with:

- *Hydrallazine 25-50 orally three times daily*

PLUS

- *Isosorbide dinitrate 10-40 mg three times daily if additional therapy is required*

Mitral valvuloplasty may be performed in pregnancy, if the clinical state warrants this. Mitral

valve prolapse is a common valvular abnormality in pregnancy. As blood volume expands, the murmur and click may disappear. This lesion does not normally produce any haemodynamic problems.

## 8.2 *Antibiotic prophylaxis at delivery*

Normal vaginal delivery and elective caesarean section do not require prophylactic antibiotics in a patient with a normal heart or with mitral valve prolapse. However, delivery in the presence of a prolonged labour or pre-existing infection does require antibiotic prophylaxis.

Antibiotic prophylaxis is **routinely** indicated for patients with **established valvular disease**.

Delivery should occur at a hospital maternity unit.

A suggested regimen for a patient arriving in labour is:

- *Gentamicin 2 mg per kg intravenously*

PLUS

- *Ampicillin 1 gram intravenously followed by ampicillin 500 mg intravenously 6 hours later*

The same regimen can be used in patients:

- not admitted in labour; given just before vaginal delivery or caesarian section
- with spontaneous membrane rupture; give antibiotics on admission to the unit
- at rupture of the membranes to induce labour; the first dose being given just before

the procedure occurs.

### 8.3 Cardiac arrhythmias in pregnancy

The same principles apply as in the non-pregnant patient (see Chapter 4). The following list is a guide to antiarrhythmic drug safety in pregnancy. For most of the drugs, experience is too limited for a firm recommendation to be made.

**Table 6. Recommendations for antiarrhythmic therapy in pregnancy**

<b>Drug</b>	<b>Recommendation</b>
Atenolol	Associated with foetal growth retardation
Atropine	Safe
Digoxin	Safe
Lignocaine	Safe
Propranolol	Safe; may induce foetal bradycardia
Verapamil	Insufficient data; avoid if possible

While beta-blocking drugs are commonly listed as medicines to avoid in pregnancy, clinical trials with oxprenolol in pregnancy-related hypertension have revealed no excess of foetal abnormalities despite prolonged exposure *in utero*. The only cardiovascular medicine incriminated in retarding foetal growth is atenolol.

## Infections of the cardiovascular system and their prevention

### *Bacterial endocarditis*

Treatment should be –given intravenously  
-prolonged  
-used in high concentrations throughout

If bacterial endocarditis is suspected take three blood cultures at three separate times before starting antibiotics.

### **Empirical therapy where the organism is unknown /culture negative endocarditis**

Penicillin G 1.8 Gm. IV 4-hourly PLUS

Cloxacillin 2Gm.IV 4-hourly PLUS  
Gentamicin 80 mg IV 8-hourly –adjust maintenance dose according to renal function

### **Streptococcal endocarditis**

Penicillin 1.8 Gm. IV 4-hourly for 4 weeks PLUS  
Gentamicin 80 mg.IV 8-hourly for 2 weeks –adjust dose/dose frequency according to renal function

**Enterococcal endocarditis** a less sensitive organism than *S.viridans* and the penicillin/gentamicin regimen above may need to be continued for 6 weeks .

**Staphylococcal endocarditis-** if a cloxacillin –sensitive organism :-

Cloxacillin 2Gm. IV 4-hourly for 6 weeks

In other circumstances consult with infectious disease/microbiology specialist.

### ***Prevention of bacterial endocarditis.***

**Low-risk** –with structural heart disease but no prosthetic valve/previous endocarditis

**Local anaesthetic** –amoxicillin 3 Gm. orally one hour before surgery, 1.5 Gm 6 hours after procedure

**General anaesthetic**—ampicillin 2 Gm.IV at induction followed by 500 mg orally 6 hours after the procedure

**High risk-** prosthetic valve(s) or previous endocarditis, any type of procedure

-ampicillin 2 Gm. at induction followed by ampicillin 500 mg IV or amoxicillin 500 mg orally 6 hours after the procedure. WITH

gentamicin 1.5 mg/kg IV at induction of (general) anaesthesia or commencement of the procedure

### ***Prevention of recurrences of rheumatic fever***

Rheumatic fever (and later valvular heart disease) are not uncommon in Tuvalu. Prophylaxis against further attacks is vital .

**If the rheumatic fever did not involve the heart**

Benzathine penicillin 1.2 megaunits every 4 weeks for 5 years or up to 18 years of age.

