Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- males of South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Acute phase proteins

Acute phase proteins

- CRP
- procalcitonin
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:

- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

*plays a more significant role in other mammals such as mice

Hyperlipidaemia: drug adverse effects

The following table compares the side-effects of drugs used in hyperlipidaemia:

Drugs	Adverse effects
Statins (HMG CoA reductase inhibitors)	Myositis, deranged LFTs

Ezetimibe	Headache
Nicotinic acid	Flushing, myositis
Fibrates	Myositis, pruritus, cholestasis
Anion-exchange resins	GI side-effects

Hypercalcaemia: management

The initial management of hypercalcaemia is rehydration with normal saline, typically 3-4 litres/day. Following rehydration bisphosphonates may be used. They typically take 2-3 days to work with maximal effect being seen at 7 days

Other options include:

- calcitonin - quicker effect than bisphosphonates
- steroids in sarcoidosis

There is a limited role for the use of furosemide in hypercalcaemia. It may be useful in patients who cannot tolerate aggressive fluid rehydration

Alkaline phosphatase

Causes of raised alkaline phosphatase (ALP)

- liver: cholestasis, hepatitis, fatty liver, neoplasia
- Paget's
- osteomalacia
- bone metastases
- hyperparathyroidism
- renal failure
- physiological: pregnancy, growing children, healing fractures

The table below splits the causes according to the calcium level

Raised ALP and raised calcium	**Raised ALP and low calcium**
• Bone metastases	• Osteomalacia
• Hyperparathyroidism	• Renal failure

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia

- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure

- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia

- nephrotic syndrome
- cholestasis
- hypothyroidism

Body mass index

Body mass index (BMI) is calculated by dividing the weight (in kilograms) by the height (in metres) squared

BMI	Old classification	NICE classification
< 18.5	Underweight	U nderweight
18.5 - 24.9	Normal	Normal
25 - 29.9	Overweight	Overweight
30 - 34.9	Obese	Obese I
35 - 39.9	Clinically obese	Obese II
> 40	Morbidly obese	Obese III

Vitamin deficiency

The table below summarises vitamin deficiency states

Vitamin	Chemical name	Deficiency state
A	Retinoids	Night-blindness (nyctalopia)
B1	Thiamine	Beriberi • polyneuropathy, Wernicke-Korsakoff syndrome • heart failure
B3	Niacin	Pellagra • dermatitis • diarrhoea • dementia
B6	Pyridoxine	Anaemia, irritability, seizures
B7	Biotin	Dermatitis, seborrhoea
B9	Folic acid	Megaloblastic anaemia, deficiency during pregnancy - neural tube defects
B12	Cyanocobalamin	Megaloblastic anaemia, peripheral neuropathy
C	Ascorbic acid	Scurvy • gingivitis

- bleeding

D	Ergocalciferol, cholecalciferol	Rickets, osteomalacia
E	Tocopherol, tocotrienol	Mild haemolytic anaemia in newborn infants, ataxia, peripheral neuropathy
K	Naphthoquinone	Haemorrhagic disease of the newborn, bleeding diathesis