

PostScript

LETTERS

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.¹ However, use of enzyme replacement with glucosylceramide glucosidase lowered tissue levels of glucosylceramide (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,¹ the organism binds to GlcCer and acidic glucosphingolipids.

It follows then that depleting glucosphingolipids 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, one 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.¹

Lowering cellular glucosphingolipids has indeed been shown to reduce adhesion of pathogens.² Mice depleted of their glucosphingolipids resisted colonisation of the urinary tract.³ Interference with HIV-1 progression by glucosphingolipid depletion is especially exciting.⁴ 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.⁵ These include the use of chlorpromazine, tamoxifen, verapamil, RU-486 (mifepristone), antiandrogens, all-trans retinoic acid, and cycloserine. Glucosamine, 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 sphingomyelin 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 should be helpful.) The level of ceramide can also be lowered by stimulating its conversion to sphingomyelin by reaction with lecithin; ergo, eat extra lecithin. GlcCer, the simplest glucosphingolipid, is normally degraded by hydrolysis, which can be speeded by phosphatidylserine, available as a food supplement.

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References

- 1 **Margalit M**, Ash N, Zimran A, *et al*. Enzyme replacement therapy in the management of longstanding skeletal and soft tissue salmonella infection in a patient with Gaucher's disease. *Postgrad Med J* 2002;**78**:564-5.
- 2 **Svensson M**, Lindstedt R, Radin NS, *et al*. Epithelial glucosphingolipid expression as a determinant of bacterial adherence and cytokine production. *Infect Immun* 1994;**62**:4404-10.
- 3 **Svensson M**, Frendeus B, Butters T, *et al*. Glycolipid depletion in antimicrobial therapy. *Mol Microbiol* 2003;**47**:453-61.
- 4 **Hug P**, Lin HM, Korte T, *et al*. Glucosphingolipids promote entry of a broad range of human immunodeficiency virus type 1 isolates into cell lines expressing CD4, CXCR4, and/or CCR5. *J Virol* 2000;**74**:6377-85.
- 5 **Radin NS**. Treating glucosphingolipid disorders by chemotherapy: use of approved drugs and over-the-counter remedies. *J Inher Metab Dis* 2000;**23**:767-77.

Phantom lymphadenopathy. An association with chronic fatigue syndrome

Shee reports an association between chronic fatigue syndrome (CFS) and what he regards as a "phantom lymphadenopathy".¹ However, his failure to observe "true lymphadenopathy" in patients with CFS complaining of swollen lymph glands does not exclude a real, albeit subclinical enlargement of those glands, because he did not compare their dimensions with the ones that were measurable before the appearance of patients' complaints.

As someone who suffered from CFS and reported on its dramatic resolution thanks to old and new drugs for Addison's disease,² I clearly remember that my lymph nodes, just a few days after the abrupt onset of CFS, became mildly painful and began to swell gradually. This slow process of enlargement lasted approximately one month. However, even when my lymph glands stopped swelling further (but continued to be mildly painful), their dimensions were still clinically within normal limits. This may indirectly explain why Shee found that "careful examination did not confirm lymphadenopathy" in CFS patients with "self diagnosed enlarged lymph glands".

Shee proposes some explanations for his patients' complaints about their lymph glands, but surprisingly fails to mention adrenal 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.³ As a consequence of their common adrenal abnormalities,³ CFS⁴ and Addison's disease⁵ also share an additional feature, namely, impaired production of dehydroepiandrosterone sulphate, which is secreted from the adrenal glands.⁴

Shee points out that general and neurological examination and other investigations were normal in all patients with CFS. His article, however, does not specify whether those investigations also included an assessment of adrenal function. Hypocortisolism, for example, despite being present in CFS (as well as in Addison's disease),³ is not mentioned in Shee's article as a possible explanation for the symptoms of his patients with CFS and, therefore, he probably omitted to measure their cortisol levels.

In view of the 42 clinical features that CFS shares with Addison's disease,^{2,3} I believe that a careful evaluation of the adrenal function of patients with CFS would have enlightened Shee more than did all other investigations combined.

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References

- 1 **Shee CD**. Phantom lymphadenopathy. An association with chronic fatigue syndrome. *Postgrad Med J* 2003;**79**:59-60.
- 2 **Baschetti R**. Chronic unexplained fatigue. *Postgrad Med J* 2002;**78**:763.
- 3 **Baschetti R**. Chronic fatigue syndrome: a form of Addison's disease. *J Intern Med* 2000;**247**:737-9.
- 4 **Kuratsune H**, Yamaguti K, Sawada M, *et al*. Dehydroepiandrosterone sulfate deficiency in chronic fatigue syndrome. *Int J Mol Med* 1998;**1**:143-6.
- 5 **Hunt PJ**, Gurnell EM, Huppert FA, *et al*. Improvement in mood and fatigue after dehydroepiandrosterone replacement in Addison's disease in a randomized, double blind trial. *J Clin Endocrinol Metab* 2000;**85**:4650-6.

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.

By John Launer. (Pp 264; £21.95.) Radcliffe Medical Press, 2002. ISBN 1-85775-539-1. ****

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 for an unquestioning grateful 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 undermining 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 find this excellent book both thought provoking and useful. Already, I have changed my opening greeting to "What would you like to tell me about?"

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How To Survive in Anaesthesia. 2nd Edition

By Neville Robinson and George Hall. (Pp 191; £22.50.) BMJ Books, 2002. ISBN 0-7279-1683-1.****

This is aimed at trainees in their first year of anaesthesia. The book's lighthearted, easy reading style cleverly passes on the tips and tactics that experienced anaesthetists use to avoid the disasters that lurk around every operating theatre corner. The 2nd edition of this section—"Anaesthesia in the corridor" and "Anaesthetic aphorisms" (aphorism = pithy saying!) nicely complete the book with several of my own favourite aphorisms 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.

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 his first few months. The last two chapters of this section—"Anaesthesia in the corridor" and "Anaesthetic aphorisms" (aphorism = pithy saying!) nicely complete the book with several of my own favourite aphorisms 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.

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Pathways in Surgery. 3rd Ed.

Edited by Michael Hobsley and Paul Boulos. (Pp 427; £29.99.) Arnold Publishers, 2002. ISBN 0-340-631186-4.***

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.

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Statistics in Clinical Practice. 2nd Ed.

By David Coggan. (Pp 109; £14.95.) BMJ Books, 2002. ISBN 0-7279-1609-2.****

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.

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NOTICES

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 McKimm, 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 Jollie, Project Officer (tel: 020 8995, email: carol@jollie.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).

CALENDAR

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 Moonan, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (tel +44 (0)24 7652 3540; fax +44 (0)24 7652 3701; email Charlotte.Moonan@warwick.ac.uk).