PostScript

BOOK REVIEWS

The Century of Mendelism

Editors Robert A Peel, John Timson. London: The Galton Institute. 2000. ISBN 0 950 40666 X.

This is a collection of elegantly written, informed, and informative essays on some current issues of genetics in relation to society, health, and other matters. Most of these were papers read at the 2000 annual conference of the Galton Institute. The general topic "The Century of Mendelism" is introduced appropriately by Peter J Bowler's "Rediscovery of Mendelism", which expresses doubts that it really was rediscovery, but rather discovery with reversion to Mendel's findings as support of the results.

Bowler, like others before him starting with Curt Stern in 1967, also questions the significance of Tschermak's role in the "rediscovery". Mark Ridley in "Genetics in the new millennium" covers some of the same territory as in his "Mendel's Demons" (2000).

The Galton Lecture was given by Robert G Resta on "Genetic counselling - its scope and limitations". To Madge Macklin he attributes invention of the designation "medical genetics", in the 1930s. He gives the date of Lejeune's discovery of trisomy 21 as 1957 (not 1959) and refers to Victor McKusick as a paediatrician. These are minor errors; on the whole, the discussion of the goals of genetic counselling and its limitations, as well as the question of whether genetic counselling should always be non-directive, is balanced.

In Colin Tudge's essay on "Problems of genetic engineering", he suggests it might better be called "genetic gardening", particularly when referring to genetically modified organisms (GMOs). He gives a discussion of ethics and morality unexpected in such a presentation. He looks, for example, at the great principles underlying the major religions, as given by Ramakrishna: humility, respect for fellow human beings and other fellow sentient creatures, and reverence for the Universe.

Sandy Raeburn discussed genetic issues in insurance and employment and how to prevent unfair discrimination.

The Galton Institute is not to be confused with the Galton Laboratory. The latter designation was coined by Lionel Penrose in 1954 to describe the department at University College London that was originally called the Department of Eugenics. Penrose used it on his headed notepaper until the name of the department was changed to Department of Genetics in 1956. Many who worked in the Galton Laboratory in the 1950s and since have intense affection and loyalty for that name.

The Galton Institute evolved about 10 years ago from the National Institute of Eugenics which was established at University College London from a bequest of Francis Galton (1822-1911). As stated by the cover blurb, the "Galton Institute is a learned society founded in 1907. Its four hundred members are drawn from a wide range of disciplines including the biological and social sciences, medicine, law, and administration. One-fifth live abroad. The Institute holds an annual conference ... and publishes the proceedings. It also publishes a quarterly newsletter. Membership of the Institute is open to all who support its aims" [which are not stated in the blurb].

The current president of the Galton Institute, Professor J S (Steve) Jones of UCL, is definitely not a eugenicist but is an effective communicator and leading ambassador for human genetics to the public.

Victor A McKusick

Myotonic Dystrophy

3rd ed. Major Problems in Neurology Series. Peter S Harper. (£55.00.) London: Harcourt. 2001. ISBN 0 7020 21520

As with the second edition of this book, published back in 1989, this third edition is an excellent account of clinical and scientific aspects of myotonic dystrophy. The book is easy to read, sustaining this reviewer's attention to scan the whole book in a single sitting, while subsequently being of value as a reference for closer consultation on specific clinical and scientific details. As stated in the preface, the book is aimed at "clinicians ... who encounter myotonic dystrophy in its numerous aspects and who need a broad overview of all the different areas" and "research scientists ... trying to interpret ... their work in terms of the broader effects on the disease". The book is aimed well. "Broad overview", "broader effects" - myotonic dystrophy involves a variety of clinical systems and presents to a variety of physicians, and the value of this book is in this wide scope, to inform about clinical and scientific areas.

The book is divided into 14 chapters. All but one of these is written by Peter Harper, thus ensuring continuity of style. The Introduction and Background gives an excellent overview of the disorder, noting the "avoidable catastrophes" that are known to occur in myotonic dystrophy. There follows an excellent chapter on the clinical features of the disease, written by one with immense clinical experience. Advice such as examining for myotonia, even when patients deny its existence, and the sections on social aspects of disability in the disorder are particularly pertinent. The chapter on other myotonic disorders gives a useful overview of the clinical disorder of proximal myotonic myopathy (PROMM), with a useful table comparing the clinical features of this with those of myotonic dystrophy and with helpful clarification on the nomenclature of DM1 and DM2 in relation to the differing phenotypes. There then follows a series of chapters outlining the clinical features resulting from involvement of specific systems, including smooth muscle, the brain, the eye, and the endocrine system. These chapters are

a mine of useful information. Figures such as "25% of patients consider their gastrointestinal symptoms to be the most disabling feature of the disorder" stuck with this reviewer. There is a clear table detailing practical recommendations for surgery and anaesthesia in myotonic dystrophy, both pre- and postoperatively. The sections on the complications of pregnancy in the disorder are similarly clearly presented and informative. A separate useful chapter follows on the disorder in infancy and childhood.

