

HYPERLIPIDAEMIA

(High blood fats)

Year 1

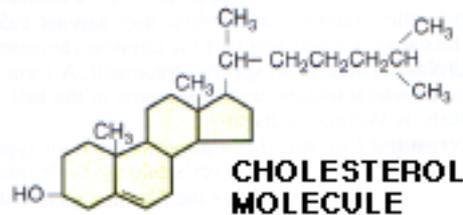
General information

LIPIDS

The term lipids refers to all blood fats, but particularly the fats cholesterol and triglyceride. Hyperlipidaemia is the presence of an excessive amount of these fats in the blood.

CHOLESTEROL

A yellow/white fatty substance called cholesterol is responsible for a large proportion of the heart attacks, strokes circulatory problems and kidney disease in the Western world. Yet cholesterol is essential for the normal functioning of the human body. It is responsible for cementing cells together, is a major constituent of bile, and is the basic building block for sex hormones (oestrogen and testosterone). Only in excess (when the patient is said to have hypercholesterolaemia) is it harmful.



About seventy percent of the body's cholesterol is actually manufactured in the liver, and only thirty percent is obtained through the diet. If too much cholesterol is carried around in the blood stream, it may be deposited in gradually increasing amounts inside the arteries. Slowly, the affected artery narrows, until the flow of blood is sufficiently obstructed to cause the area supplied by that artery to suffer. If that area is the heart, a heart attack will result; if it is the brain, a stroke will occur. This deposition of fat is known as **arteriosclerosis**, or hardening of the arteries.

The level of cholesterol in the body is determined by **inherited traits and diet**. The people most affected by high levels of cholesterol are overweight middle-aged men. Women, and some normal weight people may be affected too, but not as frequently.

A low level of cholesterol may also be due to an inherited genetic trait, but may also occur with malnutrition. Provided food intake is adequate, a low cholesterol is of no clinical significance.

It has been proved that if cholesterol levels that are within normal limits, the risk of heart attack is greatly reduced. It is therefore important for anyone who feels they may be at risk, and everyone at 40 years of age, to have a blood test to determine their cholesterol level. For this test to be accurate, it is necessary to starve for 12 hours (usually overnight) , and avoid alcohol for 72 hours before the blood sample is taken.

If the total cholesterol level is below 4.5 mmol/L, there is no need for concern. If it is above 5.0 mmol/L, the doctor will probably order tests to find out what types of cholesterol are present. **Lower levels of cholesterol are of concern in patients who have diabetes, a history of heart attack or stroke, smokers and with some other diseases.** Levels should also be lower in young people than old, and males than females.

There are two main subgroups of cholesterol - high density (which protect you from heart attacks and strokes) and low density (which are bad for you). The **ratio** between these two types of cholesterol will determine the treatment (if any) that is required.

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If the patient is found to be in the high risk group, there are several measures they can take to bring the levels back to normal. The first step is to stop smoking, limit alcohol intake, take more exercise and lose weight if obese. If these measures are insufficient, doctors will recommend a diet that is low in fat and cholesterol. On this, some people return to within normal cholesterol levels after a month or two.

Once the fatty deposits of cholesterol are deposited inside the arteries, they remain there permanently. There are new drugs that may partially remove these deposits over many years, and surgical techniques are available to clean out clogged arteries, but diet has little effect at this late stage. As in all diseases, prevention is much better than cure.

TRIGLYCERIDES

Triglycerides are a type of fat also known as VLDL (very low density lipoproteins). They are formed when one of a group of fatty acids (oleic acid, stearic acid and palmitic acid) combines with glycerol. Triglycerides are found in most animal and vegetable fats and form an essential part of the human diet. Only when eaten in excess, or excessively concentrated in the bloodstream, do they become a problem. Oral contraceptives may also be responsible for raising the blood triglyceride level.

High levels of triglycerides in the blood (**hypertriglyceridaemia**) predisposes towards an increased risk of strokes and heart attacks, as the excess triglyceride is deposited along with cholesterol on the inside wall of arteries to cause hardening of the arteries (arteriosclerosis). The cholesterol levels are more important than those of triglyceride in this process.

