potential, and there is pressure to increase the number of recognised training posts. Some expansion will be needed to satisfy projected needs, but care is being taken to avoid the imbalance between junior staff and consultants troubling so many specialties.

Such careful planning might suggest that those clinical geneticists now in training have before them a certain future. This may be far from the truth, however, since the demands for new posts come at a time of financial stringency. Regional authorities must be persuaded of the real need to develop the service geneticists provide, and this latest report should be drawn to their attention. They may be helped in their decision by the fact that geneticists make relatively modest demands for ancillary support and that the nature of their work tends to be cost effective in helping to reduce the burden of handicap. If new consultant posts are not soon established this will expose the peculiar vulnerability of doctors in the later stages of specialist training.

It is almost nine decades since the rediscovery of Mendel's work marked the beginning of genetics as a clinical science. Gestation is now complete and medicine has given birth to a distinct specialty; let us hope that weight gain is rapid.

JOHN BURN

Research Fellow,
Clinical Genetics Unit,
Institute of Child Health,
London WC1N 1EH
(MRC grant number G8203878);
Honorary Senior Registrar in Clinical Genetics,
The Hospital for Sick Children,
Great Ormond Street,
London

[1] Medical Research Council/Department of Health and Social Security Joint Working Group on Genetics. *Counselling and service implications of clinical genetics research.* London: Medical Research Council, 1980.
[2] Clinical Genetics Society Working Party. The role and training of clinical geneticists. Report. *Eugenics Bulletin* 1983;suppl 5:1-30.
[3] Alberman E. The epidemiology of congenital defects: a pragmatic approach. In: Adinolfi M, Benson P, Giannelli F, Seller M, eds. *Paediatric research: a genetic approach.* London: Spastics International Medical Publishers, 1982:1-27.
[4] Weatherall SJ. *The new genetics and clinical practice.* London: Nuffield Provincial Hospitals Trust, 1983.
[5] Johnston AW. Training of medical geneticists. *J Med Genet* 1978;**15**: 260-1.

Standardisation of oral anticoagulant treatment

The dose of oral anticoagulants is still based on the result of a biological assay of the change in coagulation which they induce, because there is no accurate biochemical test available to quantify the defect in coagulation. The biological assay in use today is similar to that devised by Armand Quick 50 years ago,[1] to which he gave the name prothrombin time: it is the recalcification time of plasma after the addition of thromboplastin. The result is expressed as either a ratio or an index to a normal control or as percentage activity compared with that in normal plasma diluted in physiological saline or absorbed plasma.[2 3] Various sources of thromboplastin have been used—bovine, human, porcine, simian, and so on—so that the optimum level of anticoagulation varies with the type of assay used.

Early attempts at standardisation were made by Biggs and Denson[4] and by Poller[5]: the latter introduced the "Manchester comparative reagent" as a thromboplastin which might act as a reference material against which all other thromboplastins could be compared. British Comparative Thromboplastin[6] was then adopted and results expressed as the British Corrected Ratio; this is the material and method which are still widely used in Britain. The International Committee on Thrombosis and Haemostasis established five reference materials to give a suitable range of comparative thromboplastins.[7 8] After an international trial to standardise these materials the World Health Organisation in 1976 established the International Committee on Thrombosis and Haemostasis reference material 67:40 as the primary World Health Organisation reference thromboplastin. This was a combined thromboplastin containing fibrinogen and factor V and derived from human brain. Secondary World Health Organisation reference thromboplastins were established in 1979, one from rabbit brain without added coagulation factors (International Committee on Thrombosis and Haemostasis reference material 70:178) and a second from bovine brain combined with these factors (International Committee on Thrombosis and Haemostasis reference material 68:434). They were given "calibration constants" of 0·5 and 1·0 respectively, based on various calibration studies.[7-9] The use of these World Health Organisation reference materials is restricted to national reference centres and they are not readily available for the calibration of commercial thromboplastins. Their limited availability coupled with several doubts about their technical suitability as reference materials led the International Committee on Thrombosis and Haemostasis to propose that a supranational thromboplastin calibration study should be undertaken by the European Community Bureau of Reference. They have now developed three secondary reference thromboplastins in sufficient quantity to allow manufacturers and others to calibrate successive batches of their own products.[10 11]

It is difficult to compare one thromboplastin with another because there is no straight line relation through the origin between sets of plasma from normal people and plasma from patients receiving anticoagulant treatment.[12] The phenomenon is probably due to a variation in the interaction of thromboplastin with coagulation factor deficiencies and the presence of varying quantities of abnormal coagulation factor proteins. These problems may be overcome for the therapeutic range of anticoagulant treatment by using a rectilinear relation of the logarithms of the prothrombin times, calculated by using an orthogonal regression equation, the slope being used as a index of the relation.

