

Dr. Luyman



Guidelines

For

Management of Hyperlipidemia

**Ministry Of Health
Brunei Darussalam**

FOREWORD



It gives me great pleasure to see the remarkable development and progress of our medical and health services in Brunei Darussalam. The Ministry of Health, in its endeavor to achieve excellence in medical care encouraged evidence-based guidelines for management of common conditions suitable for our country's needs.

Cardiovascular disease is a leading cause of mortality and morbidity in Brunei Darussalam. Our recent National Nutritional Status Survey in 1997 showed a significant concern on the prevalence of cardiovascular risk factors. Hyperlipidemia is one of the important and modifiable risk factor.

The consensus guidelines are designed to be user friendly and I hope this will provide standardized management of Hyperlipidemia both in government and private sector throughout the country. Achieving the targets for management of hyperlipidemia will go a long way in improving the health of the nation.

I would like to take this opportunity to thank and congratulate the committee members for this worthwhile task in compiling the Consensus Guidelines on the Management of Hyperlipidemia in Brunei Darussalam and I hope similar efforts will continue to update it in the future with new evidence emerging. Last but not least, I wish you all the best in your future undertakings.

A handwritten signature in blue ink, appearing to be 'Laila Jasa'.

Dato Seri Laila Jasa Haji Ahmad Bin Dato Paduka Matnor
Permanent Secretary, Ministry of Health
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INTRODUCTION

Cardiovascular diseases are important causes of morbidity and mortality in Brunei Darussalam¹. Coronary heart disease (CHD) forms the bulk of these. The disease is multifactorial. The most important risk factors are smoking, hypertension, diabetes and hyperlipidemia. All of these are prevalent in Brunei Darussalam and they are all modifiable.

Although lipids were first implicated in the development of atheromatous lesions some 150 years ago, it was only in the 1950s that Framingham Heart Study² and Multiple Risk Factor Interventional Trial (MRFIT)³ firmly established the positive correlation between elevated serum cholesterol and coronary artery disease. Recent landmark trials (WOSCOP⁴,45⁵) have confirmed the beneficial impact of lipid lowering in primary and secondary prevention of coronary heart disease.

Dietary modifications, cessation of smoking, exercise and weight reduction form the cornerstone of any coronary prevention strategy. Where appropriate, pharmacotherapy with lipid lowering drugs should be instituted.

Treatment of hyperlipidemia should be risk stratified. It is most cost effective in those with highest risks i.e. those with CHD, cerebrovascular or peripheral arterial disease. Those with multiple risks will also benefit.

CLASSIFICATION OF HYPERLIPIDAEMIA

Primary Hyperlipidemia: Familial

Secondary Hyperlipidemia:

- Diabetes Mellitus (Increased TG, Decreased HDL)
- Hypothyroidism (Increased Cholesterol)
- Chronic Renal Failure (Increased TG)
- Nephrotic Syndrome (Increased Cholesterol, TG +/-)
- Cholestasis (Increased Cholesterol)
- Pregnancy (Increased TG)
- Drugs: diuretics, contraceptives, steroids (Increased TG/Chol, Decreased HDL)

Classification based on Therapeutic Considerations

RAISED LEVELS OF		
	LIPOPROTEIN	SERUM LIPIDS
HYPERCHOLESTEROLAEMIA	LDL	Cholesterol
MIXED HYPERLIPIDAEMIA	LDL + VLDL	Cholesterol + Triglycerides
HYPERTRIGLYCERIDAEMIA	VLDL	Triglycerides

LIPID MEASUREMENT

Reminder: Levels are affected if measured during acute stress or illness. In acute myocardial infarction cholesterol level may be spuriously low between 24 hours post infarction to 3 months. Certain drugs like thiazide diuretics, steroids, beta-blockers etc also affect lipid levels.

Fasting of 12-14 hours is generally recommended for measurement of lipids. Lipid levels show biological variability. Because of this and laboratory variability *more than one measurement are usually required before initiating an action*, especially in borderline cases. Such cases should be repeated after 6-8 weeks.

