HIV infection and seizures

EDITOR.—We read with interest the article from Dr Garg.1 We are just finishing a case-control study about risk factors for new onset seizures among HIV infected patients. All HIV infected patients hospitalised between 1 January 1992 and 31 March 1999 entered the study. Those suffering from any type of recent onset seizure were included as “cases”. Two “controls” per case were randomly chosen matched by year of hospitalisation. Semiological type of seizure, CD4+ lymphocyte counts (dichotomised at 200 cells/ml), HIV infection clinical stage (dichotomising C or B or A), opportunistic HIV related central nervous system (CNS) diseases, CNS pathologies not related to HIV, age and sex, were registered.

Fifty four patients were included as cases. Their general clinical characteristics were in accordance with those of Garg’s. Most of them had generalised tonic-clonic seizures (generalised 49, partial four, not classifiable one), and their causes, summarised in table 1, were mostly in relation to opportunistic HIV related CNS diseases (36/54 cases). Nevertheless, CNS pathologies not related to HIV or with no specific cause could be identified in a significant number of cases (8/54 and 10/54 respectively). Patients generally showed considerable immunosuppression (CD4+ counts <200 cells/ml in 93% of cases), and had previously suffered from other AIDS defining pathologies (86.5%).

We hypothesised that immunosuppression, HIV clinical stage, and CNS HIV related opportunistic diseases were independent seizure risk factors. Crude univariate and multivariate analyses were done by means of Fisher’s exact test and logistic regression and the results, summarised in table 2, were expressed as odds ratios with the corresponding 95% confidence interval and Fisher’s exact test or likelihood ratio p values (SPSS 8.0 for Windows).

Crude univariate analysis disclosed that immunosuppression, HIV clinical stage, and several CNS HIV related opportunistic diseases behaved as important risk factors, as well as CNS pathologies unrelated to HIV, analysed as a group, did. However, when dichotomised CD4+ lymphocytes counts, HIV clinical stage, and relevant CNS pathologies were simultaneously introduced, in conjunction with sex and age as potential confounders, in a logistic regression model, immunosuppression and HIV infection clinical stage lost all their influence, while the effect of most HIV related CNS opportunistic diseases was maintained or even enhanced, in the same way as occurred with CNS pathologies unrelated to HIV.

Neither immunosuppression nor HIV clinical stage behave as independent risk factors, and their apparent implications are explained through HIV opportunistic CNS pathologies. CNS toxoplasmosis and CNS lymphoma are very strong risk factors of new onset seizures in HIV infected patients. The role of multifocal progressive leukencephalopathy and HIV unrelated pathologies, though not to be doubted, appear to be much smaller. The implication of HIV by itself appears weak, if at all, and the elucidation of its role would require further well designed cohort or case-control studies in which the diagnosis of HIV encephalopathy would be done on a neuropathological basis in cases as well as in controls, a condition very difficult to fulfil in common clinical practice.

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The author responds:

I am grateful to Dr Gaspar and Dr Álvarez for their interest shown in my article. In their study Gaspar and Álvarez observed that HIV related CNS opportunistic infections (for example toxoplasmosis) and CNS lymphoma were strong risk factors of new onset seizures in HIV infected patients. An almost similar observation was made by Rothman et al.1 In their study these authors tried to determine which neurological signs or symptoms were predictive of new focal lesions on a cranial computed tomography study in HIV infected patients,1 and 110 patients who had new or changed neurological signs or symptoms were subjected to cranial computed tomography. Twenty seven patients (24%) had focal cerebral lesions seen on computed tomography of which 19 (18%) were new lesions. New onset seizures were identified in their clinical finding and were strongly associated with new abnormalities seen on computed tomography. In this study also the most common intracranial lesion among patients with CD4+ counts >200 cells/ml was toxoplasmosis, while cerebrovascular accidents (ischaemic or haemorrhagic) were most common in those with CD4 counts <200 cells/ml. So, I agree with Gaspar and Álvarez that HIV infected patients who have new onset seizures are more likely to have a definite focal abnormality, which in majority of cases are caused by readily treatable opportunistic CNS infections.