The amount of triglyceride present in the blood can be readily measured in a pathology laboratory. For an accurate result, it is necessary for the patient to fast for twelve hours and avoid alcohol for three days before the test. A level below 2.3 mmol/L is considered normal.

Low levels of triglyceride occur in malnutrition, while high levels can be an inherited trait or may be associated with a wide range of conditions including obesity, the nephrotic syndrome (kidney disease), chronic kidney failure, diabetes mellitus, hypothyroidism (under active thyroid gland), Cushing syndrome, pancreatitis, hypopituitarism (under active pituitary gland under the brain), acromegaly (enlargement of bones), glycogen storage diseases, alcoholism, pregnancy and the use of drugs (eg. oral contraceptives, steroids).

RISK FACTORS

A family history of hyperlipidaemia is a very strong risk factor for developing the same problem.

A diet high in animal fat is another significant risk factor.

Obesity does not necessarily result in hyperlipidaemia. Skinny people may have a high lipid level, and obese people have a normal lipid level.

Exercise plays a minimal role in hyperlipidaemia.

SYMPTOMS - HISTORY

Unfortunately, the only symptoms of hyperlipidaemia are often the onset of a myocardial infarct or stroke.

Other non specific symptoms may include impotence and xanthoma (skin nodules).

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SIGNS - EXAMINATION

A sign is clinical evidence of a disease or deformity.

A lump, fever, rash, noise or unusual appearance, are all signs.

Exp: = Explanation of sign Int: = Interpretation of sign Phys: = Physiology of sign

Arcus Senilis

Exp: An opaque ring in the peripheral cornea with a clear zone separating it from the limbus

Int: (+) Occurs invariably with advancing age, hypercholesterolaemia

Phys: Deposition of lipids in periphery of cornea

Xanthelasma

(Xantheloma Palpebrarum)

Exp: Yellow-brown nodules in soft tissues around eye

Int: (+) Primary biliary cirrhosis, elderly, hyperlipidaemia, cholestasis

Xanthomatosis

Exp: Cluster of pale yellow papules on a red patch of skin, often on buttocks

Int: (+) Hypertriglyceridaemia, other hyperlipidaemias, diabetes mellitus, biliary cirrhosis, cholestasis

Phys: Deposition of excess circulating lipids in skin

POSSIBLE CAUSES

The causes of hyperlipidaemia are **excess animal fat in the diet** and a **genetic predisposition**.

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INVESTIGATIONS - PATHOLOGY, RADIOLOGY ETC.

RI = Reference interval (normal value) Ind: = Indication for performing test
INT: = Interpretation of results Phys: = Physiology of investigation

Cholesterol, Serum

RI: 2.2 - 6.5 mmol/L (150 - 250 mg/100 mL)

Neonate 0.2 - 4 mmol/L

Recommended levels -

- general population <5.5 mmol/L

- risk factors (eg. diabetes, heart disease, smoking, hypertension, family history) <4.0 mmol/L

Ind: Obesity, hypertension, heart disease, diabetes mellitus

Int: HIGH - Hypercholesterolaemia (LDL:HDL ratio?), familial, hypothyroidism (ETR, TSH?), diabetes mellitus (glucose?), nephrotic syn., chronic hepatitis, cirrhosis, lipaemia, porphyria, protein deficit, hypergammaglobulinaemia, anorexia nervosa, elderly, pregnancy

LOW - Acute hepatitis, Gaucher's disease, hyperthyroidism, acute infections (FBC?), uraemia, myocardial infarct, malnutrition, familial

Phys: Level determined by metabolic functions that are influenced by diet and heredity. 70% of cholesterol occurs as low density lipoproteins. No alcohol for 72 hours and no food for 12 hours before test

HDL

See High Density Lipoprotein Cholesterol, Blood

High Density Lipoprotein Cholesterol, Blood [HDL]

