Clostridium difficile: methods and protocols

P. Mullany, A. P. Roberts eds. New York: Humana Press/Springer Verlag, 2010. ISBN 978-1-60327-364-0. 228 pp. €94.95. £85,50 (Hardback).

This book is Volume 646 of the 'Methods in Molecular Biology' series published by Humana Press, which is now part of the Springer Science and Business Media group. The series can be found in the Springer protocols website and individual chapters may be accessed there (www.springerprotocols.com). Indeed, it was possible to review the book online at the Springer main web page, although such a prospect did not appeal to this reader.

Following a review chapter on the clinical disease, the contents are what one would expect from a book concerned solely with practical methods (i.e., a sequential series of steps covering the methods in question, dotted with practical hints and tips). The book contains a strong emphasis on molecular genetic methods including typing (e.g., pulse-field gel electrophoresis, ribotyping, toxin typing of the PaLoc region), multilocus sequence typing (MLST; for evaluating more fundamental evolutionary genetic changes) and methods for studying gene control regions and comparative microarray analysis of the organism. As opposed to random mutagenesis, controlled gene manipulation has only become feasible within the past few years following the introduction of methods devised for clostridia in the laboratories of Nigel Minton and Julian Rood, and both get chapters on their respective methods.

There is little for those attempting to study the pathogenesis of *Clostridium difficile* with host epithelia, which perhaps reflects the difficulties of working with pathogens of the intestinal tract. Two experimental animal models are covered (guinea pig and mouse) as they yield different outcomes: aggressive disease in guinea pig and milder disease in the mouse. One chapter on human intestinal epithelial response includes protocols for real-time polymerase chain reaction (PCR) methods on tissue culture cells (e.g., Caco-2, HT-29, etc.) along with immuno-fluorescence imaging of tight junction (occludin) and a very scanty outline of what is needed to measure transepithelial electrical resistance. A couple of chapters do not provide any figures or data illustrating a typical experiment. Is it that useful to see a protocol for imaging occludin changes – not a dramatic visual change at the best of times – without knowing what to look for?

Another limitation to such books is that they tend to preach to the converted. The introductory sections for most chapters are too short to provide anything but the briefest of introductions to the methods. Space presumably prevents a critical review of the results and their interpretation. Thus, only someone who knows what MLST is will seek out the appropriate chapter. It would seem to me that replacing the first chapter on clinical disease with a more hard-nosed review of what the methods can and cannot do at the end of the book is more appropriate to the type of reader interested in experimental methodology.

Some of the figures and photomicrographs are poor (e.g., those on pages 12, 44, 113, 140, 141 and 208). These monochrome photomicrographs are close to useless, not due to the absence of colour but because the murky images fail to illustrate anything useful. However, the publisher tells me that something has gone wrong with the reproduction process, as the pictures should be in colour. So, while the book is physically very robust with a nice glossy hard cover, the smaller font text has that very slight tendency to break up in the Abstract sections of some chapters.

The target audience of such a book is probably not diagnostic laboratories. Only the chapter on isolation and cytotoxin testing (Michael Wren) originates from such a laboratory, but research laboratories will find it valuable. *C. difficile* has been an increasing clinical problem in the UK, if not further afield, and this is reflected in the predominantly UK/European authorship.

The practical and theoretical concerns presented by this organism have developed since the publication of the book. The evidence for the need for both or just one of the toxins to cause the disease in animals has continued. The nature and use of intestinal markers such as lactoferrin and bacterial enzymes (GDH) in faeces as predictors of infection have all been published subsequently. Assuming the chapters were written in 2008 (as judged from the latest references) these topics were not covered.

It is all too easy to say that this is a useful book for those interested in the organism, but that is probably true. I am quite sure that typing and MLST methods, for example, are generic and could be found in many other books. If so then a book on *C. difficile* should concentrate on methods specific to the organism in question (e.g., details of specific isolation methods, purification and labelling of the toxins, details of the sequenced genome) but then it can argued that the emphasis is on molecular genetic methods. A circular argument, no doubt.

In summary, specialists and beginners at the bench will want the collection of methods applicable to their organism to be found in one place, and that is what this type of book offers.

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Hematopathology: Genomic Mechanisms of Neoplastic Diseases

D. Crisan ed. Heidelberg: Springer Verlag, 2010. ISBN 978-1-60761-261-2. 370 pp. €159.95 (Hardback).

The past few decades have witnessed the slow and steady encroachment of 'practical' genetics into pathology. The present volume summarises the position for haematologists in a series of nine highly technical and unashamedly academic chapters.

The first sets the scene with an overview of molecular techniques, ranging from specimen collection and processing to the extraction of nucleic acids, and concludes with a description of seven types of polymerase chain reaction. Chapter 2 is devoted to classical and molecular cytogenetic analysis of haematolymphoid disorders, focusing on karyotypic and other methods for determining chromosome abnormalities (e.g., inversion, deletion, etc.). The principal technique in this area, fluorescence *in situ* hybridisation (FISH), is explained, and is then applied to diseases such as myelodysplastic syndrome, the leukaemias

and the lymphomas. Chapter 3 then moves on and discusses using these cytogenetic and molecular tests in diagnostic work-ups; for example, in differentiating the host of different lymphomas, whereas Chapter 4 looks at molecular pathology of precursor lymphoid leukaemias.