Selection of patients: It is important to stratify patients for lipid estimation.

- Patients with known atherosclerotic diseases like CHD, CVA, and peripheral vascular disease.
- Patients with high risk for developing CHD like diabetes mellitus, hypertension, hyperlipidemia & family history of CHD.
- Patients with risk factors (refer to Table)

MAJOR POSITIVE RISK FACTORS
<ul style="list-style-type: none">• Diabetes Mellitus• Hypertension• Cigarette Smoking• HDL Cholesterol < 0.9 mmol• Family History of myocardial infarction or sudden cardiac death prior to 55 years of age in male parent or sibling and prior to 65 years of age in female counterparts.• Age > 45 in Males, > 55 in Females or premature menopause not on HRT
NEGATIVE RISK FACTOR
<ul style="list-style-type: none">• HDL Cholesterol > 1.6 mmol/L
OTHER FACTORS TO CONSIDER
Obesity, Sedentary Life Style, Elevated Fibrinogen Level, Elevated Lipoprotein (a), Homocysteinaemia should be considered in selected group of patients. Many of them operate through the other risk factors mentioned above.

Which Lipid Tests to Order: In the group without known CHD or other vascular atherosclerotic disease i.e. *primary prevention*, initial estimation of *serum cholesterol only will suffice*. If the level is **high** for that category of risk then Full Lipid Profile i.e. HDL, LDL, TG can be ordered.

Patients targeted for *secondary prevention* i.e. with underlying CHD, CVA, and PAD *full lipid profile* will be indicated.

TARGET LEVELS

	TARGET LEVELS	
	Total Cholesterol (mmol/L)	LDL Cholesterol (mmol/L)
PRIMARY PREVENTION Low Risk (Less than 2 Risk Factors)	< 6.5	< 4.1
PRIMARY PREVENTION Moderate Risk (More than 2 Risk Factors)	< 5.2	< 3.4
SECONDARY PREVENTION High Risk (CHD, CVA, PAD)	< 5	< 2.6

Guideline according to NCEP¹¹

TG target levels are not well established. Suggested value < 2.3 mmol/L

	LIPID LEVELS	LIPID MEASUREMENT INTERVALS
Low Risk Less than 2 Risk Factors	Normal	5 Years
	Raised	6 monthly till normal Review 1 year
Moderate Risk More than 2 Risk Factors	Normal	3 years
	Raised	3 monthly till normal Review 6 months – 1 year depending on level of risk
High Risk CHD, CVA, PAD +/- Other Risk	Normal	1 year
	Raised	3 monthly till normal Review 6 months – 1 year depending on overall risk and lipid level

Guideline according to NCEP¹¹

WHEN TO INTERVENE?

The purpose of intervention in patients with hyperlipidemia is to prevent the development of atherosclerotic diseases especially Coronary Heart Disease.

- **Primary Prevention:** This means preventing the development of disease. Therefore people who are at high risk of developing the disease are targeted. The landmark WOSCOP Study⁴ has demonstrated the benefits of lipid lowering in this group of patients. Mass screening for hyperlipidemia is not advocated as it is not cost effective and there may be inadequate follow-up and counseling.
- **Secondary Prevention:** This means that progression and complications are checked by controlling hyperlipidaemia in patient who have already developed CHD or other atherosclerotic disease like cerebrovascular or peripheral vascular disease. There are several recent trial that indicate that aggressive lipid lowering strategy will:
 - Decrease total and coronary artery disease mortality and morbidity (4S⁵, LIPID Study⁶, CARE trial⁷ etc)
 - Reduce the incidence of thrombotic strokes (CARE trial⁷, LIPID Study⁶)
 - Stabilize the plaque, improve endothelial function and reduce inflammation (RECIPE Trial^{8, 9, 10})
 - There is evidence that early intervention for secondary prevention is beneficial.

HOW TO ACHIEVE TARGET LEVELS?