RI: Male 0.9 - 2.0 mmol/L

Female 1.0 - 2.2 mmol/L

Ind: Obesity, high total cholesterol

Int: LOW - Increased risk of atherosclerosis and coronary artery disease, Reaven syn., pregnancy

HIGH - Lower risk of atherosclerosis

Phys: Ratio of total cholesterol:HDL cholesterol is best prognostic marker. Should not exceed 4.5; the higher the ratio, the poorer the prognosis

LDL

See Low Density Lipoprotein Cholesterol, Blood

Low Density Lipoprotein Cholesterol, Blood [LDL]

RI: < 3.0 mmol/L

Ind: High total cholesterol

Int: HIGH - Increased risk of arteriosclerosis, heart disease and cerebrovascular disease (HDL?)

Phys: Ratio between total cholesterol and LDL important

Triglycerides, Serum

RI: < 2.3 mmol/L (< 200 µg/100 mL) after 12 hour fast

Recommended level <2.0 mmol/L

Ind: Obesity, heart disease

Int: LOW - malnutrition

HIGH - Increased risk of ischaemic heart disease and atherosclerosis, familial, nephrotic syn., chronic renal failure, diabetes mellitus, hypothyroidism, Cushing syndrome, pancreatitis, hypopituitarism, acromegaly, glycogen storage diseases, non-fasting sample, alcohol, pregnancy, drugs (eg. oral contraceptives, steroids)

Phys: Triglycerides also known as VLDL (very low density lipoproteins). Hypertriglyceridaemia may be familial or associated with diabetes and other metabolic disorders. No alcohol for 72 hours and no food for 12 hours before test

TREATMENT - MANAGEMENT

HYPERCHOLESTEROLAEMIA

This is treated initially with a diet and then medication if necessary.

Remember, there is **NO cholesterol in any fruit, vegetable or cereal**. Cholesterol is only made in the liver, and so to contain cholesterol a food must come from something that has a liver (ie. an animal or animal product).

Fatty red meats are the worst, followed by shellfish, dairy products and eggs.

A low cholesterol diet has the following rules :-

FOODS ALLOWED

Vegetables, chicken breast, cereals, margarine, fruit and nuts, dark chocolate, fish, olive oil, lean meat, pasta, skim milk, wine and beer.

FOODS TO AVOID

Sausages, hamburgers, pies, mince, chicken skin and legs, pizza, offal (liver, kidneys, tripe), roast meats (particularly surface), game meat, lamb chops, calamari, prawns, milk chocolate, eggs and egg products, oysters, and all dairy products (cream, milk, butter, yoghurt, cheese, custard).

Despite a strict diet, there are still some people who cannot keep their cholesterol levels under control. They will require further lifelong medical management by the regular use of medications (hypolipidaemics) that are designed to lower the level of fat in the blood. These are prescribed only when necessary and include atorvastatin, cholestyramine (very old fashioned), colestipol, ezetimibe, fluvastatin, gemfibrozil, nicotinic acid, pravastatin, probucol and simvastatin.

HYPERTRIGLYCERIDAEMIA

Patients with excess blood triglyceride levels can usually be controlled by a diet that excludes most animal and vegetable fat (eg. fried food, dairy products, fatty meats). A low triglyceride diet would exclude all fried food, most dairy products and fatty meats (eg. sausages, lamb chops). With hereditary disease or severe cases, medication must be taken long term as well as the diet.

HYPOLIPIDAEMICS

The term “hypo” means low (as opposed to “hyper”, meaning high), lipids are fats, and the term “aemia” refers to the blood (compare “anaemia” - lack of blood), so a hypolipidaemic (antilipidemic in the USA) is a drug that lowers fat in the blood. The fats include both cholesterol and triglycerides. An excess of either, or both, of these in the bloodstream can cause narrowing, hardening and blockage of arteries, which result in serious diseases such as strokes and heart attacks. A combination of diet and drugs are used to control excess levels of fat in the bloodstream. Diet alone may be sufficient in many patients.

