Annotations

Malformation syndromes—a diagnostic approach

The problem

Seven in a thousand children are born with multiple malformations:¹ many of them will have one of the thousand or so malformation syndromes that have been described in the published reports. All malformation syndromes are rare and it is unlikely that the average clinician, or even the experienced dysmorphologist, will be able to recall all of them and to keep up to date with new reports. Nevertheless, a correct diagnosis is essential before recurrence risks and prognosis can be assessed.

A diagnostic approach

How should the paediatrician approach the diagnostic problem of a child with abnormal physical features or multiple malformations? A detailed pregnancy and family history with information on parental ages and illnesses, exposure to teratogens or mutagens, consanguinity, and possible pointers to intrauterine deformation should be taken. Clinical examination should include objective measurement of abnormalities such as hypertelorism or widely spaced nipples. Physical abnormalities should be documented in detail. For example, the designation of polydactyly is not sufficient—it can be of different degrees, may be pre- or post-axial, and be associated with syndactyly or other digital abnormalities. Wherever possible good clinical photographs should be obtained. Chromosome analysis is essential, together with other investigations for developmental delay where appropriate.

Having marshalled all the clinical information, there are two main roads to diagnosis:

Gestalt recognition.² Where the main abnormality consists of an unusual facial appearance, a diagnosis can sometimes be made by pattern recognition. Conditions such as Down's, Williams', Noonan's, and fetal alcohol syndromes are often diagnosed in this way. This approach is perilous for the inexperienced. If the dysmorphic features are reminiscent of a particular syndrome, but all the features do not quite fit, the child should not be given a diagnostic label. If there are any doubts, it is helpful to reassess

the child in 6 months or a year's time, as the characteristic facial features of many syndromes become more noticeable with age.

A recognisable combination of malformations. Where malformations are present, it is often easier to search for a diagnosis in the published reports by concentrating on a specific abnormality. These malformation 'handles' may be ranked in order of usefulness. For example, a single palmar crease is found unilaterally in 2 to 4% of normal individuals and is present in low frequency in a number of syndromes—it is not therefore a good handle. Anal atresia, on the other hand, has well documented associations with other malformations and is the subject of extensive reviews.³ When present, it is a good starting point when trying to establish a diagnosis.

Further aids to diagnosis. Searching for a diagnosis through appropriate 'handles' is aided by the use of standard text books. Smith's monograph on *Recognizable patterns of human malformation*,¹ contains a useful appendix of lists of syndromes manifesting particular abnormalities. Unfortunately, only syndromes covered in the book are listed and these make up, at most, 20–30% of those reported. Finding recently reported malformation syndromes that are not in the text books is difficult, as they are not referenced in *Index medicus* under specific malformations. It is also likely that many malformation syndromes have not yet been described in the medical literature, as only individual cases have been seen by different clinicians.

Methods are needed to retrieve obscure published reports and to tap the accumulated, unpublished experience of clinicians. Consultation with local, national, or international experts is often fruitful, but a more systematic approach is needed. Computer technology lends itself to the solution of both these problems. One approach is to index all reported malformation syndromes using a master list of physical abnormalities. The computer data base can then be searched by asking for syndromes with specific combinations of these abnormalities. Various refinements may be incorporated to allow a

'loose', as against a 'tight', search (for example, a search could be made for all syndromes with hand abnormalities, rather than all syndromes with polydactyly). This simple approach lends itself to implementation with microcomputers, which are relatively cheap and accessible, and such a system has already been developed in London.⁴ In a more ambitious approach the computer is programmed to assess a list of physical abnormalities and to produce a ranked list of possible diagnoses—at present, however, this entails the use of a large main frame computer.⁵ Both systems need to be evaluated.

Computers can also be used to store data on undiagnosed cases which can then be compared to define new syndromes. Since this approach requires input from many clinicians, informal dysmorphology meetings, where paediatricians and clinical geneticists discuss difficult or unusual cases, are a useful source of information. Such a group meets regularly at the Institute of Child Health in London.

The correct diagnosis of rare dysmorphic syndromes cannot be dismissed as 'stamp collecting'. In these days of increasingly sophisticated prenatal tests such as fetoscopy, accurate recurrence risks must be assessed for the correct management of future pregnancies. Every effort should be made to

establish a diagnosis in all cases, and this process should include searches of published reports and access to computer systems and panels of experts.

References

- ¹ Smith DW. *Recognizable patterns of human malformation*. 3rd ed. Philadelphia: WB Saunders, 1982.
- ² Gorlin RJ. Diagnosis of craniofacial anomalies: subjective evaluation/gestalt. *Birth Defects* 1980;xvii[5]:35–46.
- ³ Pinsky L. The syndromology of anorectal malformation (atresia, stenosis, ectopia). *Am J Med Genet* 1978;1:461–74.
- ⁴ Winter RM, Baraitser M. A computerized data-base for the diagnosis of rare dysmorphic syndromes. *J Med Genet* 1983;in press.
- ⁵ Buyse M. Centre for birth defects information services. *Birth Defects* 1980;xvii[5]:83–91.

R M WINTER
Kennedy Galton Centre,
Harperbury Hospital,
Radlett,
Hertfordshire WD7 9HQ

AND
MICHAEL BARAITSER
Department of Clinical Genetics,
Institute of Child Health,
30 Guilford Street,
London WC1