New primary and secondary reference materials may be required in the future, so that an agreed international method of standardisation of thromboplastin is essential. To this end a workshop on thromboplastin calibration was held recently at the University of Leiden under the auspices of the Boerhaave Committee for Postgraduate Education. It was proposed that the slope of the relation of any thromboplastin to the primary international reference preparation should be designated the "international sensitivity index" in accordance with the recommendations of the World Health Organisation.[13] Manufacturers were urged to introduce a house standard for their thromboplastin and to indicate either on the label or on an insert the slope relating the batch of material to the primary international reference thromboplastin. If this procedure were generally accepted the prothrombin ratio for an individual test could be converted to an international ratio—the "international normalised ratio," defined as the expression of the prothrombin time ratio as measured and corrected to take

account of the thromboplastin calibration slope. This method of reporting would greatly benefit patients taking oral anticoagulant drugs who move around the world and whose dosage is dependent on prothrombin time testing in several different laboratories.

If an international normalised ratio is accepted, the results of different therapeutic trials may be compared which will facilitate agreement on the optimum therapeutic ranges. The haemostasis and thrombosis task force of the British Committee for Standardisation in Haematology supports an earlier recommendation that a single thromboplastin range of 2·0-4·0 should be adopted for all clinical conditions.[14 15] This is known to be safe[16] but different optimum ratios have been proposed for different medical conditions—venous prophylaxis, arterial prophylaxis, and manifest thrombosis with variations for inpatients, outpatients, and surgical procedures.[17] Prothrombin ratios of up to 5·0 using British Comparative Thromboplastin have been considered acceptable for patients in hospital provided that there are no contraindications,[18] but such a level might be equivalent to a ratio of 3·1 if tested with rabbit thromboplastin. At present recommendations for optimum ratios must be related to the type of thromboplastin and to the mode of expression of the ratio, especially when a percentage in terms of saline dilution of the plasma is used. Here a 10% activity might correspond to an international normalised ratio of about 6·5. Use of an agreed international normalised ratio might avoid much confusion. The British Comparative Thromboplastin is generally accepted in Britain, so that a change to an international normalised ratio would cause little disturbance; an international normalised ratio of range 2·5-4·0 would correspond to a British Corrected Ratio of range 2·4-3·8 and an international normalised ratio of 5·0 to a British Corrected Ratio of 4·6. A major step towards the achievement of a standard ratio would be made if all workers on future trials reported their results as an international normalised ratio. Acceptance of this and the definition of optimum ranges for various clinical conditions together with quality control of laboratory tests[19] and rigorous therapeutic control[20] should ensure that oral anticoagulant treatment is rendered both safe and effective in the future.