Fat-lowering hypolipidaemics include tablets in the **statin** class which are generally more convenient, effective and have fewer side effects than the older medications such as clofibrate and probucol (tablets), colestipol and cholestyramine (powders to mix with water) which are taken after meals to remove fats from the blood. These older medications can be useful additive treatment to the statins and in some diabetics and obese patients, but they

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interact with a number of other medications that may be essential for the patient's well-being. The powders must always be mixed with water, and not swallowed dry.

The drugs in the **statin** class include atorvastatin (Lipitor), cerivastatin (Lipobay), fluvastatin (Lescol, Vastin), pravastatin (Pravachol), rosuvastatin (Crestor) and simvastatin (Lipex, Zocor). Side effects may include constipation, diarrhoea, excess wind, nausea and headache. They should not be used in pregnancy or severe liver disease. Regular blood tests are necessary to check liver function and fat levels.

Cholestyramine (Questran) is an old-fashioned medication used to reduce blood cholesterol, the itch of liver failure, and in some other intestinal diseases. Side effects may include constipation, belly discomfort, excess wind, heartburn and a rash. It must be used with care in pregnancy, and not in gall bladder disease. The powder must always be mixed with water, and not swallowed dry.

Clofibrate (Atromid S) and **ciprofibrate** are other older style medications that reduce both blood cholesterol and triglyceride levels. Side effects may include nausea, vomiting and diarrhoea. They must be used with care in pregnancy, and not in patients with liver failure.

Colestipol (Colestid) is a hypolipidaemic used in difficult cases. Its most common side effect is constipation. It must not be used in patients with diabetes or thyroid disease. The powder must always be mixed with water, and not swallowed dry.

Ezetimibe (Ezetrol) is used as an additional therapy in combination with a statin medication in patients whose cholesterol cannot be controlled by other medications. Side effects may include muscle pains and liver stress.

Gemfibrozil (Jezil, Lopid) also reduces both blood cholesterol and triglyceride levels. Side effects may include heartburn, belly pains, nausea and diarrhoea. It must be used with caution in pregnancy, and may reduce fertility.

Nicotinic acid is one of the oldest medications used to reduce blood cholesterol and triglycerides, and it also aids poor circulation. Side effects may include a rash, itch, nervousness, heart changes and stomach upsets. It must be used with care in pregnancy, and not in patients with peptic ulcer or a recent heart attack.

Probucol (Lurselle) is reserved for patients with severe high blood cholesterol level. Side effects may include diarrhoea, nausea, excess wind and belly pains. It must be used with care in pregnancy, and not in patients with a recent heart attack or heart disease.

Fenofibrate and **bezafibrate** are less commonly used medications in this class.

The use of hypolipidaemics, which tend to be expensive medications, is now so widespread in developed countries that more is spent on this class of medication than any other.

In simple terms:-

- Use a STATIN first
- ADD EZETIMIBE to statin if statin not controlling cholesterol
- SUBSTITUTE EZETIMIBE for statin if statin not tolerated
- ADD PROBUCOL OR COLESTIPOL OR FIBRATE in difficult cases
- For HYPERTRIGLYCERIDAEMIA use GEMFIBRIZOL first
- Others rarely used

PROGNOSIS

Patients who can reduce their cholesterol and triglyceride levels to normal with diet and/or medication can expect to have a normal quality and quantity of life.

Untreated hyperlipidaemia leads to premature heart attacks, strokes and peripheral vascular disorders (eg. ulcers on feet).

ADDITIONAL INFORMATION

For reference only

DETAILS OF MEDICATIONS USED TO TREAT HYPERLIPIDAEMIA

STATINS

The statins are a class of medications that act to reduce the level of cholesterol and triglyceride in the blood by reducing their rate of production in the liver. They are the most commonly used hypolipidaemics. They include pravastatin, simvastatin, fluvastatin, rosuvastatin and atorvastatin.

