had been treated for short stature with testosterone. In both series the majority of patients reached their predicted height and fared slightly better than untreated patients. However, patients with anorhca who were treated intensively with testosterone did even well and on average appeared to have lost about 3 in (8 cm) potential growth.10 R. Greene and L. S. Carstairs1 also found that androgen treatment did not appear to reduce adult height. On the contrary, the final heights of 27 men who had been treated as children with testosterone exceeded the predicted heights by up to 9 in (23 cm). The significance of this finding is uncertain because a control group of untreated patients was not available, and the apparent benefit of treatment may merely reflect a general underestimation of predicted height.

Androgen therapy carries other potential risks, particularly when high doses are used. In theory the secretion of gonadotrophin may be suppressed, but there is no evidence that this is a serious long-term hazard.9 More important, gynecomastia, jaundice, and abnormal liver function tests have been reported, and treatment of aplastic anaemia with anaabolic steroids may be associated with the development of hepatoa.

Though cautious treatment probably carries little risk, present evidence does not indicate that adult height can be increased to a significant extent, and the advice13 that "wisdom suggests that the pediatrician stay his hand in the ‘usual’ case” still holds good. In the few cases in which treatment is deemed necessary because of severe emotional difficulties, testosterone, possibly given as a depot injection (testosterone enanathate) is probably the best choice. Such treatment will lead to virilization and is contraindicated in girls. In boys it should probably be deferred until the patient is 11-12 years old and the bone age is above 9 years.14 Treatment should be started with relatively low doses and given for limited periods. Bone age must be followed closely, and, if it appears that bone maturation is outstripping growth, treatment should be reduced or stopped.

5 Hubbell, D., and Myant, D. R., Archives of Disease in Childhood, 1962, 37, 516.
10 Foss, G. L., Archives of Disease in Childhood, 1965, 40, 66.

Disorders of Lipid Metabolism

The relationship between arterial disease, hyperlipidaemia and diet seems undoubted, though it is certainly complex. Accordingly, the "lipid profile" has arrived in many hospitals throughout the country. But physicians are uncertain about its evaluation and what treatment may or may not be indicated. While the increased demand for estimations of blood lipid reflects the clinician’s increasing concern to prevent or delay the onset of arterial disease, there is still no consensus on when or how he should intervene. A symposium organized by the Association of Clinical Pathologists highlights recent advances in the knowledge of lipid metabolism and shows how fairly simple techniques can provide most of the diagnostic information required.1

We are reminded that cholesterol is not a harmful substance but an essential structural element of cell membranes, an obligatory precursor of bile acids and steroid hormones, and a constituent of plasma lipoproteins. N. B. Myant reviews its physiology and transport and discusses the mechanisms by which some agents effectively lower its concentration in the plasma.

Plasma triglycerides are also related to arterial disease, and an account of normal triglyceride metabolism provides a basis for comparison with states of abnormal lipid metabolism (D. S. Robinson). Phospholipid metabolism will be less familiar to most clinicians, and D. Gompertz focuses our attention on lecithin as the most important glycerophosphatide, both in the membrane systems and in lipid-transporting mechanisms.

Advances in analytical methods have provided the means for advancing our knowledge of lipid metabolism. The two techniques most widely used have been ultracentrifugation, followed by chemical analysis of the separated fractions, and electrophoresis. These techniques have enabled the hyperlipidaemias and hyperlipoproteinaemias to be classified, and this work provides the basis for the lipid profiles now emerging from our laboratories. D. G. Cramp comments on the collection of samples and on the estimation of triglycerides, cholesterol, and free fatty acids. K. Carlson (Sweden) gives detailed information on ultracentrifugation and electrophoresis, and provides useful data on the variations in triglyceride and cholesterol concentration with age and sex.

Diet influences triglyceride metabolism, and there is increasing interest in the role of triglycerides in atherosclerosis and coronary heart disease. The nature of the dietary fat accompanying carbohydrate may determine the effect of carbohydrate on the plasma triglycerides (Ian Macdonald), and this relationship is probably of greater importance in real life than the separate effect of either fat or carbohydrate. Of particular interest is the possible effect of the blood viscosity and the coagulation-fibrinolysis mechanism of the hypertriglyceridaemia induced by carbohydrate or fat.

