HYPERLIPOPROTEINAEMIAS-INVESTIGATIONS

Laboratory tests are required for the establishment of hyperlipoproteinaemia, type of abnormality and thus confirmation of underlying pathogenicity. There is also need for assessment of response of patients to treatment-dietary or following the use of lipid lowering drugs and serial monitoring of blood lipid values are required for this purpose.

Ideally the blood sample for lipid analysis should be collected after overnight fast. There should have been no dietetic restriction before the screening test. Prior alcohol consumption also alters lipid profile and especially triglycerides may become raised even with one or two drinks.

Serum is sufficient for simple lipid tests; however, if specialized tests are required, plasma is necessary and edetic acid (2.5-4.0m mol/1) as anticoagulant be used.

Lipoproteins are labile, and analysis should be carried out soon after collection or within few days, samples being stored at -4°C.

In general, total cholesterol and triglyceride determinations should be carried out.

The laboratory should follow standard procedures for lipid analysis and run internal and external quality control procedures. In plasma left undisturbed overnight at 4°C, chylomicrons float to the surface, while VLDL remains in suspension. This can provide distinction between hypertriglyceridaemia due to fasting chylomicronaemia and that due to an increase in VLDL without the necessity to perform electrophoresis.

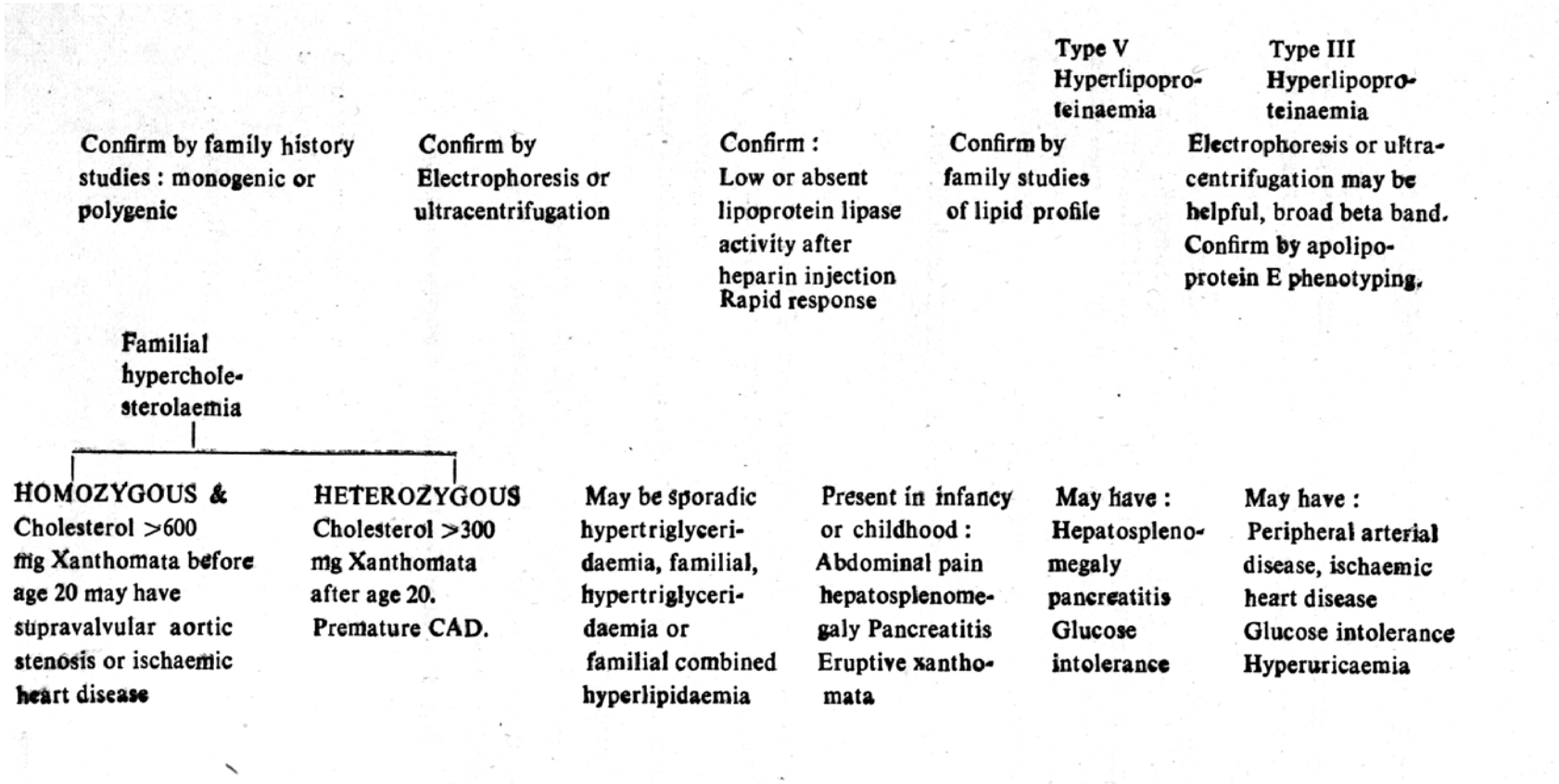
Lipoprotein electrophoresis (Agarose gel gives the best separation).

