Deep-vein Thrombosis

"Sudden death of unknown aetiology" would be a more truthful description of death following pulmonary thromboembolism, for we do not yet know why blood suddenly clots in the deep veins and later breaks free into the circulation as an embolus.

That it can do so even in apparently healthy people, with little or no clinical manifestations, was discussed recently by H. A. Fleming and Sheila M. Bailey. They emphasized the need to be aware of this possibility because slight premonitory signs and symptoms such as faintness and tiredness, if interpreted correctly, can lead the physician to start life-saving treatment. These patients are not in fact healthy, for a person who has a pulmonary embolus must have some change in his peripheral venous circulation that predisposes to thrombosis. Unfortunately we know little more about the abnormalities that initiate thrombosis than Virchow did in 1846.

The present-day management of deep-vein thrombosis is threefold: prophylaxis, by anticoagulant therapy; treatment with anticoagulants after diagnosis in the hope of preventing further thrombosis and to give some protection from subsequent pulmonary embolism; and investigation into the cause or causes of the initial thrombosis.

The value of prophylactic anticoagulants has been established in several studies, particularly in orthopaedic and traumatic cases. It reduces the incidence of deep-vein thrombosis and lessens the frequency of pulmonary embolism. However, S. Sevitt has said: "We have found it impossible to separate full anti-thrombotic protection from an increased haemorrhage rate." Thus we must set the risk of haemorrhage and the complicated work of the haematological control of the anticoagulant against the protection it gives. In general the advantages outweigh the disadvantages. Haematological control is particularly important, for the whole purpose of treatment is defeated if an adequate level of anticoagulation is not achieved. At present the giving of anticoagulant drugs must be classed as non-specific therapy, for it is not certain that excessive coagulability of the blood is the prime fault. Other forms of prophylaxis such as bandaging the legs, raising the foot of the bed, and early ambulation after illness or operation have not yet been proved to be of value, though articles supporting and rejecting them abound.

Treatment with anticoagulants after the thrombosis is likely to be most effective if given as soon as possible, but early

3 —— Lancet, 1964, 1, 1159.
19 Hewson, W., Experimental Inquiries, 1772. London.
diagnosis is difficult. Oedema of the ankle, the most reliable sign, is present only in the advanced state; tenderness in the calf is unreliable as an indication. An increase of skin temperature with delayed cooling of the limb after exposure is a useful early sign, for some patients who develop this abnormality show other signs of deep-vein thrombosis later. However, few physicians would use it as the sole indication for administering anticoagulants. The anatomy of the deep veins between the muscles can be well displayed by phlebography, but this procedure is inadequate for detecting deep-vein thrombosis because the intramuscular sinuses are not shown up. Attempts to detect thrombi by labelling the plasma with iodine-131-fibrin have still to be proved and will probably not be generally applicable.

Heparin is the drug of choice for the initial treatment of both deep-vein thrombosis and pulmonary embolism, for it appears to hasten the resolution of local symptoms in the legs, improve the survival rate from pulmonary embolism, and also perhaps to relieve coincidental bronchospasm by preventing the release of serotonin from thrombin from the platelets in the thrombus. But it does not seem to reduce the incidence of post-phlebitic complications in the leg. Thrombolytic agents such as streptokinase will lyse pulmonary emboli, but there has not yet been a properly controlled clinical trial, with the use of diagnostic pulmonary angiography or lung scanning, comparing the effects of streptokinase with those of heparin. Until this is done heparin must be given to the severe case, but for those less ill streptokinase is the more logical treatment. The massive-dose treatment of M. Verstraete and colleagues offers a regimen that does not require the assistance of a specialist haematologist but should not come into general use until the value of thrombolytic agents has been indisputably proved. The same arguments apply to the use of streptokinase for deep-vein thrombosis. At least one paper suggests that thrombolysis in peripheral veins is poor, and the belief that there is no risk of causing a pulmonary embolus is based on the experience of a relatively small number of cases.

Research into the aetiology of venous thrombosis may disclose a better means of prophylaxis. The most promising field at present lies in study of the changes in blood coagulability by computer techniques and in study of the platelets. It seems certain there are changes in the platelets post-operatively and in association with certain diseases, including carcinoma, that could initiate thrombosis. The advent of drugs which can alter platelet activity may provide better prophylaxis of thrombosis. The role of stasis is still undecided. W. Hewson and S. Wessler have shown that venous blood clots very slowly in vivo even when it is in complete stasis. The changes in the flow of venous blood in muscles after operation or during bed rest are still not known. N. L. Browse has shown that the arterial inflow, and so presumably the venous outflow, of the calf muscles is reduced after surgical operation, but the effect of post-operative activity on the flow of venous blood in muscle requires further evaluation. The argument whether or not changes of activity and the flow of venous blood have any causal role in the development of deep-vein thrombosis will not be settled until we can make the diagnosis with some degree of certainty.

Changes of the vein wall deserve more study, for though they are often passed over as being unimportant they may not be. Normal veins are a potent source of a plasminogen activator substance, and it has been suggested that peripheral thrombolysis may be under neurogenic control. This property may play a part in preventing thrombosis and encouraging recannulation after thrombosis.

What can the future hold? We may hope for a clearer understanding of the known aetiological factors—always remembering that a hitherto unknown factor or principle may await discovery. From this we go on to specific prophylaxis, but an urgent need at present is to improve our methods of diagnosis.

### Retinal Detachment in Renal Failure

In retinal detachment the rod-and-cone layer separates retina from the pigment epithelium, so that the potential space of the embryonic optic vesicle reopens. One important cause of detachment is the formation of haemorrhagic, exudative, or serous fluid in this potential space. This abnormality may occur in renal failure, usually when hypertension exists also. Sir Stewart Duke-Elder, in his classical Textbook of Ophthalmology, cites references before 1905 giving a cumulative incidence of detachment in such cases as 7 out of 132 cases, or 5%. Nowadays retinal detachment as a complication of renal failure is undoubtedly much less common because of improvements in treatment, in particular efficient antihypertensive drugs.

Recently L. Lapco and colleagues described eight such cases. The detachment is often bilateral and usually occurs, as would be expected, in the lower half of the retina. There is considerable impairment of visual acuity, the patient complaining of "a curtain or a dark cloud in front of the eyes." The patients were all hypertensive and had severe renal failure, the blood urea being above 100 mg./100 ml. in all patients and averaging 300 mg./100 ml. In all patients except one there was a low serum sodium and evidence of overhydration, indicating severe dilutional hyponatraemia, and in the majority there was hypoalbuminaemia.

The most important observation was the gratifying response to peritoneal dialysis. In all patients there was reattachment of the retina as the exudate was reabsorbed with removal of fluid by dialysis. This was accompanied by considerable loss of weight and a rise in serum sodium as well as a fall in blood urea. Visual acuity improved, in some cases to full normal vision. Retinal detachment in uraemia should be regarded as an immediate indication for removal of fluid, either by haemodialysis or peritoneal dialysis, in order that reattachment may occur before there is irreversible damage to the rods and cones in the detached portion. W. S. Buchanan and P. P. Ellis reported a single case in which resolution of the eye signs occurred after bilateral nephrectomy and subsequent successful kidney transplantation.

Retinal detachment of similar type is also prone to occur in pregnancy toxemia. J. A. S. Bosco reported ten such cases, with bilateral retinal detachment in seven. In nine of the patients the toxemia was considered to be of severe degree on

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