Barry Lewis discusses the classification scheme initiated by Frederickson and colleagues3 and emphasizes that a knowledge of the plasma concentrations of cholesterol and triglyceride and of the plasma lipoprotein pattern is sufficient for the selection of treatment for most patients with hyperlipidaemia. But it is essential to realize that the accepted classification implies only that we recognize a particular lipoprotein pattern present at the time of the examination. We are classifying the plasma and not the patient4 and there is only a limited relationship between the serum lipoprotein patterns and the underlying pathogenesis. A particular abnormal lipoprotein pattern may be caused in several different ways. At present it seems reasonable to use the World Health Organization's classification, but it represents merely a convenient shorthand for communication. As a general guide to the selection of treatment it may be somewhat complicated. In any case of hyperlipidaemia there must be a diligent search for underlying disease, and when the condition is not clearly secondary, an investigation of first degree relatives.
The secondary hyperlipidaemias are common, and Alan Chait discusses such causes of them as diabetes mellitus, alcohol, chronic renal disease, hypothyroidism and gout. No lipoprotein pattern is specific for any of these, and the pattern may vary from time to time in the same patient.

Lars A. Carlson (Sweden) describes a classification with only three classes based on plasma cholesterol and triglyceride levels. He has used it in prospective studies of the relationship of plasma cholesterol and triglyceride levels to ischaemic heart disease. The rate of new attacks of coronary infarction increased linearly with the concentration of both triglycerides and cholesterol, and he states that the frequency of new attacks depends more on triglyceride levels than on cholesterol levels. As he defines "normal" cholesterol as being below 280 mg per 100 ml, his conclusions on the independent role of triglycerides as a risk factor needs cautious assessment.

Cholesterol, particularly in the form of the olate, is the main lipid to accumulate in atherosclerotic lesions; triglycerides are never more than a minor component. Once inside the arterial wall, the sterol cannot be metabolized therein and is a highly sclerogenic agent. C. W. M. Adam reviews the pathogenesis of atherosclerosis and emphasizes the general view that the main source of the cholesterol esters in atherosclerotic lesions is the plasma. He considers that cholesterol deposited in the arterial wall would be difficult to absorb and throws some doubt on the therapeutic reversibility of atherosclerosis. However, in an addendum he refers to recent work which shows considerable regression in the atheromatous coronary arteries of rhesus monkeys first fed on an atherogenic diet and then returned to a low in lipids and rich in corn oil.

Hypolipoproteinaemia may be a primary condition genetically determined or secondary to some disease. June Lloyd describes the rare but fascinating primary disorders which have contributed greatly to our understanding of the function of the plasma lipoproteins, which are apparently important for the normal functioning of many organs. Beta-lipoprotein appears to be essential for the transport of triglycerides out of cells, and normal alpha-lipoprotein appears essential for cholesterol ester metabolism. Both these plasma lipoproteins help to preserve the integrity of the nervous system and maintain the normal composition of the erythrocyte membrane, and beta-lipoprotein has an additional function as a carrier of carotenoid and of vitamin E in the circulation.

Bile acids are essential to lipid metabolism, facilitating the digestion of triglycerides, the absorption of monoglycerides and fatty acids, and the absorption of cholesterol and the fat-soluble vitamins. R. Hermon Dowling reviews the normal enterohepatic circulation of the bile acids and discusses the effect of diet, and particularly dietary fat, on this circulation. There is indirect evidence that the hypocholesterolaemic action of polyunsaturated fats may result in increased faecal loss of bile acid with a parallel increase in bile acid synthesis and hence in the metabolism of cholesterol.

The treatment of lipid disorders is mainly concerned with the prevention of long-term vascular complications. But in the absence of symptoms the patient is apt to follow his prescribed regimen laxly. Furthermore, many physicians remain unconvinced that the lowering of blood cholesterol levels will decrease the incidence of ischaemic heart disease, so that the combination of an unwilling patient and an unconvinced doctor promises little therapeutic success. Den-