Four classes of lipoproteins are separated by electrophoresis (CM, B, Pre-B), largest and least dense are the chylomicrons. Chylomicrons remain at origin and this Type I can be identified. Progressively smaller in size and greater in density are the very low density lipoproteins VLDL, low density lipoprotein, LDL and high density lipoprotein, HDL.

In the instances with total cholesterol >300 mg/dl, the excess may be due to pre-Beta fraction which will show broad beta band on electrophoresis (Type III).

A rare variation is increase in alpha lipoproteins (induced by oestrogens) and such type of hyperlipoproteinaemia as such does not require drug therapy.

PROSPECT FOR SCREENING :
Family History of Premature CAD
Hyperlipidaemia or Impaired Glucose Tolerance
History of Recurrent Pancreatitis
Presence of Xanthelesma, Lipaemia Retinalis
Or Arcus Juvenilis.
Primary
Primary Hyper-lipoproteinaemia
Secondary
Exclude hypothyroidism, chronic renal failure, the nephrotic syndrome, diabetes, alcohol excess, primary biliary cirrhosis, contraceptive pill or oestrogen treatment, Beta blockers or thiazides, Gout ?
Is plasma turbid ?
Cream layer on top of stored plasma
Cream layer on top with turbid infranant layer
No
Yes
Is serum triglyceride concentration normal?
Is serum cholesterol concentration normal ?
Is serum chylomicron level raised
Is serum triglyceride concentration raised ?
Yes
No
No
Yes
Yes
Type IIa Hyperlipo-proteinaemia
Type IIb Hyperlipo-proteinaemia
Type IIb or Type IV
Type I Hyperlipo-proteinaemia
Xanthomata eruptive
Xanthomata tuberous


Type V Hyperlipoproteinaemia
Type III Hyperlipoproteinaemia
Confirm by family history studies : monogenic or polygenic
Confirm by Electrophoresis or ultracentrifugation
Confirm : Low or absent lipoprotein lipase activity after heparin injection Rapid response
Confirm by family studies of lipid profile
Electrophoresis or ultracentrifugation may be helpful, broad beta band. Confirm by apolipoprotein E phenotyping.
Familial hypercholesterolaemia
HOMOZYGOUS & Cholesterol >600 mg Xanthomata before age 20 may have supravalvular aortic stenosis or ischaemic heart disease
HETEROZYGOUS Cholesterol >300 mg Xanthomata after age 20. Premature CAD.
May be sporadic hypertriglyceridaemia, familial, hypertriglyceridaemia or familial combined hyperlipidaemia
Present in infancy or childhood : Abdominal pain hepatosplenomegaly Pancreatitis Eruptive xanthomata
May have : Hepatosplenomegaly pancreatitis Glucose intolerance
May have : Peripheral arterial disease, ischaemic heart disease Glucose intolerance Hyperuricaemia

Etectrophoretic pattern can be used for LDL/HDL ratio which can be used as risk index.

Ultra-centrifugation gives[5] the precise nature of the density value of lipoprotein affected. Procedure is possible only where ultra centrifuge is available and is also time consuming.

HDL cholesterol estimation is done by treating the serum with heparin and magnesium which precipitates LDL and VLDL. Thc concentration of cholesterol in the supernatant is determined, this is taken as HDL. Similarly VLDL and LDL cholesterol concentration can be calculated with reasonable accuracy from total cholesterol, triglyceride and HDL cholesterol concentration, provided there is no chylomicronaemia and triglyceride is not in excess of 400 mg/100 ml.

LDL cholesterol-Totat cholesterol (Triglyceride + HDL cholesterol).

Specialized laboratory tests

Apolipoproteins

Recent investigation has resulted in charaeterization of the protein components (apoproteins) and even determination of their primary structure.

Immunological methods are in vogue for determination of apolipoproteins. Each apoprotein is designated by namenclature based on C-terminal arninoacid.

Important amongst these are :

Apo-A	better discriminator for HDL cholesterol.
Apo-B	discriminator for LDL, cholesterol.
Apo,C	
Apo-E	discriminator for familial dyslipoproteinaemia.

LDL Receptor

LDL receptor studies are done on fibroblast cultures. These are research procedures done at advanced laboratories and assist in recognition of genetic penetrance and basic mechanism of hyperlipoproteinaemia.

The chart on the previous pages assists in approach to hyper1ipidaemia.