Infections and glycolipids

A recent case report in the journal described a Gaucher’s disease patient, dangerously infected with salmonella that responded poorly to antibiotic treatment. However, use of enzyme replacement with glucosylceramide gluco-oxidase lowered tissue levels of glucosyl-ceramide (GlcCer), and produced a slow but dramatic improvement. The article points out that infection is an important aspect of the genetic disorder. I would like to mention important observations that explain this unfortunate complication and their significance for many patients with infections.

Many research studies have shown that a wide variety of bacterial and viral infections involve binding of the organism to a glucosphingolipid in the cell surface. Patients with Gaucher’s disease accumulate not only GlcCer, but also some of the more complex glucosphingolipids formed from GlcCer. This second order accumulation explains why these patients are susceptible to infection. In the case of salmonella,’ the organism binds to GlcCer and acidic glucosphingolipids.

It follows then that depleting glucosphin- gloipids in people should reduce the number of binding sites for infectious agents and, possibly, prevent the development of new infections. If the glucosphingolipids already bound to infectious particles are in a reversible equilibrium, we can expect that a decrease in the body’s total glucosphingolipid content will force the infectious particles to leave the body, one way or another. This, basically, is why enzyme replacement helped the Gaucher’s patient.

Lowering cellular glucosphingolipids has indeed been shown to reduce adherence of pathogenic species. Mice depleted of their glucosphingolipids resisted colonisation of the urinary tract. Interference with HIV-1 progression by glucosphingolipid depletion is especially promising. Studies of this sort utilised inhibitors of GlcCer synthase.

Other approaches can also achieve reductions in cellular glucosphingolipids. Caloric restriction has long been known to extend life, slowing the appearance of infections, cancer, atherosclerosis, and other serious illnesses. Brief fasting or caloric restriction might prove helpful in fighting a current infection. This approach should also be helpful for micro-organisms that bind primarily to glycoproteins.

Other means of slowing glucosphingolipid synthesis have been described. These include the use of chlorpromazine, tamoxifen, ver- pamit, RU-486 (mifepristone), antiandrogens, all-trans retinoic acid, and cyclolizer. Glu- cosamine, widely used to prevent joint pain, should compete against glucose, lowering the level of uridine diphosphoglucose.

Biosynthesis of the GlcCer precursor, ceramide, can be slowed by inhibiting sphingomy- elin hydrolysis. This can be done by avoiding arachidonic acid, a stimulator of the enzyme. Dietary fats should therefore be restricted to olive and canola oil. Glutathione, the major thiol in cells, slows sphingomyelin hydrolysis and should be maintained at a high level by eating a glutathione precursor, N-acetyl cysteine. 3-O-Methyl sphingomyelin is a direct inhibitor of the hydrolase. Supplementing the diet with modest amounts of antioxidants will protect glutathione against oxidation. Carnitine, available as a food supplement, helps lower tissue fatty acids by speeding their oxidation. (Since ceramide is formed from two molecules of fatty acid, general fat depletion might be helpful.) The level of ceramide can also be lowered by stimulating its conversion to sphingomyelin by reaction with lecithin; ergo, eat extra lecithin. Glc- Cer, the simplest glucosphingolipid, is normally degraded by hydrolysis, which can be speeded by phosphatydilserine, available as a food supplement.

Shere proposes some explanations for his patients’ complaints about their lymph glands, but surprisingly fails to mention adre- nal insufficiency as a possible cause of those symptoms. Enlargement of lymph nodes is one of the many of clinical features that CFS shares with primary adrenal insufficiency. As a consequence of their common adrenal abnormalities, CFS and Addison’s disease also share an additional feature, namely, impaired production of dehydroepiandroster- one sulphate, which is secreted from the adrenal glands.

I believe that a careful evaluation of the adrenal function of patients with CFS would have enlightened Shere more than did all other investigations combined.

R Baschetti
Retired Medical Inspector of the Italian State Railways, CP 671, 00010–970 Fornelles [CE], Brazil, baschetti@bayenet.com.br

References


BOOK REVIEWS

The reviewers have been asked to rate these books in terms of four items: readability, how up to date they are, accuracy and reliability, and value for money, using simple four point scales. From their opinions we have derived an overall “star” rating: * = poor, ** = reasonable, *** = good, **** = excellent.

Narrative-based Primary Care: a practical guide.


The progressive decline in GPs’ morale has resulted not only from an increasing workload, but also from awareness that patients,
the NHS, and GPs themselves now place less value on the work that GPs perform. Having progressed from the traditional role of simply dispensing medicine and wisdom with an unquestioning patient, GPs need to address the challenges of clinical governance, evidence-based medicine and patient empowerment, while maintaining their own sanity and even self respect.

Narrative-based medicine focuses on enabling a patient to “tell his story”. This forms the basis of an interaction where the listener’s intervention serves to “improve” the story. By embracing the patient’s narrative, GPs can understand his “agenda” and negotiate a management plan that is more likely to be acceptable and to work. John Launer guides the reader from the theory into the practice and teaching of this approach within the GP consultation. This requires the GP to become an expert listener (not just to what the patient says, but also how and when), and to become more reflective and honest (both intellectually and emotionally). Putting this into practice involves repeatedly testing ideas or beliefs (I was struck by the analogy to the approach of Popper) without underestimating expertise, and then acting within “currently accepted systems of thought”, which will change over time. Open minded and reflective GPs, particularly those involved in teaching, will benefit both thought provoking and useful. Already, I have changed my opening greeting to “What would you like to tell me about?”

