Fundamentals of Genetic Epidemiology. Muin J Khoury, Terri H Beaty, Bernice H Cohen. (Pp 283; £35.00.) Oxford: Oxford University Press. 1993.

This is the first book which attempts to pull together all aspects of genetic epidemiology from the design of family studies through to linkage mapping and association studies. The major problem with producing a book on genetic epidemiology is to decide on the approach; either a single author could produce a detailed treatise on one aspect (as did Elizabeth Thompson, for example, in *Pedigree Analysis in Human Genetics*) or multiple authors might venture to produce a broader span. These authors (an epidemiologist, a statistical geneticist, and a human geneticist) took the latter approach and produced a largely seamless, readable volume where topics flow easily from one to another (and presumably from author to author). The book covers four broad areas: background and fundamentals of genetic epidemiology, population studies of genetic traits and genetic factors in disease, family studies (including segregation and linkage analyses), and applications of genetic epidemiology in medicine and public health. Many topics are covered in impressive detail, for instance, the case control study focusing on family history and the methods of segregation analysis. This probably represents both the strength and the weakness of the book (depending upon the reader's interests), the strength because of the detail of the methods but the weakness is that, in some instances, the text "catalogues" without giving indications of the reasons for choosing one method over another (for example, when to study extended families instead of nuclear families for segregation analysis).

Overall this is an admirable effort which should make many graduate student's life easier. There are few places where most of the covered topics are reviewed in any more detail than presented here, and this volume effectively ties the topics together. The one person that this book probably cannot help is the scientist who has performed a study and is having trouble interpreting the results of complex analyses as in perhaps segregation or linkage analysis; such detail is beyond even this volume.

D T BISHOP

The Calculation of Genetic Risks: Worked Examples in DNA Diagnostics. Peter J Bridge. (Pp 208; £37.00.) Baltimore: Johns Hopkins University Press. 1994.

At first glance this looks rather an old fashioned book. Flicking over the pages gives a powerful flavour of a time when almost all DNA diagnostics required an informative pedigree, typed for one or two two-allele markers, with a hard sum at the end. No PCR dot blots in those days, you had to really understand the genetics! A happy few people developed a great skill at reducing almost any genetic problem to a Bayesian calculation, done by hand on a suitably large piece of paper. Like people who can do the foxtrot, they are to be envied for their accomplishment – but isn't it all a little obsolete?

Not at all, says Peter Bridge. To use a computer package intelligently and safely, you need to have in reserve the ability to do the calculation by hand, at least approximately,

so as to appreciate which factors contribute to the risk. And the current computer packages cannot cope with several factors which can crucially affect the final risk, such as germinal mosaicism or the risk of maternal cell contamination. So there are chapters on Bayesian risk calculations for X linked and for autosomal diseases, using the pedigree alone or including biochemical or DNA data or both. There is also a chapter on linkage and lod scores which, characteristically, concentrates on showing how you can work the scores out by hand in suitable pedigrees.

The numerous worked examples raise most of the issues which need to be appreciated by anyone reporting genetic risks, whether they use a pencil or a computer to derive the numbers. It is not a general manual for genetic counsellors, being almost entirely focused on mendelian diseases where linked markers can help, nor does it deal with zygosity or paternity testing. Looking at the competition (and there is not much), Young's *Introduction to Risk Calculation in Genetic Counselling* (OUP 1991) covers a wider field, but has only 30 pages on using linked markers. Within its chosen area, Bridge's book is very thorough. Every combination of pedigree structure and marker data is discussed, with numerous tables showing the result of systematically varying one or more parameters. To me it has a strong flavour of somebody who has achieved total familiarity and total command of Bayesian methods through blood, sweat, and tears, and is now setting out his wealth of rather homespun lore for the benefit of non-mathematical readers.

Thus what you get is closer to a bench cookbook than an illustration of the intellectual outlines of the subject. There is a tendency to produce rules which work, rather than principles. For example, I don't think Bayes's hypothesis is ever formally stated, though it underpins the whole book. Whether you like this or not is a matter of taste, but it is no doubt a deliberate choice of emphasis, to make it user friendly to non-statisticians. If you worked your way through, you would undoubtedly build up a very substantial competence in risk estimation. And even in these days of direct mutation analysis, experience shows that you need genetic knowledge to understand what the result means. So the body of knowledge about how genetic markers should be used, which has been built up in DNA diagnostic laboratories over the past 10 years, is by no means obsolete, and this book does a service in codifying it.

ANDREW P READ

Chromosomes: A Synthesis. Ed R P Wagner, M P Maguire, R L Stallings. (Pp 523; \$89.95.) New York: Wiley-Liss. 1994.

Books on chromosomes can generally be classified into two categories: those written by biologists not working with human chromosomes in which the biological part is well presented, but data useful to those interested in medical and human cytogenetics are scarce or lacking, and those written by experts in human chromosomes in which the fundamental genetic part is absent or insufficiently presented. The present book falls into the first category. Written by well known experts, it is what it says, a synthesis of the knowledge of chromosomes in general. It is subdivided into the following chapters: (1)

Basic Chromosome Structure; (2) Chromosome Organization; (3) Chromosomes and the Cell Cycle; (4) Genetic Recombination; (5) Variations in Chromatin Organization and Amount; (6) Transcription and Its Regulation; (7) Chromosome and Gene Activity in the Interphase; (8) Gene Linkage and Chromosome Maps; (9) Organization of Genomes and their Chromosomes; (10) The Evolution of Genomes and their Chromosomes.

