Pain is then considered at the two ends of the life spectrum—in children and in older people. It is difficult to imagine what direction these two chapters should take. They fall somewhat short in the analysis of pain in relation to sociodemographic variables—such as gender—but attempt to give prevalences. I might have been more interested to understand more about the interpretation and perception of pain in these two groups and found myself wondering at the end of the chapter what the prevalence figures really meant.

The book then goes on to consider pain in a number of different conditions. The choice is interesting, although somewhat eclectic, including fibromyalgia and chronic widespread pain, chronic post-surgical pain, phantom limb pain, central post-stroke pain, migraine and headache, facial pain, tempro-mandibular disorder pain, neck pain, shoulder pain, low back pain and knee pain. It was not clear why the editors chose these particular conditions. If the book is to be concerned with populations, then I would suggest that any future edition should consider pain in arthritis (although the chapter on knee pain considers this a little) and pain in cancer. That said, however, each of the chapters is extremely well written and researched and there is a particularly valuable meta-analysis looking at migraine. These chapters would be of enormous value to anyone with a particular interest in those individual topics. The authors have made an enormous effort to prepare systematic reviews and are to be commended for the amount of work and consideration given to these individual chapters.

In summary, the book is a useful introduction to epidemiological approaches in the management of pain and provides excellent resource material for the individual topics considered. It does not include all pain—no textbook ever could—but it is a worthy addition to the bookshelves of individuals studying pain and epidemiology.

IRENE J HIGGINSON


Epidemiology aims to elucidate mechanisms of disease and disease transmission and identify susceptible subgroups in the population. Contributors to this book are concerned with measurement of associated biological markers with a strong emphasis on genetic characteristics. Host genotype can influence the risk of infection and disease development, just as it can predispose to non-transmissible multifactorial disease. In Chapter 1 Eric Engels and Thomas O'Brien provide a comprehensive and clear overview of epidemiological design theory and analysis, which sets the rest of the book in context. The applications of cohort and case-control designs and measures used to quantify risk are well explained. Not every strong association is causal and the possible influence of confounding or chance in assessing risk based on genotype is also addressed.

The rise of bacterial strains with pathological phenotypes and the development of multi-drug antibiotic resistance has highlighted a need to identify and monitor their origin and spread. In Chapter 2 Eric Brown summarizes current Polymerase Chain Reaction (PCR)-based techniques for bacterial genotyping and strain discrimination, including repetitive PCR fingerprinting, rDNA PCR (‘ribotyping’) and randomly amplified polymorphic DNA PCR. The protocols, as in the other chapters with methodological bias, are set out in separate panels adjacent to commentary in the text, a visually effective format. The most accurate and powerful method for bacterial strain discrimination remains DNA sequence analysis and references for several strategies are given.

Chapter 3 considers the complicated issues of detection and quantification of viral targets, using Human Immunodeficiency Virus (HIV) as a model. The sequence heterogeneity within and between HIV groups makes the design of efficient single primer pair/probe systems for detection of variants extremely difficult. The first part covers general principles of PCR primer design, based on Shirley Kwok’s extensive investigations of the effect of mismatch to targets on amplification efficiency. Advice given on increasing assay sensitivity and reducing false positives makes this section well worth consulting in any experimental situation where sensitivity and specificity in PCR is proving problematic. The second part of the chapter provides detailed protocols for the extraction, amplification, detection and quantification of HIV RNA and DNA, which will be of primary interest to virologists working in this area.

