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LETTERS TO THE EDITOR

A clinical and genetic database for management of familial adenomatous polyposis

Cachon-Gonzalez *et al* (*J Med Genet* 1991;28:681-5) describe their experience with four linked DNA markers (π 227, C11p11, YN5.48, and ECB27) flanking the familial adenomatous polyposis (FAP) locus. They conclude that "lod scores are sufficiently high to allow the use of these probes in presymptomatic diagnosis". In the absence of large bowel adenomas or extra-colonic manifestations of the FAP gene, a Bayesian approach to risk assessment, incorporating age of onset and DNA data, may guide clinical screening policy. We have developed a computerised regional register for FAP (called 'MegaBASE/FAP') which facilitates both risk assessment and coordination of screening examinations for the extended families of index patients.

The core of the register software is the pedigree and this can be viewed on screen and printed out for use in the clinic. The main database contains information relating to administrative, screening, surgical, pathological, and genetic aspects of patient management, and this can be viewed and edited either on a text based screen or directly on the pedigree.

From the genotypes stored on each family member, input files for the LINKAGE¹ programs can be written automatically within the database, which also contains a built in age of onset curve specified as 20 liability classes. The time consuming and error prone manual creation of LINKAGE files is thereby avoided, making risk evaluation both simpler and more reliable.

Cachon-Gonzalez *et al* have suggested that closely linked markers might now be usefully incorporated in the modern management of FAP. By integrating clinical and genetic information our database has facilitated this development for families with FAP in our region.

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1 Lathrop GM, Lalouel JM. Easy calculations of lod scores and genetic risks on small computers. *Am J Hum Genet* 1984;36:460-5.

High proportion of twins in carriers of fragile X syndrome

Vogel¹ hypothesised that the extraordinarily high mutation rate in fragile X (fra X) syndrome can be reduced to conventional proportions if moderately increased fertility of clinically unaffected females (CUF) is assumed. The author concluded that this may be the result of an equilibrium between an increased reproduction rate in CUF and a decreased fertility in their affected relatives, and that equilibrium would require more than a doubling of the reproductive rate especially in CUF. An indicator of fertility in women is the dizygotic twinning rate, which

is a consequence of an increase in ovarian stimulation by FSH (follicle stimulating hormone) and is influenced by maternal age and birth order.²

We have studied 65 women diagnosed as obligate carriers in 44 Spanish families with fra X syndrome in our Molecular Genetics Unit. In 10 of these carriers (15%), twins were observed in their progeny, with one carrier having three cases (total no = 12). Six cases were dizygotic and in the remaining six zygosity could not be determined. In total, the 65 carriers had 213 children and the twinning within this group was 1/18, in contrast with the twinning in our population of about 1/70 births.³

Similar data were reported by Fryns⁴ in a study of the progeny of 144 obligate female carriers with a high incidence of twinning at 1/35 births (18/642), and Sherman and Turner⁵ found that the twinning rate in their fra X carriers was 1/42 births (18/752), significantly higher than the twinning rates in their respective countries. Fryns concluded that these observed two to four-fold increases in the frequency of twinning among fra X carrier women may be evidence for a dysregulation of the cortico-hypothalamo-hypophysal axis in fra X syndrome. In support of this, large ovaries and ovarian cysts have been reported in heterozygous fra X syndrome girls,⁶⁻⁸ oligomenorrhoea and premature menarche have been reported in several related fra X carrier mothers in a large Dutch pedigree,⁶ and at least two cases of precocious puberty have been reported in fra X girls.^{9,10}

We think that our results are in agreement with the hypotheses of Vogel and Fryns and indicate once more the importance of performing more accurate investigations regarding ovarian stimulation, fertility, and fra X syndrome.

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BOOK REVIEWS

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International Nomenclature of Diseases. Vol VI. **Metabolic, Nutritional and Endocrine Disorders.** (Pp 464; SFr 25.00.) London: The Council for International Organizations of Medical Sciences and the World Health Organization. 1991.

It is a difficult but very important job to define disease names that can be used internationally and which are unlikely to change rapidly. The Council for International Organizations of Medical Sciences and the World Health Organization, together with their many eminent advisors, are to be congratulated on doing just that. This is volume VI and the first to be of particular interest to geneticists. Further volumes are planned and these will include ones on musculoskeletal disorders, immune disorders, and diseases of the eye. *International Nomenclature of Diseases* is complementary to the *WHO Classification of Diseases* and neither replaces nor duplicates it.

For inclusion in these directories, a disease must be a well defined pathological entity, and the name for it should be simple, unambiguous, and descriptive. I am thankful that the use of numbers, initials, and eponyms are avoided where possible, although they are listed under synonyms. Older names for enzymes are also listed under synonyms and are indexed, so there is no difficulty about learning to use the correct name. There are brief notes on each disease and these are a model of precision and clarity.

The wide scope of this book is shown by its divisions into sections on inborn errors of metabolism (all genetic), disorders of steroid and endocrine metabolism, disorders of red cells and of haemoglobin, disorders of platelets and clotting, amyloidoses, collagenoses, muscular dystrophies, nutritional defects, diabetes mellitus with its syndromes, and endocrine tumours. There are also included some benign metabolic conditions so that they may be identified as 'non-diseases'.

The authors recognise that individual enzyme defects will be caused by different genes, and even by genes at different loci. Therefore they have chosen the enzyme defect as a basis for naming most of the diseases in this book. This is of great practical value. Only in the amyloidoses are DNA mutations included in the definition. It seems a good idea to use DNA mutations rarely, since they are being recognised at such a rate that disease names which incorporate them will have to be modified and expanded in the near future. It is helpful to a non-biochemist to have the biochemical basis of disease so clearly and correctly described in this handbook. As an example of how the editors are obsessed with correctness, the reader is even shown how to write glucose 6-phosphate and glucose-6-phosphatase.