LETTERS TO THE EDITOR

The real cost of aspirin

EDITOR,—In the context of coronary heart disease the poor perception of the hidden cost of aspirin¹ partly stems from under-recognition of alternative therapeutic strategies for achieving the objective of primary or secondary prevention of myocardial infarction during long term use. A prime example is the use of warfarin, which, in patients who already have a strong indication such as atrial fibrillation, for its long term use, can serve as a satisfactory alternative therapeutic strategy. This is because, in its own right, anticoagulation to a target international normalised ratio (INR) of 1.4–2.0 can reduce the risk of myocardial infarction by 47% in high risk males aged 45–69.² This compares favourably with the 34% reduction in myocardial infarction risk achievable with aspirin in chronic stable angina.³

For secondary prevention of myocardial infarction, prospective studies show at least comparable efficacy between warfarin (adjusted to target INR of 2.4–4.8),^{4,5} and aspirin,⁶ while, in the meta-analytic context (antedating the comparison between aspirin and trapidil),⁶ data from the Antiplatelet Trialists Collaboration are less favourable than data from anticoagulant trials on the basis of “numbers needed to treat”.^{7,8} Statins are an alternative and powerful modality both for primary and secondary prevention of myocardial infarction in patients with modest as well as a marked increase in plasma cholesterol concentrations.⁹ As with warfarin,^{2,5,6} their benefit extends to primary prevention of stroke,¹⁰ the latter objective currently not achievable with aspirin.¹¹ In the presence of either coronary heart disease, hypertension, or diabetes, angiotensin converting enzyme blockade can reduce myocardial infarction risk by 20%, a spin off being a 23% reduction in heart failure risk.¹²

Secondary prevention of myocardial infarction as well as primary prevention of heart failure after myocardial infarction, comprise two end points also achievable with β -adrenergic blockade in conventional, and in low doses, respectively.^{13,14} This raises the possibility of a highly beneficial drug interaction between the two modalities, perhaps unlikely to be enhanced by coprescription of aspirin, given the possibility of an adverse interaction between aspirin and enalapril.¹⁵

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1 Burgess MI, Densem CG, Brooks NH, et al. The real cost of aspirin. *Postgrad Med J* 2000;76:734–5.

2 MacCallum PK, Brennan PJ, Meade TW. Minimum effective intensity of oral anticoagulant therapy in primary prevention of coronary heart disease. *Arch Intern Med* 2000;160:2462–8.

3 Juul-Moller S, Edvardsson N, Jahnmatz B, et al. Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. *Lancet* 1992;340:1421–5.

- 4 Smith P, Arnesen H, Holme I. The effect of warfarin on mortality after myocardial infarction. *N Engl J Med* 1990;323:137–52.
- 5 ASPECT Research Group. Effect of long-term oral anticoagulant treatment on mortality and cardiovascular morbidity after myocardial infarction. *Lancet* 1994;343:499–503.
- 6 Yasue H, Ogawa H, Tanaka H, et al. Effects of aspirin and trapidil on cardiovascular events after acute myocardial infarction. *Am J Cardiol* 1999;83:1308–13.
- 7 Rabbani LE, Loscalzo J. Atherothrombotic insights into secondary prevention after acute myocardial infarction. *Can J Cardiol* 1993;9:739–47.
- 8 Miller DB. Secondary prevention for ischaemic heart disease. Relative numbers needed to treat with different therapies. *Arch Intern Med* 1997;157:2045–52.
- 9 Maron DJ, Fazio S, Linton MF. Current perspectives on statins. *Circulation* 2000;101:207–13.
- 10 White HD, Simes J, Anderson NE, et al. Pravastatin therapy and the risk of stroke. *N Engl J Med* 2000;343:317–26.
- 11 Steering Committee of the Physicians' Health Study Research Group. Final report of the aspirin component of the ongoing Physicians' Health Study. *N Engl J Med* 1989;321:129–35.
- 12 Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high risk patients. *N Engl J Med* 2000;342:145–53.
- 13 Golstein S. β -blockers in hypertensive and coronary heart disease. *Arch Intern Med* 1996;156:1267–76.
- 14 Rochon PA, Tu JV, Anderson GM, et al. Rate of heart failure and 1-year survival for older people receiving low-dose β -blocker therapy after myocardial infarction. *Lancet* 2000;356:639–44.
- 15 Nguyen KN, Aursnes I, Kjekshus J. Interaction between enalapril and aspirin on mortality after acute myocardial infarction: subgroup analysis of the cooperative new Scandinavian Enalapril Survival Study II (CONCENSUS II). *Am J Cardiol* 1997;79:115–19.

