A156E1[11] probes in the PWS/AS region) showed the PWS/AS region to be present twice in the marker (data not shown).

The parents of the index patient are illiterate, went to a school for children with learning difficulties, and have a simple job in a sheltered environment. They have had no seizures.

In 18 out of 32 lymphocytes analysed in the mother, the same marker was present. The karyotype of the father was normal. The marker was not found in 100 lymphocytes from the maternal grandparents. Sibs of the mother were not available for further study and we have no information on their mental status.

Numerous cases of small familial inv dup(15) supernumerary markers have been reported.[2357] Apparently, most of these markers have no adverse phenotypic effects. Many of these familial cases have been ascertained accidentally by prenatal screening. To our knowledge, however, only three familial cases of inv dup(15) where mental retardation was a feature have been reported.[12-14] All retarded probands in these three families inherited the marker from their mother. One of these mothers was not retarded herself, but she was a proven mosaic. Another two families, ascertained through mentally retarded probands, have been reported. However, in these cases it was not likely that the mental retardation could be attributed to the inv dup(15), since other carriers of the familial marker were not retarded.[513] In both families the inv dup(15) was small and unlikely to contain the PWS/AS region. Finally, one report concerned a prenatal diagnosis of an inv dup(15) in a carrier mother, who was described as "mentally slow". No information on the development of the child was presented.[15]

In the present report another family is described, in which an inherited inv dup(15) is associated with mental retardation. To our knowledge this is the second familial case where the presence of additional copies of the PWS/AS region was shown by molecular techniques,[14] and the first familial inv dup(15) in which two extra copies of this region were identified. This case confirms that an inv dup(15) may be inherited, even when two copies of the PWS/AS region are present in the marker. The phenotype caused by such a large marker, however, does not always have to be severe, but may be milder owing to a mosaic state, as illustrated by the mother of our index case. The use of FISH probes for the PWS/AS region appears to be of importance in counselling parents, who may be mosaics for an inv dup(15) supernumerary marker, with respect to the expected phenotype of their non-mosaic offspring.

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Simple tests for rhodopsin involvement in retinitis pigmentosa

Retinitis pigmentosa (RP) is an inherited retinal degeneration affecting approximately 1 in 5000 people.[1] The genetic basis of RP is complex, with X linked, autosomal dominant, and autosomal recessive inheritance, and multiple loci for each form. This makes it difficult for diagnostic laboratories to provide useful information to RP patients and their families, especially in dominant RP, which maps to at least eight different loci. However, our work on dominant RP over the last five years indicates that there are three simple tasks which a clinical genetics diagnostic laboratory could carry out as a starting point for DNA analysis, each of which have a reasonable chance of providing useful information.

Published estimates for the frequency of rhodopsin mutations as a proportion of dominant RP range from 20 to 31%,[2-4] but our own recent analyses in large families suggest a figure as high as 50% (Inglehearn *et al*, manuscript in preparation). Rhodopsin is therefore a good candidate gene for patients with a dominant family history, and it has also been implicated in several cases of recessive RP.[5 6] The markers which have been used in the past to exclude rhodopsin as a candidate RP gene are C17 (D3S47), the RFLP marker first linked to ADRP at 3q21,[7] and a microsatellite in intron 1 of the gene itself.[8] However, C17 is now estimated to be some 18 cM from rhodopsin[9] while the intragenic microsatellite has a heterozygosity of only 33%. We have therefore placed the rhodopsin gene on the microsatellite map of Gyapay *et al*[10] by linkage analysis in rhodopsin RP families. Haplotype analysis (data not shown) locates the rhodopsin gene in a 5 cM gap between markers D3S1589 (heterozygosity 0·68) and D3S1292 (heterozygosity 0·85). By pooling data in linked families we obtained maximum lod scores of 8·55 at $\theta = 0{\cdot}07$ from marker D3S1589 and 21·75 at $\theta = 0{\cdot}02$ for marker D3S1292. These are therefore highly informative microsatellite markers with which to test for rhodopsin linkage in dominant RP.

Screening for mutations in the rhodopsin gene is also complex, since over 60 have now been reported.[11] The Pro-23-His mutation was found to account for 12% of US ADRP.[12] However, this has not been reported in any other populations[13] and is now thought to represent a founder effect. Two other mutations have been reported in different populations. Pro-347-Leu has been seen in US, UK, German, and Japanese patients[4] and three other base substitutions have been found at the same site. Similarly, Thr-58-Arg has been reported in both US and UK populations. These are therefore probably mutation hotspots for rhodopsin mutations leading to ADRP and may be worth screening in dominant and sporadic cases of RP. This can be done by a simple assay involving PCR amplification followed by restriction digestion, using *Msp*I for codon 347 (destroys a site)[14] and *Dde*I for codon 58 (creates a site).[15] Our own data on screening for these mutations showed five patients with the codon 347 Pro-Leu substitution and two with the codon 58 Thr-Arg substitution. These were identified in a sample of 120 RP patients who attended the Moorfields Eye Hospital genetic clinics and gave a family history indicating dominant RP. It is worth noting that both codon 58 pedigrees have a rare sectorial RP phenotype. Sectorial RP cases should therefore be made a priority in testing for the codon 58 mutations.

In summary ADRP families can quickly be assessed for linkage to rhodopsin, using markers D3S1589 and D3S1292, which span the locus. In addition around 6% of dominant RP cases can be characterised by simple PCR/restriction digestion tests at codon 58 and 347 of the rhodopsin gene.