Each chapter contains a historical introduction, a box or boxes highlighting the main points, instructive illustrations, and a short summary. The medical genetics reader will especially enjoy the chapters on genetic recombination, transcription, and organisation of genomes. I found the chapter on the interphase not sufficiently up to date and lacking important newer aspects relevant to medical genetics. Likewise, the linkage and mapping paper does not deal thoroughly with chromosomal mapping methods, such as microdeletion mapping, phenotypic mapping, candidate gene approach, and mapping through structural chromosomal rearrangements. Among structural chromosome rearrangements, for example, no mention is made of the rare types of unbalanced segregation and of insertions. The impact of chromosome aneuploidy on the phenotype is not discussed. The new molecular methods recently introduced for the study of cryptic chromosome aberrations and aberrations which cannot be fully clarified with the traditional techniques are not appropriately dealt with to enable researchers to use them in cytogenetic laboratories. The rate of 1:200 for unbalanced chromosome aberrations in man is probably too high (p 274); likewise, the statement that deletions and duplications occur at random in all chromosomal segments (p 285) is most likely not true in man.

The nomenclature used is in many parts not that common and generally accepted in medical genetics. I found only very few typing errors and obvious errors in the field of medicine. The references in general are up to date to about 1990.

To summarise, the present book is useful for medical geneticists wanting to obtain an introduction to chromosomes in biology. It is not a standard book for cytogenetics, including human cytogenetics, and it is also not of high value for biologists wanting to learn medical aspects of cytogenetics. For such a work which would consider the rapid progress during the last years, medical cytogeneticists will still have to wait.

A SCHINZEL

Genes V. Benjamin Lewin. (Pp 1272; £29.95.) Oxford: Oxford University Press. 1994.

Previous editions of *Genes* will be familiar to most readers of this journal. The text is widely used in undergraduate teaching as well as by those of us who need to update our general knowledge of molecular biology from time to time. The author suggests that "studying genetics essentially means dealing with DNA, and in many respects *Genes* could be viewed as a textbook of modern genetics". For the editor of *Cell*, it is eminently logical to consider that what is going on inside the cell is paramount. The basic organisation of the

book remains unchanged from the previous edition, with sections on: DNA as a store of information; Translation: Expressing genes as proteins; Constructing the cell; Control of prokaryotic gene expression; Perpetuation of DNA; Organization of the eukaryotic genome; Eukaryotic transcription and RNA processing; The dynamic genome: DNA in flux; and Genes in development. Post-translational events, the intracellular localisation of proteins, the control of the cell cycle, and RNA processing are now treated in more molecular detail. The development section in fact comprises three rather specific chapters, about 40 pages each, on vertebrate immunobiology, embryonic development of *Drosophila*, and oncogenes. Few human examples are used, except in two of these last three chapters: the two page discussion of imprinting gives just one mouse example.

A consequence of this approach is that other aspects of genetics get little treatment. For example, mitosis is discussed mostly in terms of the cell cycle; meiosis with Mendel's first and second laws figure concisely in the introductory chapters; and recombination, after two paragraphs mentioning its evolutionary significance, is analysed solely in terms of the mechanisms involved. There is brief mention of topics such as minisatellite repeats and their use in gene mapping and DNA profiling, but it would be hard for the student to appreciate their significance.

Genes has gone through five editions in a decade. The weight of the text has increased over the last three editions from 1.3 kg through 1.9 kg to the present 2.8 kg. Part of this growth is accounted for by the increased content, but much of it is because of the use of a larger type face. The book is well produced with many diagrams, now in full colour. Bigger does not necessarily mean better, so just how good is the latest version? The book tells an interesting story over a wide field, and it tells it clearly and generally with commendable accuracy. But it tells it in a "Just So" manner. Unlike the earliest editions, which tried to show what kind of work had led to the conclusions presented, experiments are not consistently integrated into the presentation of the topics. Molecular methods are described, but PCR rates just one page of text and one diagram of the basic procedure; I did not find a description of RT-PCR. The author explicitly states that the control of bacterial gene expression is now treated in terms of DNA-protein interaction rather than the original genetic characterisation. This makes for a clear presentation, but at a rather different level of understanding. Present day students often seem to find it difficult to think in genetic as well as molecular terms and this text would not help them. The book is excellent in its own terms, but before using it for teaching, it would be important to ensure that the very molecular approach is compatible with course objectives.

ALISTAIR STEWART

Molecular Genetics of Sex Determination. Ed S S Wachtel. (Pp 518.) London: Academic Press. 1994.