L S Levene
General Practitioner, Leicester, UK

How To Survive in Anaesthesia. 2nd Edition

This is aimed at trainees in their first year of anaesthesia. The book’s lighthearted, easy reading style cleverly passes on the tips and techniques that experienced anaesthetists use to avoid the disasters that lurk around every operating theatre corner. The 2nd edition of the book has been reduced in physical size to facilitate carrying around operating theatres and wards as a pocket book for easy reference. The book is presented in three parts. The first part covers the “nuts and bolts” of anaesthetic practice with chapters dedicated to airway management, vascular access and fluid therapy, anaesthetic equipment, and monitors. The second part has eight chapters on “crises and complications” and the third part titled “Passing the gas” gives practical advice on administering anaesthesia for the common types of surgery that a trainee is exposed to in the first few months. The last two chapters of this section—“Anaesthesia in the corridor” and “Anaesthetic apherotics” (apheresis = pitty saying!) nicely complete the book with several of my own favourite apherotics included. Throughout the book are numerous pink boxes presenting the important information of the chapter or important management plans for a problem in a concise form; these are listed at the beginning of the book for easy reference.

A splendid read. Only one word of caution—some of the politically incorrect messages of the last chapter should be taken with a pinch of salt.

P Spiers
Consultant in Anaesthesia and Critical Care.
Leicester General Hospital, UK

Pathways in Surgery. 3rd Ed.

Teaching medicine is an art, constantly undergoing change, with mechanisms for imparting knowledge being continuously challenged and criticised. Certain aspects of medicine, and in particular surgery, will always need to be didactic and some of my best memories from medical school emanate from forcefully delivered lectures which left no room for lateral thinking, a far cry from today’s problem orientated learning processes.

The editors and authors have combined both styles and have sought to provide a comprehensive textbook covering all aspects of surgery, both core general surgery and relevant subspecialties. The book seeks to provide a “roadmap” for common symptoms and signs and has been divided up into non-emergencies and emergencies. The style and arrangement of the book are different from other textbooks of surgery. The focus is on symptoms and signs which the surgical trainee is likely to encounter, and works backwards to show how one can identify which of several possible diseases produced that clinical picture. I have to say that I found this quite difficult and rather unstimulating, though this probably represents my own medical training in a more traditional didactic environment. The book suffers from a minimum of colour, presumably for economic reasons, which makes reading and assimilating more difficult.

Nevertheless, overall this book is very comprehensive, offers great value for money, and probably lends itself very well to today’s problem orientated approach to medical education.

B Moran
Consultant Surgeon, The Hampshire Clinic, Hampshire, UK

Statistics in Clinical Practice. 2nd Ed.

This book starts by describing how statistics are used to summarise data in numerical and graphical form. Particular topics included are different forms of data, measures of central tendency and dispersion, and the normal distribution. Further chapters deal with probability and how statistics can be used in interpreting clinical data and drawing conclusions. Topics described here are sensitivity, specificity, p values, confidence intervals, standard error, and statistical power. The final chapters deal with statistical modelling including linear regression and assessment of bias.

The text is clearly and concisely written with many worked examples and questions to explain the concepts. I would highly recommend the book to both qualified health professionals and students in training who want a basic understanding of statistics and how they can be used to interpret clinical papers. It will also be of value to those wanting an introduction to research methodology. The book is reasonably priced at £14.95.

R A Hart
Consultant Gastroenterologist, West Norwich Hospital, Norwich, UK

Teaching and learning in clinical contexts: a resource for health professionals
A new web based learning programme for clinical teachers has been launched (www. clinicalteaching.nhs.uk). It has been developed as part of a London Deanery initiative to develop web based educational packages to support training of doctors and other health professionals. The project has been led by Dr Shelley Head, Dean of Postgraduate Medicine at the London Deanery and managed by Judy McKinn, Head of Curriculum Development at Imperial College School of Medicine. The Steering Group is chaired by Dr Diana Wood, Deputy Dean for Education at Bart’s and the Royal London Medical School; membership includes representatives from each of the London medical schools and from the Faculty of Health and Social Care Sciences at Kingston University.

For further information contact: Carol Jollic, Project Officer (tel: 020 8995, email: carol@jollic.fsworld.co.uk).

NHS Education for Scotland e-Library
Readers who work for the NHS in Scotland might like to know of a new initiative launched by NHS Education for Scotland. The Scotland e-Library is a virtual collection of healthcare information resources designed to ensure delivery of high quality healthcare services focusing on evidence based care and best practice (www.elib.scot.nhs.uk). For further information contact: Dr Ann Wales, NHS Scotland Library Service Development Coordinator (tel: 0141 223 1551; fax: 0141 223 1403; email: ann.wales@ nes.scot.nhs.uk) or Nicola Carlyle, Communications Officer (tel: 0141 247 6602; fax: 0141 225 9970; email: nicola.carlyle@ nes.scot.nhs.uk).

Warwick University Short Course
7–10 July 2003: Techniques and applications of molecular biology: a course for medical practitioners. A four day residential course for those in the medical profession wishing to improve their understanding of the principles and applications of genetic engineering techniques. Details: Dr Charlotte Moanan, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (tel: 0044 (0)24 7652 3540; fax +44 (0)24 7652 3701; email Charlotte.Moanan@warwick.ac.uk).