SIMVASTATIN

The hypolipidaemic medication simvastatin was the first statin drug released. It is used as a tablet to lower excess blood levels of cholesterol. It was released in the late 1980's and has radically improved the treatment of arteriosclerosis and other diseases caused by excess cholesterol. It is very safe and generally well tolerated. The usual dosage is 10 to 80 mg. a day taken at night.

It should not be used in pregnancy unless no alternative available, and is not for use in breastfeeding or children. Regular blood tests to check blood fats and liver enzymes are necessary. Use simvastatin with caution in liver and kidney disease, and do not prescribe it if the patient is suffering from severe liver disease or myopathy (muscle disease).

Side effects are uncommon but may include constipation, diarrhoea, excess wind, nausea and headache. Unusual effects may include vomiting, heartburn, back pain, muscle pain, dizziness, sleeplessness, cough, bronchitis, pins and needles sensation, rash, sinusitis, blurred vision and depression. Yellow skin (jaundice) or severe muscle pain and weakness are rare and severe effects that require urgent medical attention.

Simvastatin may interact with anticoagulants (eg. warfarin), niacin, nicotinic acid, digoxin, verapamil, gemfibrozil, cyclosporin, nefazodone, ketoconazole, itraconazole, macrolide antibiotics (eg. erythromycin, clarithromycin), immunosuppressive treatment and the herbs alfalfa, fenugreek, garlic and ginger as well as grapefruit juice.

Liver stress is the only likely effect of an overdose.

Hypolipidaemics do not cure high cholesterol problems, only control them, so if the medication is ceased, the cholesterol problem will recur. They are therefore designed for long term use.

Other medications in the statin class have similar effects and complications.

ATORVASTATIN

Atorvastatin (Lipitor) was introduced in 1998 and is now the world's most prescribed hypolipidaemic. It is used to very effectively lower blood cholesterol level in a dose between 10 mg. and 40 mg. taken orally once a day. It is designed for long-term use as it controls high cholesterol but does not cure the problem. Stopping the medication without advice from a doctor may lead to a rapid increase in cholesterol to the pre-treatment level. High cholesterol levels increase the risk of a heart attack or stroke.

It is not to be used in pregnancy, breast feeding, children or if the patient is suffering from active liver disease or if previous adverse effects (eg: muscle pain or weakness) were experienced from other medication used to lower cholesterol. It must be used with caution in liver and kidney disease. Regular blood tests to check cholesterol level and liver function are advisable.

Side effects are uncommon but may include altered bowel habits (diarrhoea or constipation), indigestion, heartburn, nausea, headache, belly pain, sleeplessness, a rash, itch or muscle and joint pain. Rarely swelling of the face or lips, muscle pain, muscle damage or tingling in hands and feet occur.

Interactions may occur between atorvastatin and digoxin, erythromycin, rifampicin, phenytoin, oral contraceptives, immunosuppressives, antifungals, other medications used to lower cholesterol levels and the herbs alfalfa, fenugreek, garlic, ginger. Liver and muscle damage are possible with an overdose.

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EZETIMIBE

There are a large number of medications available to lower excessively high cholesterol, but one of the most effective (and expensive) is ezetimibe (Ezetrol). Released in 2002 it acts to reduce the absorption of cholesterol from the gut, and is normally used in conjunction with medications in the statin class, but is sometimes used alone, particularly in the USA.

It must not be used in patients with gall bladder disease, and must be used with caution in pregnant women, children and in those with liver disease.

Side effects may include muscle and joint pain, liver stress and pancreas inflammation.

The normal dose is 10mg a day.

PROBUCOL

Probucol is a hypolipidaemic medication used as a tablet to control an inherited high blood cholesterol level that does not respond to other treatment. It should be used with caution in pregnancy. It is not for use in breastfeeding, or if suffering from heart failure, heart electrical abnormalities, irregular heartbeat or a recent heart attack. Use probucol in children only if medically essential. Regular blood tests to check liver enzyme and blood cholesterol levels are necessary and a low cholesterol diet must be maintained.