Dr Burgess responds on behalf of the authors:

Dr Jolobe's comments seem rather indirectly related to our work. The objective of our study was to evaluate the prevalence of aspirin associated side effects and make a comment on the potential cost implications. We certainly did not intend to evaluate the relative value of aspirin compared to other agents used in patients with coronary artery disease. His letter reviews some important data on the use of other agents in this patient group and we would concur with the comments about the use of statins, angiotensin converting enzyme inhibitors, and β -blockers for the secondary prevention of coronary events. These drug groups appear to have an additive effect.

Hyperthyroidism induced by β -human chorionic gonadotrophin

EDITOR,—We wish to raise three important points regarding the diagnosis, aetiology, and management of β -human chorionic gonadotrophin (β -hCG) induced hyperthyroidism.¹

(1) β -hCG induced hyperthyroidism is characterised by very high concentrations of β -hCG and these may cross react in some assays for thyroid stimulating hormone (TSH)^{2,3} giving apparently normal rather than suppressed TSH values. Since many laboratories offer TSH as the first line test in investigating thyroid dysfunction, the diagnosis of β -hCG induced hyperthyroidism may, therefore, be missed.

(2) β -hCG exists as several isoforms depending on carbohydrate content. Desialated isoforms, which are produced more abundantly in cases of β -hCG induced hyperthyroidism, have greater thyrotrophic

activity than the commoner sialated isoforms.^{4,5} Therefore, the quality rather than quantity of β -hCG is important in the development of β -hCG induced hyperthyroidism. This also explains why pregnancy, with high β -hCG concentrations comparable to those reported in this case, is not usually associated with thyrotoxicosis.

(3) Tumour β -hCG induced hyperthyroidism may require standard antithyroid treatment, but almost invariably responds to effective tumour chemotherapy. Tumour relapse may also be associated with recurrence of the thyrotoxicosis.²

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- 1 Ismail M, Bhat RV. Thyrotoxicosis of a rare aetiology. *Postgrad Med J* 2000;76:799–800.
- 2 Gama R, Smith MGM, White WF, et al. Hyperthyroidism from an embryonal carcinoma. *J R Soc Med* 1997;90:446–7.
- 3 Lemon M, Bevan BR, Li TC, et al. Thyroid function in trophoblastic disease. *Br J Obstet Gynaecol* 1987;94:1084–8.
- 4 Mann K, Schneider N, Hoermann R. Thyrotrophic activity of acidic isoelectric variants of human chorionic gonadotrophin from trophoblastic tumours. *Endocrinology* 1986;118:1158–65.
- 5 Pekary AE, Jackson IMD, Goodwin TM, et al. Increased in vitro thyrotrophic activity of partially sialated human chorionic gonadotrophin extracted from hydatiform moles of patients with hyperthyroidism. *J Clin Endocrinol Metab* 1993;76:70–4.

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.

Teaching & Learning Communication

Skills in Medicine. By Suzanne Kurtz, Jonathan Silverman, and Juliet Draper. (Pp 245; £35.) Radcliffe Medical Press, 1999. ISBN 1-85775-273-2. ****

This book provided an evidence based guide to the teaching and learning of communication skills. The book is based on the principles of adult education and includes advice on how to integrate communication skills teaching. It includes useful boxes which communications skills facilitators can use to help them guide small group sessions.

This is a useful book for communications skills teachers in undergraduate and most postgraduate medicine in this country. It is well written, carefully structured, and easy to read. It gives a contemporary and practical view of communications skills teaching and should be highly recommended to communications skills teachers.

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Narrative Based Medicine. Edited by Trisha Greenhalgh and Brian Hurwitz. (Pp xvi + 286; £19.95.) BMJ Books, 1998. ISBN 0-7279-1223-2.***

After two introductory contributions, the remaining 23 chapters (written by 29 contributors) are arranged under the following section headings: "Illness stories", "Narrative in medicine", "Learning and teaching narrative", "Understanding narrative in health care", and "Broader perspectives on narrative in health care". There is also an appendix (by the editors) which contains valuable suggestions for further reading, followed by an adequate index.

But what is *narrative based medicine*, and what has it to offer? The subheading of the book ("Dialogue and discourse in clinical practice") is probably more revealing in this context than the main title. In a foreword (written by H Brody) the reader is told (and this is reiterated in chapter 1) that ... "after two and a half years of being taught on the assumption that everyone is the *same* (my italics) the student has to find out for himself that everyone is different...". "Most people (the reader is also told) would have said as recently as 1982 that stories are an unimportant and uninteresting feature of medicine".