In Chapter 4 Michael Dean, Bernard Gerrard and Rando Allikmets examine mutation detection by Single Strand Conformation Polymorphism (SSCP) and Denaturing High Performance Liquid Chromatography (DHPLC). The principle advantage of SSCP is its speed and use of standard laboratory equipment. The authors claim high sensitivity, but this requires the additional effort of varying gel running temperatures and matrix composition to generate conditions for alternative conformations. Preparation of the traditional long thin acrylamide gel is described but no mention is made of the alternative, ABI 310 capillary electrophoresis, which operates under temperature-controlled conditions, makes for higher throughput in automated loading and substitutes fluorescence for radioactivity. Multiplexing is useful for a larger number of samples but as any practitioner of this method knows, interpretation of long SSCP gel patterns with even a single loading can present a challenge. In DHPLC, DNA molecules are eluted by size from a non-porous column in an increasing gradient of acetonitrile at temperatures determined by a melting algorithm. Heteroduplexes denaturing at lower concentrations than homoduplexes are detected as peaks with shorter retention times. After an expensive initial outlay on apparatus, this rapid, non-radioactive, automatable, high sensitivity method is probably superior to most other mutation detection methods available.

Attention has recently turned from rare Mendelian disorders to the more intractable and arguably more pressing problem of understanding the aetiology of complex diseases resulting from relatively common genetic variation. Full genome association studies require costly individual genotyping of large DNA banks. In Chapter 5 Lisa Barcellos, Soren Germer and William Klitz describe methods in which DNA from many individuals sharing disease status are combined for genotyping, with allele frequency differences determined between the case and control pools. Nuclear or trio families can also be used. The need to quantify individual DNA samples to fix equal template concentrations is a tedious pre-requisite to this approach, involving duplicate
Determinations in each sample, a substantial task in large cohorts, and re-quantitation of duplicates differing by 5%. Simultaneous detection of several groups of Short Tandem Repeat (STR) markers with overlapping sizes is possible on the ABI automatic sequencer using different fluorescent dyes. Most of the high throughput Single Nucleotide Polymorphism (SNP) genotyping methodologies require varying degrees of post-PCR processing, but in one method, by monitoring allele-specific PCR in real time, delay in mismatch amplification can be used to determine minor SNP allele frequencies of a few per cent.

Single-sperm typing provides an efficient means of measuring recombination frequencies by direct determination of the haplotype of each meiotic product, using PCR to identify alleles at multiple polymorphic sites along the chromosome. In Chapter 6 Michael Cullen and Mary Carrington describe fluorescence activated cell sorting to isolate individual sperm and whole genome amplification using random primers to provide PCR templates. For multiple SNP typing, multiplex PCR requires a set of compatible allele-specific primers, which also create differences in product length for multiple allele detection in a single lane. The authors only describe radioisotope-based methods for detection of STR and SNP alleles, however resolution of fluorescent labelled multiplex PCR products on the ABI sequencer is an obvious and probably preferable alternative.

The HLA class I and II loci are the most polymorphic coding sequences in the human genome. In Chapter 7, Henry Ehrlich and Elizabeth Trachtenberg review current PCR-based methodologies. The reverse blot has proved a major advance in HLA typing. Although it demands specific hybridization to a large set of immobilized probes under a given set of conditions and minimal secondary structure in the labelled target single stranded PCR product, a number of commercially available tests now incorporate this method. Recent introduction of capillary based systems (e.g. ABI 310) has increased throughput and decreased the cost of chain termination sequencing using fluorescent tags, but it still remains an expensive procedure not ideally suited to large scale or routine clinical typing.

In epidemics caused by the sudden emergence of a strongly pathogenic parasite strain, knowledge of its evolutionary origin is often a first step in devising strategies for its control. The final chapter, contributed by Austin Hughes, Jack da Silva and Federica Verra takes a philosophical rather than practical approach and deals with the conceptual background to some of the commonly used methods of molecular sequence analysis and their application to data of epidemiological relevance. Numerous references are given for those interested in a mathematical treatment of the issues covered. The true phylogenetic tree illustrating the actual relationships among genes or organisms is in general unknown, so statistical methods based on comparison of sequences are used to reconstruct it. The strengths and weaknesses of the main approaches to construction and testing reliability are reviewed.

This book provides both comprehensive background information and detailed protocols for the practical analysis of the aetiology of disease in the post Human Genome Project era. Although the emphasis is on infectious disease exposure, progression and susceptibility, sections relevant to complex disease and the effective design of molecular genetic approaches make this a volume of significant general interest.

SANDRA O’DELL