The fifth chapter provides a thorough discussion of the molecular pathology of the acute myeloid leukaemias, listing all relevant chromosome aberrations and mutations, and explains the precise molecular lesions that lead to disease, such as the inappropriate activation of tyrosine kinase genes that have downstream roles in apoptosis, proliferation and differentiation. Chapter 6 offers similar explanations in the lymphomas, such as how certain mutations generate fused genes and therefore their protein products.

Chapter 7 is perhaps my favourite as it deals with probably the most well-characterised genetic lesion, that of the Philadelphia chromosome and its characterisation as a *BCR-ABL1* fusion producing altered tyrosine kinase activity. What follows is a fascinating account of the development of the tyrosine kinase inhibitor imatinib, and how this serves as a template for the development of other drugs. This chapter also describes a second mutation, *JAK*2 V617F, and its role in other disease such as polycythaemia rubra vera.

Chapter 8 explains deletions, translocations and trisomy leading to chronic lymphocytic leukaemia, and also looks at high-throughput molecular methods (e.g., gene array) to assess these mutations. The book concludes with a Chapter on targeted therapies, such as monoclonal antibodies (e.g., to CD20) and small molecule drugs (e.g., the tyrosine kinase inhibtors and drugs inducing apoptosis).

Each chapter is heavily referenced (often over 100) with full-colour photographs and diagrams. It is certainly an example of a highly technical reference volume that has been put together with great care by undoubted academic experts. Consequently, it will find a home in regional cytogenetics units, but perhaps less so in routine laboratories.

A. D. Blann

Clinical Biochemistry

N. Ahmed ed. Oxford: Oxford University Press, 2010.
ISBN: 978-0-19-953393-0. 714 pp. £34.99.

Biomedical science forms the foundation of modern healthcare and spans a broad and complex subject area. The 'Fundamentals of Biomedical Science' series of books aims to blend the essential basic science with insights into laboratory practice to provide an understanding of how biology of disease is coupled to the analytical approaches that lead to diagnosis and treatment monitoring in the modern healthcare environment. *Clinical Biochemistry* is one textbook in this series of nine books and attempts to provide a knowledge resource suitable for undergraduates, trainees working in the field, and particularly those undertaking professional qualifications.

There are 22 chapters written by various authors currently active in the field. The layout of the book generally has some very nice features. Each chapter is introduced with a set of learning objectives, followed by an introduction to the subject area. The text is interspersed with excellent, clear and colourful illustrations and various coloured inset boxes which contain useful additional information. For example, there are numerous green boxes containing useful case studies, pink boxes highlighting key points from the text, orange boxes with self-check questions, and green cross-referencing boxes to other chapters and, in some cases, to other books in the series.

Unfortunately there is no consistency to the use of these features, with some chapters using the cross-referencing and information boxes more than others, and some for different purposes. Each chapter finishes with a brief summary, references for further reading, and a set of questions. The answers to these questions, coupled with some additional useful content, are available through an online resource. The book also has useful tables of reference ranges for the more common biochemical analytes, and at the end a glossary of terms

The first chapter is an introduction to the subject which lays the foundation of the modern clinical biochemistry department and features a potted history of the development of the discipline. It is a well-written and illustrated chapter covering the essential basics involved in the functioning of a modern laboratory, from method validation, quality control and quality assessment, specificity and sensitivity, accuracy and precision to the audit cycle. Another useful topic – automation – is the subject of the following chapter and covers the development and principles of the modern automated analysers and robotic systems currently found in many laboratories. The following 20 chapters cover topics such as kidney disease, hyperuricaemia and gout, clinical enzymology and biomarkers, disorders of calcium, phosphate and magnesium, biochemical nutrition, specific protein markers, to mention just a few.

The chapter on lipid abnormalities uses the blue information boxes to include interesting snippets such as the possible naming of Kringle domains after the Danish doughnut, and the discovery of statins. These tend to increase the interest factor for the reader.

The pituitary gland and its disorders are dealt with in a single chapter but is supplemented by further separate, well-focused chapters each dealing with diabetes, thyroid disease, reproductive endocrinology, and the adrenal gland. There is a well-structured and informative chapter on inherited metabolic disorders which describes the laboratory investigations that can be used to aid the diagnoses of the various disorders. Brief coverage is given to each of the groups of metabolic disorders and screening programmes for inherited disorders. Notably, there is no mention of antenatal screening for Down's syndrome.

The last two chapters provide a good overview of therapeutic drug monitoring and chemical toxicology. These aim to provide the reader with a practical insight into dealing with sampling and the laboratory investigations involved with drug analysis, and include the pros and cons of the various methodologies available for the analysis of these substances. Generally, however, only brief coverage is given to the analytical tests and thus the biomedical science student or newly qualified practitioner will not find sufficient information on the basic science which lies behind the laboratory investigations described in this book. However, when coupled with other suitable texts that cover