The contents of this book (one writer assures his readership) "allow us to see both sides of the bridge with equal vividness". What if any is the relevance of *median* longevity to the individual? What is it like to suffer from cancer or a stroke, or survive to the age of 78 with haemophilia? Narratives are also included of an epileptic and a sufferer from angina. The importance of literature in medicine, and the value of dialogue between doctor and patient, is highlighted. The role of anecdotes is rightly stressed. "The sick, like the poor, leave few archives behind them".

So diffuse are the contributions that this text is almost impossible to review adequately in 250 words. There is clearly much to be gained, however; but the book should be read alongside systematic texts of medicine, and *not* as an alternative to them!

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Statistics with Confidence. 2nd Ed. Edited by Douglas G Altman, David Machin, Trevor N Bryant, and Martin J Gardner. (Pp 240; £18.95.) BMJ Books, 2000. ISBN 0-7279-1375-1.***

This book is written by senior statisticians with a wealth of experience in both statistical research and teaching. The first section of the book deals with the different statistical methods including means, medians, proportions, confidence intervals, sample sizes, regression, correlation, and meta-analyses. The second

section details useful information on statistical guidelines for contributing to medical journals including the selection of the appropriate tests and presentation and interpretation of results. The final part is a reference section on notation, software for analysis, and statistical tables. A disk is included for calculating confidence intervals.

This book is well written and understandable covering the range of basic to advanced statistics. The text is very well illustrated with worked examples and references. The book will be invaluable to all health professionals wishing to start medical research and as a reference source for more experienced workers. The book and included disk is good value at £18.95.

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Introduction to Clinical Neurology. 2nd Ed. By Douglas J Gelb. (Pp 386; £22.50.) Butterworth Heinemann, 2000. ISBN 0-7506-7202-1. ****

The stimulus to write this book is the recent change in healthcare policy in the United States whereby there is a move away from the "specialist" to the "generalist". It is anticipated that the number of residency training posts in neurology may fall to possibly half the present number. This contrasts with the UK where the increasing demand for neurologists and those in other specialties is driving waiting lists higher and higher.

The stated rationale for this book is that all physicians should be familiar with the general principles of neurological diagnosis and management. Its purpose is to "focus on practical issues of management" and avoid "esoteric diagnostic distinctions with little practical relevance".

Part 1 concentrates on neurological skills. The localisation of a lesion applying basic anatomical concepts is followed by a practical description of how to perform a neurological examination and advice on how to establish the nature of the pathology. Sensible case histories are used liberally to illustrate the problems. Part 2 discusses common neurological conditions and part 3 addresses symptomatic presentations.

This is an extremely well written book which takes a practical approach to a subject which many beginners find daunting. The case histories are particularly helpful in focusing a problem, both for the inexperienced clinician and even for a trained neurologist. It will be of value to trainees for the MRCP examination and beyond, and will also provide useful diagnostic tips for their seniors.

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BOOKS RECEIVED

The receipt of these books is acknowledged and this listing must be regarded as sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed, space permitted. The journal does not publish unsolicited reviews.

The Management of Acute Pain. 2nd Edition. By Gilbert Park, Barbara Fulton, and Siva Senthuran. (Pp 210; £19.95.) Oxford University Press, 2000. ISBN 0-19-262467-9.

Q Base Surgery: 1 MCQs for the MRCS. By J S A Green and S A Wajed. (Pp 99; £22.50.) Greenwich Medical Media Ltd, 2001. ISBN 1-9000151-375.

DIARY

Techniques and Applications of Molecular Biology: A Course for Medical Practitioners

9–12 July 2001, University of Warwick, Coventry

This is 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. *Further information:* Dr Charlotte West, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL (tel 024 7652 3540, fax 024 7652 3701, email Charlotte.West@warwick.ac.uk).

Ninth Annual Pediatric Update

20–21 July 2001, Lucile Packard Children's Hospital, Palo Alto, California

This conference is presented by the Department of Pediatrics at Stanford University School of Medicine and Lucile Packard Children's Hospital. It is designed for paediatricians, family physicians, nurses, and allied health professionals and will highlight the most recent advances and issues in paediatrics. *Further information:* Lucile Packard Children's Hospital CME Office at +1 650 497 8554 or email lpchcme@medcenter.stanford.edu.