Non-Pharmacological Measures (NPM) is the mainstay of treatment of hyperlipidemia. NPM should be the sheath anchor of management in the primary prevention group. For secondary prevention NPM should be advocated either alone or along with drug therapy if indicated. Note that *drug therapy is not a substitute to NPM even in secondary prevention*. Secondary causes of hyperlipidemia should also be controlled.

- **Dietary Modification:** This can reduce cholesterol by 12-15%. It involves reducing saturated fats, cholesterol and calories. In addition it is advisable to read the label on oils or processed products with "low cholesterol" or "no cholesterol". This does not mean that these products are suitable for large consumption as they may contain high levels of saturated fats (e.g. palm oil) and they may still be high in caloric content. Patients must be referred to dietitian for detailed counseling (refer to appendix for guideline for lipid lowering diet).
- **Weight Reduction:** Obesity is associated with higher levels of TG and lower levels of HDL-C. A weight reduction of 0.5-1.0KG per week is recommended. The recommended BMI is <25 & waist to hip ratio (WHR) is 0.9 for males and 0.8 for females.
- **Exercise:** Exercise enhances the effect of dietary management, increases HDL-C & decrease plasma TG. It should be regular and adequate (30-45 min/session, 3-5 times per week. e.g. brisk walking, jogging, cycling, swimming).
- **Cigarette smoking:** It is a major risk factor for CHD. Smoking, both active and passive reduces HDL-c levels. It must be stopped and proper counseling should be arranged.

Assessing Response to NPM: Measure lipid profile 3-6 months after initiating NPM. The Lipid levels should reduce by 25%. If there is no reduction in lipids, check for patient compliance. For individuals at low risk failure to achieve the target value do not mean that dietary therapy be replaced by drug therapy. Whatever reduction is achieved will help lower the risk of CHD especially with the concomitant adoption of a healthy lifestyle.

LIPID LOWERING DIET

PRINCIPLE	AMOUNT	PRACTICAL SUGGESTIONS
Decreased total fat/oil	<30% of total caloric intake	Reduce intake of foods which are high in fat such as fried foods, fast foods, local cakes ("kuih"), fritters, 'tunking' pies, ice-cream, chocolate, canned meats, crisps, pre-fried frozen foods. Suitable cooking methods-grill / steam / microwave / bake or stir fry with minimal oil.
Types Saturated fat	7-10% of total calorie intake.	Limit intake of – butter, hard margarine, ghee, palm oil, full cream milk, condensed milk, cream, high fat cheese, beef bacon & all sausages, mayonnaise, coconut oil/milk, foods made with coconut milk such as "bingka", "kelupis", products containing hydrogenated oil and non-dairy creamers.
Monounsaturated & polyunsaturated oils/ margarine	Not more than 6tsp/day in cooking or as spreads.	Use oil and margarine made from olive, peanut, canola, sunflower, safflower, soybean or corn. Make sure to use these cooking oils only once when frying.
Protein Food Choose those that are low in saturated fat	2-3 servings/day	Choose fish, chicken without skin/fat, beans and pulses e.g. dhal, green peas & beans, "tempeh", bean curd, egg white, lean meat skimmed milk & products. Some low fat milk contain up to 50% of its original fat
Increase Intake Complex carbohydrate & fibre	20-25gms fibre/day Include 2-3 servings of fruit/day & 3-4 servings of vegetables/day	Sources of complex carbohydrates include rice, bread, pasta, noodles and tubers. Choose foods high in fibre such as fruits, vegetables, lentils and beans, unpolished rice, whole meal bread/biscuits and wholegrain cereals e.g. oats.
Reduced Dietary cholesterol	< 300 mg/day	Not more than 3 whole eggs per week. Organ meat e.g. liver, brain, kidney limit to 2-3 oz once a month. Small amount of prawns (including dried prawns) /cuttlefish/shellfish/crabs/oyster may be taken once or twice a week. "Pusu" can be eaten provided the head and entrails are removed. Avoid prawn paste ("belachan"), fish, crab or prawn roes. Foods high in cholesterol should not be concentrated on any one-day but to be distributed throughout the week.