OR

Penicillin V 250 mg orally 12 hourly for the same duration (more difficult for patient compliance)

**If the heart was involved** the above prophylactic regimen is recommended until at least 40 years of age.

Some sources recommend prophylaxis for life but there is no clear evidence base for this recommendation. It errs on the side of caution.

<b>Medicine to be infused</b>	<b>Formulation</b>	<b>Preparation</b>	<b>Infusion rate</b>
Hydrallazine	20 mg/ampoule	Reconstitute 20 mg ampoule by adding 2 ml of sterile water (concentration: 10 mg of hydrallazine/ml). Add hydrallazine solution above to 98 ml of normal saline in a metered chamber (concentration: 1 mg of hydrallazine/ml).	Infuse initially at 0.2-0.3 mg/min (12-18 ml/hr).  Maintenance dose: 0.05-0.15 mg/min (3-9 ml/hr).
Magnesium sulphate	50%, 2 ml (1 g) ampoule; 10 ml (5 g) ampoule	Loading dose: Magnesium sulfate 50%, 4 g (8.0 ml) diluted in 100 ml of dextrose 5%.  Maintenance dose: Magnesium sulfate 50% (25 ml) in 100 ml dextrose 40%.	Loading dose: Use infusion pump and run at 300 ml/hr and set total volume at 108 ml.  Maintenance dose: Infuse at 1 g/hr. Set infusion pump to run at 10 ml/hr and set total volume at 125 ml.
Labetalol	100 mg/20 ml (5 mg/ml)	Add 100 mg (20 ml) of labetalol in 80 ml of dextrose 5% in a metered chamber (concentration: 1 mg of labetalol /ml).	Recommended dose: 0.5–2.0 mg/min  Infusion rate: 30 ml/hr (0.5 mg/min) initially then titrate until diastolic blood pressure of 110 mm Hg is achieved to a maximum dose of 120 ml/hour (2 mg/min).

Dopamine	1 vial = 200 mg/5 ml	Add 200 mg of dopamine in 95 ml of normal saline or dextrose 5% in a metered chamber. After reconstitution, the concentration of dopamine in the chamber will be 200 g/ml [1 ml = 60 microdrops ( gtts) or 33 g/ gtts].	<p>To achieve enhanced renal perfusion: 2-5 g/kg/min (120-300 g/min)</p> <p>For antihypotensive effect: 5-50 g/kg/minute (300-3,000 g/min)</p> <p>For example, the infusion rate in a 60 kg patient will be:</p> <ul style="list-style-type: none"> <li>- Renal perfusion dose: 4-10 gtts/min (4-20 ml/hr)</li> <li>- Antihypotensive effect: 10-100 ml/hr</li> </ul>		
<b>Medicine to be infused</b>	<b>Formulation</b>	<b>Preparation</b>	<b>Infusion rate</b>		
Streptokinase	1 vial = 1.5 million units	Add 2 ml of normal saline to the vial containing 1.5 megaunits streptokinase. Mix the streptokinase solution to 98 ml of normal saline in a metered chamber.	100 ml/hr		
Lignocaine 2%	2% solution (20 mg/ml) vial	Discard 200 ml from 1 liter of dextrose 5% and add 2 grams (200 ml or 20 vials) of lignocaine 2% (concentration: 4 mg of lignocaine/ml).	Time	Rate (ml/hour)	Dose (mg/hour)
			1 <sup>st</sup> hour	60	4
			2 <sup>nd</sup> hour	45	3
			After the 2 <sup>nd</sup> hour for 24 hours	30	2
Lignocaine 1%	1% solution (10 mg/ml) vial	Discard 400 ml from 1 liter of dextrose 5% and add 4 grams (400 ml or 40 vials) of lignocaine 1% (concentration 4 mg of lignocaine/ml).	Time	Rate (ml/hour)	Dose (mg/hour)
			1 <sup>st</sup> hour	60	4
			2 <sup>nd</sup> hour	45	3
			After the 2 <sup>nd</sup> hour for 24 hours	30	2

Isoprenaline	2 mg/ampoule (1 mg/ml)	Add 2 mg (1 ampoule) of isoprenaline to 99 ml of normal saline or dextrose 5% in a metered chamber (concentration: 0.02 mg of isoprenaline/ml or 20 µg of isoprenaline/ml).	Initially at 3 ml/hr (1 µg/min) then titrate accordingly based on response of heart rate, blood pressure, urine output, central venous pressure and peripheral circulation up to a maximum of 60 ml/hr (20 µg/min).
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