year at school, as well as to their parents. A few genetic clinics are necessary to provide this service; ophthalmological support is essential for an accurate diagnosis, itself a prerequisite for meaningful genetic counselling.

The "new genetics," with prenatal diagnosis by chorion biopsy of genetically determined disorders, has dramatically changed the prospects of secondary prevention. Among the conditions that may now be diagnosed early in pregnancy are X linked retinitis pigmentosa,[9] choroideraemia,[10] and retinoblastoma.[11] This list should increase over the next few years, with additional autosomal recessive, autosomal dominant, and X linked conditions. Hence secondary prevention of genetically determined diseases will become increasingly important. This is yet another reason why genetic counselling should be made available to all visually handicapped children and their families.

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Laboratory control of oral anticoagulants

A several fold variation in the mean warfarin dose in different geographical locations has been reported in a recent international survey.[1] The main cause of the variation was the tissue thromboplastin in the test for the prothrombin time. North American centres, which used rabbit brain thromboplastin almost exclusively, gave more warfarin than centres elsewhere, which used human brain reagents.

This problem was resolved in Britain with the introduction in 1969 of the national system for anticoagulant control by the British Society for Haematology. A single reagent, British comparative thromboplastin, was adopted as the national reference preparation and was linked to a national system of reporting the British ratio. British comparative thromboplastin was a designated batch of the routine reagent, Manchester comparative thromboplastin, which until recently was employed by over 95% of British hospitals.

This human brain tissue extract had to be withdrawn in early 1986 because of the possible risk of contamination by human immunodeficiency virus tissue from the central nervous system. Other thromboplastin reagents are now again being used to estimate the prothrombin time in British hospitals. Does this matter or has the problem been solved by the prothrombin time standardisation system based on international normalised ratios (INR)? These ratios were introduced recently by the World Health Organisation[2,3] and are derived from calibrations of routine thromboplastin reagents against an international reference preparation. The validity of the system has been confirmed in international collaborative studies.[4-6]

The international normalised ratio is defined as the prothrombin time ratio that would have been obtained if the original WHO international reference preparation had been used. It depends on the international sensitivity index (ISI), derived from calibrating the commercial thromboplastins against an international reference preparation on the results of prothrombin times of blood from controls and patients stabilised with long term treatment with coumarin. The resulting index quantifies the responsiveness of the commercial thromboplastin to the coumarin defect in terms of the primary international reference preparation (defined as 1·0).

Surveys by the UK External Quality Assessment Scheme in Blood Coagulation have shown, however, that different international normalised ratios are obtained with the various reagents on the same test samples. There are various possible explanations. Some manufacturers are apparently not yet calibrating their reagents correctly. Secondly, coagulometers are now used in nearly half of British hospitals, and some of these may cause serious deviations from the mean result gained using the same reagent with a manual technique.

Calibration of thromboplastins are performed on samples taken from patients stabilised on long term treatment. Hospital patients in the early induction stages of treatment must not be included. In the first 7-10 days of warfarin treatment the international normalised ratios appear less dependable with some reagents because of their varying responses to depression of individual vitamin K dependent clotting factors.[7]

The problems will be resolved only by manufacturing thromboplastin reagents showing better sensitivity to the coumarin induced defect, ideally giving international sensitivity index values between 1·0 and 1·2. Few commercial reagents would qualify at present, but the accurate implementation of the international system by the manufacturers might provide them with the necessary insight and impetus to improve the quality of their reagents.

In the mean time British hospitals should report international normalised ratios with all prothrombin time results used for anticoagulant control, employ a reagent with a low international sensitivity index, and participate regularly in the UK National External Quality Assessment Surveys in Blood Coagulation.

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