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 glucosidase 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 glucosphinoglipid in the cell surface. Patients with Gaucher's disease accumulate not only GlcCer, but also some of the more complex glucosphinoglipids 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 glucosphinoglipids. It follows then that depleting glucosphinoglipids in people should reduce the number of binding sites for infectious agents and, possibly, prevent the development of new infections. If the glucosphinoglipids already bound to infectious particles are in a reversible equilibrium, one can expect that a decrease in the body's total glucosphinolipid 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 glucosphinoglipids has indeed been shown to reduce adhesion of pathogens.1 Mouse depleted of their glucosphinoglipids resisted colonisation of the urinary tract.1 Interference with HIV-1 progression by glucosphinoglipid depletion is essentially the same.2 Studies of this sort utilised inhibitors of GlcCer synthase.

Other approaches can also achieve reduction in cellular glucosphinoglipids. 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 glucosphinoglipid synthesis have been described.3 These include the use of chlorpromazine, tamoxifen, verapamil, RU-486 (mifepristone), androgens, all-trans retinoic acid, and cyclooxynase. Glucosamine, widely used to prevent joint pain, should compete against glucose, lowering the level of uridine diphosphoglucose.

Bio-synthesis 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 hydrolysis. 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 help.) 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 glucosphinoglipid, is normally degraded by hydrolysis, which can be speeded by phosphatidylserine, available as a food supplement.

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References

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". However, his failure to observe "true lymphadenopa-thy" in patients with CFS complaining of swollen lymph 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,1 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.2 As a consequence of their common adrenal abnormalities,3 CFS and Addison's disease4 also share an additional feature, namely, impaired production of dehydroepiandrosterone sulphate, which is secreted from the adrenal glands.5

Shee points out that general and neurologi-cal 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 exam-ple, despite being present in CFS (as well as in Addison's disease),1 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;4 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

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
dependence on the work that GPs perform. Having
progressed from the traditional role of simply
dispensers of medicine and wisdom for an
unquestioning grateful patient, GPs need to
address the challenges of clinical governance,
evidence-based medicine and patient empow-
erment, while maintaining their own sanity and
even self respect.

Narrative-based medicine focuses on ena-ling 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 intellectu-
ally 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
take over time. Open minded and reflective
GPs, particularly those involved in teaching,
will find the book both thought provoking and
useful. Already, I have changed my opening greeting to “What would you like
to tell me about?”

L S Levene
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How To Survive in Anaesthesia. 2nd Edition
0 7279-1631-1.

This is aimed at trainees in their first year of
anaesthesia. The book's light-hearted, easy
reading style cleverly passes on the tips and
tricks 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
covers the “nuts and bolts” of anaes-
thetic practice with chapters dedicated to air-
way management, vascular access and fluid
therapy, anaesthetic equipment, and moni-
tors. 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 two 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 in-
cluded. Throughout the book are numerous
pink boxes presenting the important infor-
mation of the chapter or important manage-
ment 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
cautionsome of the politically incorrect
messages of the last chapter should be taken
with a pinch of salt.

P Spiers
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Pathways in Surgery. 3rd Ed.
Edited by Michael Hobsley and Paul Boulis.

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 proc-
esses.

The editors and authors have combined
both styles and have sought to provide a compre-
hsive textbook covering all aspects of surgery,
both core general surgery and relevant
subspecialties. The book seeks to pro-
vide a “roadmap” for common symptoms and
drugs and has been divided up into non-
emergency 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 back-
wards to show how one can identify which of
several possible diseases produced that clini-
cal 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 envi-
ronment. 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 com-
prehensive, offers great value for money, and
probably lends itself very well to today's prob-
lem orientated approach to medical educa-
tion.

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Statistics in Clinical Practice. 2nd Ed.
By David Coggan. (Pp 109; £14.95.) BMJ

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 dis-
tribution. Further chapters deal with prob-
ability and how statistics can be used in inter-
preting clinical data and drawing conclusions.
Topics described here are sensitivity, specific-
ity, 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 recom-
end the book to both qualified health profes-
sionals 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 want-
ing an introduction to research methodology.
The book is reasonably priced at £14.95.

A R Hart
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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 devel-
oped 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 King-
ston 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 Develop-
ment Coordinator (tel: 0141 223 1551; fax:
0141 223 1403; email: ann.wales@nes.
scot.nhs.uk) or Nicola Carlyle, Communi-
cations 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 tech-
niques. Details: Dr Charlotte Moogan, Depart-
ment of Biological Sciences, University of
Warwick, Coventry CV4 7AL, UK (tel: 041
(0)24 7652 3540; fax +44 (0)24 7652 3701;
email Charlotte.Moogan@warwick.ac.uk).