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BOOK REVIEWS

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Fetal Medicine: Prenatal Diagnosis and Management. Editor André Boué. (Pp 292; £50.00). Oxford: Oxford University Press. 1995. ISBN 0 1926 1904.

With the rapid increase in mapping and cloning of genes for many human diseases, more and more prenatal diagnosis becomes technically possible. Newer methods, such as interphase FISH for prenatal diagnosis of chromosomal aneuploidies, are now beginning to emerge on the clinical scene. Faced with the prospect of being superseded almost immediately, the production of a textbook covering such an expanding field is a daunting task.

Undaunted, Boué *et al* have written a comprehensive textbook which covers a wide range of topics. They include sections on basic cytogenetics and molecular genetics, as well as detailed descriptions of the procedures involved both in prenatal sampling and in sample analysis. The book does not set out to cover all the areas of fetal medicine, and issues such as ultrasound based diagnosis, isoimmunisation, or exchange transfusion are specifically excluded. However, the use of prenatal diagnosis in the management of maternal viral infection is covered, with detailed discussion of the relative merits of specific diagnostic tests. It is clear from the text that a great resource of practical experience in prenatal diagnosis in France has been brought together, and that the authors have a deep understanding of the problems and pitfalls in fetal medicine.

The book is aimed at obstetricians, general practitioners, and paediatricians, to help them address the questions asked by their patients. There is an appropriate emphasis on detection of chromosomal aneuploidies, but the short section on maternal serum screening does not discuss the improved detection brought about by triple marker screening. A large chapter on prenatal diagnosis of single gene disorders covers both biochemical and DNA based diagnosis of a wide range of conditions. For some diseases, there are discussions of the clinical genetic issues for families at different degrees of risk. There is a considerable amount of detail on the specific DNA markers used in different monogenic conditions. All the markers mentioned are RFLPs analysed by Southern blot, which in many cases have now been superseded by PCR based microsatellites, of which there is no mention. The amount of technical detail may be somewhat overwhelming for the general reader, especially as such detail must inevitably become outdated. There is only a brief reference to PCR in the section on molecular methods, which is unfortunate, as PCR is not the mainstay of DNA technology in molecular diagnostic laboratories.

The editor has wisely included a chapter on ethical issues in prenatal diagnosis, and focuses on the ethical implications of "screening" for genetic disease in selected populations, citing the statements of the French National Consultative Committee on Ethics. Boué also rightly emphasises that prenatal diagnosis needs a multidisciplinary approach, and involves obstetricians, clinical and laboratory geneticists, and ultrasonographic expertise.

This textbook also draws together information from different disciplines, and has successfully covered a large area of the management of pregnancies at increased risk of disease. Even though the editor accepts that the volume will rapidly be superseded, the core of this textbook will remain valuable for a considerable time to come.

ANDREW GREEN

Catalog of Teratogenic Agents. 8th edition. T H Shepard. (Pp 542; £76.00.) Baltimore: Johns Hopkins University Press. 1995. ISBN 0 8018 51823.

Champions of the electronic age claim that reference books are now outdated, to be replaced by online databases and CD-ROM based information retrieval. This new edition of a well known and comprehensive catalog(ue) shows that there is still a place for high quality, well indexed, and up to date reference books. The author has built on the work of previous editions to produce a clear and well referenced book covering the teratological effects of many pharmacological agents, as well as physical agents, maternal viral infection, pesticides, specific occupations, and even such events as a maternal suicide attempt.

The style is reminiscent of other publications from the Johns Hopkins University Press, and the book has been generated by a computer program similar to that used to produce another major catalog(ue), *Mendelian Inheritance in Man*. For each entry there is a presentation of the relevant data in sequence, starting with human epidemiological studies, thence to case reports of teratogenic effects in humans, and finally to animal experiments, followed by a comprehensive reference list. The author wisely does not attempt to classify an agent into a specific grading of severity, but cites the data and allows the reader to make an appropriate interpretation. For some agents, he may preface the entry with a clear, brief summary of the issues for a particular suspected teratogen, or cite a major review of the issue.

The individual teratogenicity of illegal drugs is well covered. The practical issue of the interaction of these agents in a mother who takes several such drugs together is often more difficult to address. The teratogenicity of newer designer hallucinogens is as yet unknown, especially with the variable purity of such agents. The same caveats must also apply for new medicines coming onto the market, as their human teratogenic effects are as yet unknown, and cannot be covered in a catalogue such as this. The point about species variability in thalidomide teratogenicity is well made.

Specific entries dealing with issues such as folate deficiency, anticonvulsants, and cytotoxic agents are clear and to the point. There are the odd transatlantic differences in nomenclature which make tracking a particular agent difficult, but once found the data are well presented. There is a good and interesting entry on the teratogenicity of video display terminals, and Shepard quotes that it is a "shame that we may be terrorizing a generation of women without a clear scientific imperative to do so". This is the only indirectly expressed opinion in the catalogue that I could find, which reflects the clear thinking and scientific approach of the author.

I would recommend this book for its breadth of entries and clarity of presentation. It shows that there is still a place for a good book in a world of electronic information.

ANDREW GREEN

Principles and Practice of Sleep Medicine in the Child. R Ferber, M Kryger. (Pp 254; £33.00.) UK: Harcourt Brace & Co. 1995. ISBN 0 7216 4761 8.

There is much evidence that persistent sleep disturbance is very common and that it can have serious psychological or even physical effects, and yet this topic is often marginalised or ignored in professional teaching and training courses. Sleep disturbance specific to children generally receives even less attention. However, this book would provide a clinician