DRUG THERAPY (Only If Target Not Achieved)

Reminder Non-pharmacological measures form the mainstay in the treatment of hyperlipidemia. One must always ensure compliance of Nonpharmacological Measures before starting drug therapy. If there is any underlying secondary cause for hyperlipidemia, it should be corrected first. In those with established CHD, drug treatment is initiated in conjunction with NPM. FOUR major drugs in use are: -

Class of Drugs	Indications	Side Effects
Ion Exchange Resins Cholestyramine (Questran) 4-24 gm/day	↑ Cholesterol	GI Upset Interacts with vit. K and folic acid absorption
Fibrates Bezafibrate (Bezalip) 200-600 mg/day Gemfibrozil (Lopid) 600-1200 mg/day	↑ Cholesterol + Triglycerides	GIT upset Myositis (Caution in renal failure) Pruritis, Gallstones Rhabdomyolysis with statins
Statins (HMG CoA Reductase Inhibitor) Simvastatin (Zocor) 10-40 mg od Pravastatin (Pravachol) 20-40 mg od Atrovastatin (Lipitor) 10-40 mg od	↑ Cholesterol +/- Triglycerides	GIT Upset Myalgia Rhabdomyolysis Hepatitis Contraindicated in pregnancy and lactation

How To Initiate Drug Therapy

Hyperlipidemia	In Order Of Preference
Increased Cholesterol	1.Resin, 2.Statins
Mixed	1.Fibrates, 2.Statins
Increased Triglycerides	1.Fibrates,2.Nicotinic Acid

Combination Drug Therapy (Only in severe hyperlipidemia)

Hyperlipidemia	Drug Of Choice
Severe Hypercholesterolaemia	Statin + Resin Statin + Fibrates* Statin + Nicotinic acid* Resin + Nicotinic acid
Severe Mixed Hyperlipidemia	Statin + Fibrates* Statin + Nicotinic acid* Resin + Fibrates/Nicotinic acid

*Risk of Myositis and Rhabdomyolysis is higher with this combination

Monitoring And Duration Of Therapy

It should be stressed that these patients will be on long term therapy. It is therefore important to assess them on a regular basis in terms of response of therapy and to look out for possible side effects. After start of therapy LDL Cholesterol should be measured at 6-8 weeks and then again at 3-4 months. Long term monitoring can then be done with Total Cholesterol measurement only and full lipid profile once a year

Monitoring of ALT and Creatinine is necessary during the first 6-8 weeks with statins and Fibrates and then if necessary.

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FLOW CHART FOR MANAGEMENT OF HYPERLIPIDEMIA

High Risk	Moderate Risk	Low Risk
Coronary, Cerebral, Peripheral Arterial Disease	> 2 Risk Factors	< 2 Risk Factors
Target Total Cholesterol & LDL-C (mmol/L)		
TC < 5.0 LDL-c < 3.0	TC < 5.2 LDL-c < 3.4	TC < 6.5 LDL-c < 4.1
How To Achieve Targets (In order of Preference)		
NPM Statins Add Cholestyramine or others carefully	NPM Fibrates Cholestyramine Statins	NPM Drugs: Last Resort Cholestyramine Fibrates Rarely Statins
Followup Lab		
3monthly Lipids Till Normal Then 6-12 mth Lipids	3-6monthly Lipids Till Normal. Then 6-12 mth TC	6 monthly TC Till Normal Then 12 mth TC
Control any Secondary causes. Watch for LFT with Statins & Fibrates. Periodic review		

- Consider step down & stopping drugs after discussing with patients, based on risk profile and lab results.
- Discuss with your senior colleagues before referring to hospital. Only *very high-risk patients or those that are difficult to control on maximum treatment should be referred.*
- Ask for Lipid Panel only if required. Most of the time Total Cholesterol and Triglycerides levels will be enough to assess patients.
- Drugs are *not indicated in children* under 12 years of age. Caution in pregnancy and lactation.

Ministry Of Health, Brunei Darussalam

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