It is not until one is three-quarters of the way through the book that the chapter on the genetic basis of myotonic dystrophy is reached. This is the area in which huge advances in understanding have been made since the last edition of this book. As with the clinical chapters, this is a lucid account of the finding of the unstable CTG repeat sequence in the 3' untranslated region of the myotonic dystrophy protein kinase gene. This chapter and that following on "Molecular and cell biology of myotonic dystrophy" are concise overviews of the recent molecular biological advances. They cannot be comprehensive, but rather give an excellent grounding for those who want to delve into the more detailed scientific publications.

And what of the down sides of the book? Criticisms here relate to the publication style rather than the content. The general quality of the illustrations is fairly poor, with all figures and photographs in black and white. There is odd shading in several of the clinical photographs. The reproduction of the CT and MRI images is poor. The histological slides shown would be greatly enhanced if they were in colour. In many places the figures and legends are several pages removed from the appropriate text, making smooth reading awkward. A list of the abbreviations used throughout would be useful. More diagrams in the sections detailing molecular genetic mechanisms would be helpful.

These "publication" criticisms, however, are minor and stand in stark contrast to the excellent text. Yes, a book is always going to suffer the drawback of delay in time to publication. Advances in the molecular understanding of myotonic dystrophy have continued apace since this volume was published last year, not least with the exciting discovery of CCTG expansions within *ZNF9*, the DM2 gene, on chromosome 3q21 in August 2001. This does not mean that a volume such as this is obsolete. Far from it. The background, detailed clinical information and, I return to this word again, "broad" overview given in this work, provide an excellent, readable, and retainable account of myotonic dystrophy. I highly recommend this book.

Karen E Morrison

**Oxford Medical Databases:
London Dysmorphology
Database Version 3.0. London
Neurogenetics Database Version
3.0. Dysmorphology Photo
Library on CD-ROM Version 3.0**

R M Winter, M Baraitser. (CD, £1595.00.) Oxford: Oxford University Press 2001. ISBN 0198510780.

Most clinical geneticists are familiar with the Oxford Medical Databases and new versions

of these Databases are eagerly awaited. Version 3.0 of the London Dysmorphology Database (LDDb), London Neurogenetics Database (LNDB), and Dysmorphology Photo Library has been completely updated. This version of LDDb contains information on 3428 dysmorphic syndromes with over 33 000 references. The new version of LNDB has also been expanded and covers 3292 neurogenetic disorders and syndromes involving the central and peripheral nervous systems with over 36 000 references. Version 3.0 of the Dysmorphology Photo Library contains 12 742 photographs, 1355 more than the previous version.

Both Databases and the Photo Library are included on a single CD-ROM. Minimum system requirements for the package include PC with Pentium processor and CD-ROM drive, 32 MB RAM, 150 MB free hard disk space, VGA monitor with 800 × 600 screen resolution and, Internet Explorer 4.0. The software is compatible with all versions of Windows from Windows 95 onwards (including the recently introduced Windows XP). The Databases and Photo Library were easy to install and worked well with Windows Millennium Edition.

Like the previous versions, this version is an authoritative source of information about dysmorphic and neurogenetic syndromes. Although LDDb mainly contains information about non-chromosomal multiple congenital anomaly syndromes, it also includes information about a few distinctive chromosomal deletion or microdeletion syndromes and syndromes resulting from uniparental disomy of different chromosomes. Both Databases have a detailed record for each syndrome with information about its chromosomal location (if known or relevant), McKusick number, synonyms, gene symbol, inheritance pattern, an abstract card, a features card, references card, and photo card. The abstract card provides a compact but informative review of the syndrome. The features card contains an exhaustive list of clinical features and the references card lists all the key published references for that syndrome. The photo card is a superb collection of photographs that show the main facial dysmorphic features of the syndrome and other relevant images, such as skeletal survey, hair microscopy, etc. In the case of neurogenetic syndromes, the photo card contains CT and MRI images showing their characteristic neuroradiological features, examples of EEG changes or the changes observed on other key electrophysiological investigations and, where relevant, pictures of the characteristic neuropathology (including nerve and muscle biopsy).

One of the most useful functions of these Databases is their ability to allow the user to search for syndromes based on the features of a patient. In LDDb these include mainly clinical and/or radiological features, whereas in LNDB a search can be carried out using age at onset of neurological features, neurological and other clinical features, neuroradiological findings, changes seen on electrophysiological investigations, abnormal biochemistry, and neuropathological findings. Syndromes can also be searched for by McKusick number, inheritance pattern, or by references. References can be searched for by their title, author(s), journal, year of publication, or publisher.

