Molecular genetics as a diagnostic service

The major advances in mapping and cloning disease genes during the past few years have been applied with minimal delay to such practical areas as prenatal diagnosis and carrier detection. Following early applications for the thalassaemias, important disorders such as the muscular dystrophies, haemophilias, cystic fibrosis, and Huntington's disease have all come within the orbit of molecular genetics, and most of the other major Mendelian conditions are likely to follow in the near future.

So far these developments have been reported and analysed in terms of the individual disease or group of diseases, and there is no doubt as to their effectiveness in the context of such disorders as β thalassaemia¹ or Duchenne muscular dystrophy.² Much less attention has so far been given to the overall development of diagnostic molecular genetics and to the optimal organisation of services based not on a single disease, but on a broad range of genetic disorders. As the number of diseases where such applications are feasible increases, this overall approach becomes a matter of urgency.

Such assessments as have been done so far³ have been based largely on indirect evidence, especially in relation to the economic aspects. The reports in this issue of the *Journal* are thus especially timely, as they are based on the hard experience of units initiating and developing a molecular genetics service. Four years ago the Health Departments in England and Wales funded three centres for a trial three year period to provide the foundations of a molecular diagnostic service; simultaneously, an independent evaluation of their results and progress was commissioned to allow an objective assessment of the value of this work.

Results are presented here⁴ from one of the centres involved (Manchester), which clearly show the extent and pace with which this field has grown and matured. One of the other centres (Cardiff) has already presented comparable data from its own experience,⁵ so that a picture is now emerging as to how these techniques are being related to new discoveries, to clinical demands, and to existing genetic and other services.

A valuable and practical report giving guidelines for DNA banking also appears in this issue,⁶ which should be of real help to units setting up this important service.

The independent audit also presents its preliminary results here and gives a valuable analysis of the activity of the centres, especially the relationship of molecular genetic diagnosis to the overall work in a medical genetics department,⁷ and the costs involved in establishing and running the service.⁸ While it is too early to form more than preliminary conclusions, several points already seem clear.

First, there can be no doubt that molecular genetic diagnosis has already entered the service era and is becoming established alongside clinical genetics and cytogenetics as a well defined field of activity. The close links between the various branches of medical genetics are a noteworthy feature of the work reported and assessed here. A second relevant point is the relatively modest cost of these new services; while cost-benefit analyses are still in progress, there seems no reason to suppose that prohibitive cost will be the determining feature regarding their provision. Indeed, costs may reduce further with the incorporation of new technical advances, though it must be noted that the associated costs of genetic counselling and related clinical activities need to be fully considered in any economic analysis. A third point of importance is the 'regional' pattern that is emerging, a logical one in view of the similar organisation of other genetic services, and one that the level of activity reported fully justifies in relation to a regional population base of 2 to 4 million people. In this respect it should be noted that the structure of the National Health Service in Britain has so far proved a suitable one for the planned introduction of this service.

Many questions remain as to how future patterns of service will evolve, not surprisingly in light of the rapid changes in technology and scope of the subject. Will a 'supraregional' pattern be preferable for the rarer disorders? (Such a system has been adopted and seems to be working well for the Molecular Genetics Consortium in Scotland.) What will be the relationship between an overall regional molecular genetics service and departments with specific expertise for individual disorders, such as the haemophilias and haemoglobinopathies? Who will take responsibility for common and important disorders such as familial hypercholesterolaemia, which currently are being relatively neglected in the service context? And what will happen when the even commoner disorders, such as manic depressive psychosis and schizophrenia to name but two, have clearly defined susceptibility genes?

All these topics will be the subject for lively debate over the next few years. It is, however, encouraging that as the new field of molecular genetic diagnosis grows, it is doing so in the context of critical analysis, independent audit, and full reporting of its results, all facts which are essential if its role as an established service is to be secure in the future.

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