Familial Hypercholesterolaemia (FH) occurs in about one person in every 500 and is one of the most frequently occurring inherited conditions. It is caused by an abnormal gene resulting in exceptionally high cholesterol levels, usually between 8 and 12 mmol/l but sometimes is excess of 20mmol/l. Triglycerides are generally not increased, or if they are, only moderately. High cholesterol levels start from birth and are present throughout life. People with FH are at high risk of early coronary heart disease (CHD).

More than 120,000 people in Britain have the problem, a similar number to those who need insulin to control their diabetes. However, unlike that type of diabetes, many people with FH go undetected with tragic consequences. People with FH may be disabled or die from CHD early in life, often in their 40s or 50s, sometimes earlier.

Family Matters
FH is a genetic problem and can be passed from parent to child. Each family member has an even chance of inheriting the problem (like tossing a coin). Whenever FH is diagnosed, it is essential that all close relatives have their cholesterol levels measured so they too can start preventative treatments.

Symptoms of FH
As well as a very high cholesterol level and a strong family history of CHD, FH can sometimes be recognised by outward signs, ‘lumps and bumps’, which need the expert eye of a doctor for accurate diagnosis. Not everyone with FH has these signs. They may result from cholesterol deposits in the tendons at the back of the hands overlying the knuckles and in the Achilles tendon at the back of the ankles. The resulting swellings are called tendon xanthomata (pronounced zan-tho-mata). Cholesterol may also be deposited in the skin around the eye or eyelid. These deposits are usually yellow and are called xanthelasmas (pronounced zan-thel-as-mas). Another visible sign often seen in people with FH is a pale or white ring around the inside of the outer rim of the iris, the coloured part of the eye. The ring is called corneal arcus. Only tendon xanthomata are specific to FH. Xanthelasmas and corneal arcus can occur for other reasons as we get older.

Testing of FH in children
It may be important to identify FH in childhood, particularly in families in which CHD is occurring early in adult life. Children should be tested before the age of ten, but generally not before age two, although it is possible to test for FH soon after birth.

A diet low in total and saturated fat can be followed by children over two years of age, provided there are sufficient calories and nutrients to support normal growth. Parents may wish to seek guidance from a dietitian experienced in lipid management. Whilst opinions differ regarding the treatment of FH in children, it is recognised that they will be in a position to benefit early in adult life if their FH is diagnosed in childhood. Lipid lowering drugs should only be prescribed by a specialist clinic.

Familial Combined Hyperlipidaemia
Familial Combined Hyperlipidaemia (FCH) is another inherited disorder of cholesterol. It is characterised by having a high triglyceride level as well as high cholesterol. This condition is not as well understood as FH, but is also associated with premature coronary heart disease. The elevated blood fats may not be present in childhood, and may not appear until the 20s or 30s. Tendon deposits are not present in FCH, and cholesterol levels tend to be not quite as high as in FH. Treatment generally consists of healthy lifestyle practices and medication as discussed above.

Treatment of FH
Diet is an essential element for the treatment and management of FH, although medication is generally also necessary at some stage. There are several cholesterol lowering drugs available on prescription that are effective in treating the condition. It is important to maintain a heart healthy diet and lifestyle, even when prescribed medication, as the two complement each other.

There are currently plant sterol and stanols products that can be used in the healthy diet to help improve cholesterol lowering. These products work by blocking cholesterol absorption in the gut and can lower LDL cholesterol by up to 14%.
**DRUG TREATMENT**

Drug treatment is generally reserved for people at high risk of CHD for whom diet and lifestyle measures have failed to reduce blood lipids to acceptable levels. This will include many people with FH and most individuals who have already developed CHD. Increasingly, other groups of people, particularly those who combine more than one risk factor, such as those with diabetes, are also treated with lipid-lowering drugs. The following are the more commonly prescribed classes of drugs for treating lipid disorders.

**Statins**

- Statins come in tablet form and work by slowing down the production of cholesterol in the liver, which is where most of the body’s cholesterol is made. Statins are thoroughly tested and very effective at lowering cholesterol, LDL in particular.
- They are generally well tolerated, and reassuringly have been shown to extend life by preventing CHD. If generalised muscle aches occur, this should be reported to the doctor, although it is rare for the statins to be the cause of the muscle inflammation. Statins should not be used to treat people with liver disease, pregnant women or women who might become pregnant. Use of statins in children should be under supervised specialist care.

**Fibrates**

- Fibrates come in tablet form and are useful when both triglycerides and cholesterol are raised. These drugs tend to be well tolerated. Fibrates should not be used during pregnancy or by individuals with liver or kidney disease.

**Resins**

- Resins come in powder form and are taken by mixing with water, fizzy drinks, fruit juice or yoghurt. Resins prevent re-absorption of bile salts in the intestine, which means that more cholesterol is used up in replacing them. Resins are safe for children because they are not absorbed into the body, although extra folic acid is recommended. Many people may experience side effects such as flatulence and constipation which limit the usefulness of resins.

**Selective cholesterol absorption inhibitors**

- These drugs block absorption of dietary and biliary cholesterol in the gut. They work specifically at the brush border of the small intestine. They can help to reduce cholesterol levels by up to 18%. However, when they are combined with a low dose of statin drug they can greatly enhance the cholesterol lowering effect.

**Nicotinic acid**

- The major effect of nicotinic acid is to inhibit fatty acid release from fat cells in the body. This reduces the production of VLDL in the liver, which results in reductions of IDL and LDL. There is a subsequent rise in HDL cholesterol. Doses in the region of 2g per day are required.

**Omega-3 fish oils**

- Fish oils (1-4g daily) reduce plasma triglyceride by reducing VLDL production in the liver. Eating three portions of oily fish per week can provide the recommended amount to help prevent heart disease but if you prefer, fish oil capsules (1g daily) can provide an alternative source.
- If taking cholesterol-lowering drugs with other medicines, it is important to discuss this with your doctor. Doses of other drugs such as anticoagulants like warfarin may need to be adjusted.

**OTHER TREATMENTS**

**Apheresis**

Apheresis is a treatment similar to kidney dialysis. The patient is connected to a machine that removes the LDL or bad cholesterol from the patients’ blood. The patients’ ‘cleaned’ blood is then returned to the patient. The process takes about 3 hours to perform and has to be repeated at fortnightly intervals. The procedure is quite expensive and is only available at specialist centres and is usually reserved for specialist cases.

**Liver transplantation**

In very extreme cases, complete or partial liver transplantation can be undertaken. However, the procedure is extremely difficult and the long term effect of taking anti rejection drugs such as cyclosporine can shorten life expectancy.

**Gene therapy**

The idea of gene therapy for this condition does seem an attractive proposition. However, although early trial evidence has not been successful, there is hope that the procedure can be perfected in the future.