The title of this volume does itself a disservice by being both too inclusive as well as too exclusive. Aside from a single chapter on *Drosophila*, the contents are solidly mammalian. However, the treatment of humans extends beyond sex determination to include

molecular genetic and clinical aspects of sexual differential. As such, this book provides a thorough and current treatment of mammalian sex determination.

The book is divided into two parts. The first section begins with descriptions of the search for the mammalian Y chromosome located testis determining factor (TDF), followed by chapters detailing the basic biology of sex determination as elucidated through work on the mouse, marsupials, and *Drosophila*. The latter half of the book is devoted to human biology, with chapters ranging from sex chromosome structure through the molecular and clinical aspects of abnormal sexual development syndromes.

The initial two chapters provide an historic delineation (with much overlap) of the trials and tribulations of the search for TDF. Although these chapters may have been better located among the chapters on humans, the placement of these at the beginning of the book emphasises the intense effort to identify this gene. Substantial information has been obtained from mouse experiments, in particular relating to the genetic aspects of sex determination. These experiments are well covered, with chapters on the mouse Y chromosome structure, XX males, XY females, and X chromosome inactivation. Evolutionary conservation of X linkage across eutherians is discussed, as well as the utility of marsupials and monotremes in studying evolution and genetics of mammalian sex determination. A chapter on sex determination in *Drosophila* is well written and informative, but seems out of place in this volume. It appears in isolation without additional chapters on non-mammalian systems and offers no insights into mammalian sex determination. The remainder of the book is devoted to human sex determination and differentiation with initial orientation provided by chapters on the human Y chromosome structure and on the sequence homology between the X and Y chromosomes (which offers a particularly clear presentation of complicated information). These are followed by chapters on XX sex reversal, XY sex reversal, and X chromosome loss. The remainder of the book details genes and genetic defects associated with normal and abnormal sexual differentiation: androgen insensitivity, male pseudohermaphroditism, steroid 21-hydroxylase deficiency, and anti-Müllerian hormone activity.

Overall, the content provides a good overview and ample background on sex determination in mammals. In general, the chapters read well, and the information is detailed and complete. A fair amount of overlap occurs between chapters, particularly regarding the cloning of TDF. This may prove irritating to those who wish to read sequentially through the book, but it does allow each chapter to be complete unto itself. This book is recommended as a reference for researchers in the field of sexual development, as well as a current text suitable for graduate students.

ALAN J SCHAFER

Human Cytogenetics Database. A Schinzel. (£395.00. Annual upgrade £150, OUP estimate. Extra manuals £7.50 each.) Oxford: Oxford University Press. 1994

The long wait for the update of Albert Schinzel's *Catalogue of unbalanced chromosome*

aberrations in man has been worthwhile. In keeping with the times, this new edition comes as PC compatible software, using the software shell developed for the *London Dysmorphology Database*. The *Human Cytogenetics Database* is unarguably the most comprehensive catalogue available of the many rare cytogenetic aberrations and their clinical correlates and contains information on over 1000 autosomal chromosome aberrations. This information comes from more than 5000 references and there is now a continuing update system in place to ensure the database remains current.

The database may be used as a comprehensive source of references by those seeking details about the phenotype associated with rare cytogenetic aberrations as well as an aid to clinical and cytogenetic diagnosis. The clinical features associated with specific cytogenetic aberrations are conveniently listed, while patient clinical features are easily entered and then used to identify candidate regions of the genome that may benefit from more detailed cytogenetic assessment.

There are features in the program which will appeal to both cytogeneticists and clinical geneticists. Besides providing a list of clinical features associated with a chromosomal aberration, an extra table is created which summarises the frequency of occurrence of these features. This summary table, created from all the clinical data in the case reports from each reference, will become increasingly useful as the database expands.

Searching by using patient features uses the clinical features list created for the *London Dysmorphology Database*. For those familiar with the LDB, the likeness creates an encouraging familiarity. Searches are easily set up although clinical searches benefit from a flexible approach using knowledge about the frequency and likely specificity of the various anomalies. Likewise, clinical interpretation of cytogenetic aberrations is dependent on the accuracy of the cytogenetic detail and, occasionally, extra contributing molecular information. Rather than lessen the need for cytogenetic and clinical skills, the *Human Cytogenetics Database* highlights the value of each and how interdependent these skills are. In addition, the comprehensive reference list is easy to search or browse through.

A helpful feature of the program is the capacity to jump to the right position in a list containing several thousand items. This feature, developed for the LDB, is useful for the reference list. However, it has limited application in the main list of chromosomal aberrations which has no simple numerical code to allow a jump to a particular chromosome. The program also has a section which provides an IQ measurement, based on data from the published case reports of chromosomal aberrations associated with mental retardation. Unfortunately, this potentially useful summary statistic cannot be obtained from the program. OUP have indicated the underlying fault is minor and should be overcome by the next upgrade. One advantage of the database over the earlier book is inclusion of uniparental disomy for a number of chromosomal regions.

Further comparison with the book shows two disadvantages. The first is exclusion of sex chromosome abnormalities which makes the database less encyclopaedic. The second is the lack of a brief introductory summary for each abnormality. The summary tables do give this information in a numerical form, but this is less digestible than the format of