An important feature new to this version of the Databases is a new look user interface with a user friendly toolbar. For users who are familiar with version 2.0 of these Databases, it

is possible to configure the display to the style of the previous version with buttons instead of the toolbar. Other novel features of this version include major changes in the photo card and the photograph viewer. These include the ability to change the size of the thumbnails of the images in the Photo Library, display several or all images for a syndrome simultaneously for comparison, and import selected images of a syndrome from the Photo Library to a personal collection of images called "My Collection". It is also possible for users to import clinical photographs of their own patients into "My Collection", thus allowing comparisons to be made with the images in the Photo Library. Most picture file formats are supported, such as JPEG, Windows Bitmap, and Tagged Image File Format, making this a very useful function. There are also links from the Databases to Online Mendelian Inheritance in Man (OMIM) and Medline in case the user wishes to obtain more information about an individual syndrome or reference.

Another important feature of version 3.0 is the ability to download regular updates to both the LDDb and LNDB online, at no extra cost. This will allow the Databases to remain up to date with all recent advances, especially with respect to identification of genes for well recognised syndromes and delineation of new dysmorphic and neurogenetic syndromes.

Both Databases are relatively easy to use, even for first time users. However, a working knowledge of clinical dysmorphology and neurology is necessary to harness their full potential and in order for these Databases to be used effectively. It is difficult to find fault with any aspect of the Databases. The only drawback is the price of the combined package (£1595 + VAT for the single user version and £1125 + VAT for the single user upgrade). Although the Databases and Photo Library can all be purchased individually, the cost of each component (£595 + VAT for the single user version and £425 + VAT for the single user upgrade) is still prohibitive and will dissuade most clinicians from buying a copy for their personal use.

The clinical genetics community owes a huge debt of gratitude to the two authors of these Databases. It is difficult to envisage the practice of clinical dysmorphology and neurogenetics without access to the LDDb, LNDB, and Dysmorphology Photo Library. For most clinical geneticists faced with an unknown dysmorphic or neurogenetic syndrome, these Databases are likely to be the first port of call. A thorough search of the Databases will often suggest a diagnosis for such patients. It is this reviewer's firm belief that no clinical genetics or neurology department can afford to be without these Databases. Perinatal pathologists and paediatricians will also benefit enormously from access to them.

Mohnish Suri

Fragile X Syndrome - Diagnosis, Treatment and Research

Third edition. Editors Randi Jenssen Hagerman, Paul J Hagerman. £65.50 HB, £31.00 PB. Baltimore: The Johns Hopkins University Press. 2002. ISBN 0-8018-6844-0.

This is the third edition of a book that is already well known to clinical geneticists and genetic counsellors. Probably, just as many

scientists from the cytogenetic and DNA laboratories are familiar with the title. The first edition was printed in 1991, at the same time that the mutation that causes fragile X syndrome was identified. When the second edition appeared in 1996, much more could be written about the gene product, FMRP. Advances in understanding molecular and cellular changes in fragile X syndrome have proceeded, but in smaller increments in more specialised fields. The neuroscientific aspects of the syndrome are thus allotted more space in this new edition and, perhaps related to this, there has been an editor substitution with Paul Hagerman, spouse of Randi and molecular arm of the husband-wife collaboration, replacing Amy Cronister, who continues to make a major contribution co-authoring the chapter on genetic counselling.

To make room for new information on neuroscience, the chapter on cytogenetics of fragile X syndrome has been cut but, really, this omission should be regarded as a sound reason for retaining the second edition on the bookshelf. Happily, the opening chapter by Randi Hagerman is not shortened as it contains a wealth of clinical information including perfect illustrations of macroorchidism and the value of a Prader orchidometer. Older geneticists may wistfully recall epic estimations of testicular volume in burly men pre-1991, but new trainees need only gaze in astonishment at these pictures and perhaps give silent thanks for the trinucleotide repeat.

The essays in this edition also provide a good illustration of how one dramatic discovery, the CGG expansion, clarifies much that was previously perplexing, but also leads to many more complex questions being posed. Ted Brown's very clear chapter on the molecular biology of the fragile X mutation sits alongside Stephanie Sherman's fascinating account of the syndrome's epidemiology, but self-congratulatory feelings about one's adult learning capacity are then dashed by detailed state of play reviews of protein studies, an animal model, and the brain structural phenotype. After this, a review of the neuropsychology of the syndrome brought home to me the importance of a technical approach to the definition of behavioural phenotypes, and wound up the first half of the book.

In the second half, essays explore treatment options and give practical advice on dealing with learning difficulties and troublesome behaviours. Much of the best advice is of a general nature and is not specific to the management of children with fragile X syndrome. The chapter on drug therapies will also be of interest to the paediatrician or specialist in learning disability who supervises clinical management. The accounts of academic and psychological interventions that may improve quality of life for affected subjects and their families contain much information that is of value to teachers and therapists. To close, there are useful appendices with web and e-mail addresses for general information, educational software, and other helpful resources.

In summary, this is a book that may be read by the fireside; especially pleasing are the many paragraphs that supply historical background to major discoveries about the syndrome, but the book's main use is for reference purposes. Quite simply, it should always be consulted when considering clinical problems.

John Tolmie