N K SHINTON

Consultant Haematologist,
Coventry and Warwickshire Hospital,
Coventry CV1 4FH

[1] Quick AJ. Prothrombin in hemophilia and in obstructive jaundice. *J Biol Chem* 1935;**109**:xxiii-iv.
[2] Poller L. Oral anticoagulant therapy. In: Bloom AL, Thomas DP, eds. *Haemostasis and thrombosis*. Edinburgh: Churchill Livingstone, 1981: 725-36.
[3] WHO Expert Committee on Biological Standardization. Twenty-eighth report. *WHO Tech Rep Ser* 1977;No 610:1.
[4] Biggs R, Denson KVE. Standardization of the one-stage prothrombin time for the control of anticoagulant therapy. *Br Med J* 1967;i:84-8.
[5] Poller L. A national standard for anticoagulant therapy. The Manchester comparative reagent. *Lancet* 1967;i:491-3.
[6] Thomson JM, Chart LS. The system for laboratory control of oral anticoagulant therapy using the British comparative thromboplastin. *Journal of Medical and Laboratory Technology* 1970;**27**:207-12.
[7] Bangham DR, Biggs R, Brozovic M, Denson KWE. Draft report of a collaborative study of two thromboplastins (including the use of common abnormal plasma). *Thrombosis et Diathesis Haemorrhagica* 1970;suppl 40:341-51.
[8] Bangham DR, Biggs R, Brozovic M, Denson KWE. Calibration of five different thromboplastins, using fresh and freeze-dried plasma. *Thrombosis et Diathesis Haemorrhagica* 1973;**29**:228-39.
[9] International Committee on Thrombosis and Haemostasis. International Committee for Standardization in Haematology. Prothrombin time standardization: report of the expert panel on oral anticoagulant control. *Thromb Haemost* 1979;**42**:1073-114.
[10] Loeliger EA, Besselaar AMHP, Van den Hermans J, Van den Velde EA. Certification of three reference materials for thromboplastins. Brussels: Commission of the European Communities, 1981. (BCR information series.)
[11] Loeliger EA, Lewis SM. Progress in laboratory control of oral anticoagulants. *Lancet* 1982;ii:318-20.
[12] Kirkwood TBL. Calibration of reference thromboplastin and standardization of the prothrombin time ratio. *Thromb Haemost* 1983;**49**:238-44.
[13] WHO Expert Committee on Biological Standardization. *Requirements for thromboplastins and plasma used to control oral anticoagulant therapy*. Geneva: WHO, 1983.
[14] Blackburn EK. Long-term anticoagulant therapy. *Prescribers' Journal* 1977;**17**:73-4.
[15] Shinton NK. Therapeutic control of anticoagulant treatment. *Br Med J* 1982;**284**:1871.
[16] Barkhan P. Therapeutic range with BCTR. *Thromb Haemost* 1976;**35**:751.
[17] Loeliger EA. The optimal therapeutic range in oral anticoagulation. History and proposal. *Thromb Haemost* 1979;**42**:1141-52.
[18] Poller L. British comparative thromboplastin therapeutic range. *Thromb Haemost* 1976;**36**:485.
[19] Poller L, Thomson JM, Yee KF. Quality control trials of prothrombin time: an assessment of the performance in serial studies. *J Clin Pathol* 1979;**31**:251-3.
[20] Duxbury BMcD. Therapeutic control of anticoagulant treatment. *Br Med J* 1982;**284**:702-4.

Trends in induced abortion in England and Wales

The combination of medicine with anything to do with sex is said to have a paralytic effect on human resourcefulness. Nowhere is this more the case than with induced abortion. The subject arouses strong feelings and even violence: in the United States antiabortion groups have bombed clinics carrying out operations. The very strength of feelings both against abortion and in favour of its free availability is an argument for basing discussion—so far as possible—on objective data. Since 1968 health authorities have been responsible for providing induced abortions under the terms of the 1967 Abortion Act; they need to have reliable information for their planning.

After the 1967 Act the numbers of legal induced abortions performed on residents in England and Wales stabilised first at between 100 000 and 110 000 a year (equivalent to abortion rates of 11·5 per 1000 women aged 15 to 44).[1] These rates—considerably lower than those in the rest of northern Europe and North America—then began to fall in the early 1970s, when contraception became much more widely available. Since 1978, however, the numbers have increased progressively—to 120 600 in 1979 and 128 550 in 1981.[2 3] In the hyperactive world of abortion politics such figures tend to be given more importance and meaning than is justified. In particular, reference must always be made to the age structure of the base population at risk and its related fertility patterns, aspects of which may fluctuate considerably over comparatively short periods of time.

A study[4] analysed the trends in induced abortion and fertility using a novel method of statistical modelling developed by Osmond and Gardner for use with cancer mortality data.[5 6] This method separates the contributions of factors associated with age, period, and cohort, which are clearly likely to play important and varying parts in patterns of fertility and abortion. The analysis showed that the age specific abortion rates increased from 1968 until about 1973, when the rates peaked for all ages; rates then declined until 1977 but have subsequently returned to higher levels. Two important conclusions emerged. Firstly, the recent changes were parallel to changes in the fertility rate; and, secondly, recent cohorts of women have shown a tendency to resort to abortion more readily.