Side effects may include diarrhoea, excess wind, nausea and belly pains. Unusual side effects may include pins and needles sensation, noises in ears, rash, heartburn, impotence, palpitations, headache and blurred vision. An interaction with cholestyramine is possible.

It is normally used in only the most difficult cases of high blood cholesterol levels.

GEMFIBRIZOL

Gemfibrozil (with the common trade name of Lopid) is a hypolipidaemic medication used to reduce excessive blood levels of cholesterol and triglyceride.

It should be used in pregnancy only if medically essential, and is not for use in breastfeeding and children.

Patients must remain on a low fat diet, and regular blood tests are necessary to check blood fat levels, liver enzymes and blood cells. Do not prescribe gemfibrozil if the patient is suffering from severe liver or kidney disease, gall stones, or trying to get pregnant as drug may reduce fertility.

Common side effects may include heartburn, belly pains, diarrhoea, tiredness, nausea and muscle pain, while less common ones may be vomiting, eczema, rash, dizziness, constipation and headache. Stop the medication if disabling muscle pain occurs.

Gemfibrozil interacts with anticoagulants (eg. warfarin), cerivastatin, colestipol, alfalfa, fenugreek, garlic and ginger.

Introduced in 1995 it is a medication that is particularly effective and safe in the treatment of excess blood levels of triglycerides and cholesterol.

FENOFIBRATE

Fenofibrate is a hypolipidaemic medication that lowers blood fat (cholesterol) levels. It should not to be used in pregnancy and breastfeeding, or if suffering from gall stones, other gall bladder disease, severe liver or kidney disease.

Common side effects are nausea, diarrhoea and rash, while unusual ones are a headache, tiredness and dizziness. It is not available in all countries and normally only used in patients who are resistant to other medications.

CURIOSITY

Questran (cholestyramine) is a very old fashioned, and unpleasant to take, powder that is used to treat hypercholesterolaemia. It may still be used to treat intractably high cholesterol levels but is more commonly used in the 21st. century to control persistent diarrhoea in patients with severe coeliac disease.

OTHER INVESTIGATIONS

For reference only

Apolipoproteins, Serum [Apo]

RI: ApoA1 1.0 - 1.8g/L
ApoB 0.8 - 1.6g/L
Ind: Atherosclerosis
Int: LOW - Increased risk of atherosclerosis
Phys: Immunoassay. May be measured as an alternative to HDL and LDL

Homocysteine, Serum

RI: 0.5 - 2.2 nmol/mL
Ind: Family history of myocardial or cerebral infarct
Int: HIGH - Homocysteinaemia, atherosclerosis, increased risk of thrombotic events such as myocardial or cerebral infarct, folate deficiency, lack of vitamin B6 or B12.
Phys: Cystathionine beta-synthase deficiency causes congenital atherosclerosis. Detected by measuring homocysteine which is an abnormal metabolite. Metabolic pathway may be additionally stressed by methionine loading. Excess homocysteine damages the vascular endothelium.

Lipids, Total Plasma

RI: After fasting 12 hours, 400 - 600 mmol/L
Ind: Obesity, hypertension
Int: HIGH - Hyperlipidaemia, atherosclerosis, diabetes, hypothyroidism
Phys: Specific type of hyperlipidaemia is determined by measuring the cholesterol and triglyceride components of the total plasma lipids

Very Low Density Lipoprotein Cholesterol, Blood [VLDL]

RI: < 1 mmol/L
Ind: Hypercholesterolaemia
Int: HIGH - Reaven syn.

CURIOSITY

Wine contains between 80 and 90% water, 8 to 15% alcohol (more in fortified wines), sugar (less in dry wines), and acids. There are also trace amounts of minerals, vitamins and amino acids (the building blocks for proteins). Wine also contains the most potent antioxidants known which are probably the main ingredient to give health benefits, mainly by converting the bad low density cholesterol into the good high density ones.

TOTALLY, COMPLETELY AND UTTERLY USELESS INFORMATION

There is no cholesterol in pure chocolate, but some added dairy fats will contain cholesterol. Dark chocaholics rejoice!

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