Another important point raised by Gaspar and Álvarez is about the role of direct HIV infection of the brain in the pathogenesis of new onset seizures in patients with AIDS. It has been suggested that in patients with seizures who have no definite identifiable disease of the brain, cerebral HIV infection seems to be the most likely cause of seizures. In a series by Wong et al17 patients within the “non-identified” group (comprising of 32 patients) underwent postmortem examination of brain; only six of them had characteristic pathological changes suggestive of HIV encephalopathy.1 So, in all HIV infected patients with normal imaging studies and normal cerebrospinal fluid examination the seizures cannot be attributed to HIV infection of brain. In a recent prospective study Pascual-Sedano et al reported that in the majority of such patients the new onset seizures were either because of antiviral drug toxicity or were related to some metabolic

Table 1 Presumed aetiologies of new onset seizures in the 54 HIV infected patients included as cases in our study

<table>
<thead>
<tr>
<th>CNS pathologies related to HIV</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal</td>
<td>29</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>19</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>6</td>
</tr>
<tr>
<td>Progressive multifocal</td>
<td>4</td>
</tr>
<tr>
<td>leukencephalopathy</td>
<td>7</td>
</tr>
<tr>
<td>Diffuse</td>
<td>5</td>
</tr>
<tr>
<td>HIV encephalopathy</td>
<td>5</td>
</tr>
<tr>
<td>Tuberculous meningitis</td>
<td>1</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>1</td>
</tr>
<tr>
<td>CNS pathologies not related to HIV</td>
<td>8</td>
</tr>
<tr>
<td>Infectious endocarditis</td>
<td>2</td>
</tr>
<tr>
<td>Cranioencephalic trauma</td>
<td>2</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>1</td>
</tr>
<tr>
<td>Neurophilus</td>
<td>1</td>
</tr>
<tr>
<td>Foscarnet therapy</td>
<td>1</td>
</tr>
<tr>
<td>Gloma</td>
<td>1</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 2 Results of univariate and multivariate analysis of hypothetical risk factors of new onset seizures in our HIV infected patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate (Fisher’s exact test)</th>
<th>Multivariate (logistic regression)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
</tr>
<tr>
<td>CD4+ count (&lt;200 cells/ml)</td>
<td>7.49</td>
<td>2.18</td>
</tr>
<tr>
<td>HIV infection clinical stage (C or B or A)</td>
<td>4.05</td>
<td>1.68</td>
</tr>
<tr>
<td>CNS toxoplasmosis</td>
<td>21.17</td>
<td>5.92</td>
</tr>
<tr>
<td>CNS lymphoma</td>
<td>17.72</td>
<td>2.12</td>
</tr>
<tr>
<td>HIV encephalopathy</td>
<td>3.43</td>
<td>1.03</td>
</tr>
<tr>
<td>Progressive multifocal leukencephalopathy</td>
<td>4.72</td>
<td>0.84</td>
</tr>
<tr>
<td>CNS pathologies not related to HIV</td>
<td>3.43</td>
<td>1.03</td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>3.43</td>
<td>1.71</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval; LLR = logarithm of the likelihood ratio.
Medical restrictions to driving: awareness of patients and doctors

EDITOR,—We were interested to read the article by Kelly et al on the awareness of patients and doctors of medical restrictions to driving published recently. It reported that “Doctors’ knowledge of current licensing policy and action to be taken if a patient was not eligible to drive was poor”.

This led us to conduct our own research among hospital doctors, general practitioners (GPs), and medical students. We used the doctors’ questionnaire from the study by Kelly et al to investigate local knowledge of driving restrictions. We interviewed 50 hospital doctors from a variety of specialties (14 house officers, 12 senior house officers, 14 registrars, and 10 consultants) at the Queen Elizabeth Hospital, Birmingham; 23 GPs from five different practices around Birmingham with experience ranging from GP registrar to those qualified 30 years; and 30 fourth year medical students. Participation was voluntary and anonymous.

Our results were similar to those reported by Kelly et al. Knowledge of the age at which licences should be reviewed for fitness to drive was generally around the correct age of 70 years (see table 1). When asked to name conditions that should be reported to the Driving Vehicle Licence Authority (DVLA) epilepsy, stroke, and diabetes were the most frequently given answers in all three study populations. Four hospital doctors and one medical student did not know that conditions should be reported to the DVLA. Nobody stated that the patient’s insurance company should be informed. Table 2 summarises the knowledge of specific restrictions among the three study populations.

For the five conditions for which specific restrictions were selected an average of 15.6% of GPs gave correct complete advice, while hospital doctors scored 14.6%, and medical students 5%. A χ² test demonstrated that there was no significant difference in knowledge between GPs and hospital doctors (p=0.85). Interestingly, 83% of GPs said that they would obtain further information about driving restrictions from leaflets produced by the DVLA, while only 16% of hospital doctors and no medical students knew about such publications.

These results appear to agree with the findings of Kelly et al. They indicate that there may be a failure to communicate driving restrictions to patients as many medical practitioners are unaware of the existence of details or specific features of present legislation. GPs’ spontaneous knowledge of driving restrictions is generally poor. However, with frequency of cardiac and endocrine conditions increasing, it could be argued that the high levels of awareness and access to DVLA publications may be sufficient to advise patients accurately. The success of this strategy will depend on basic knowledge being sufficient to know when to refer to such information.

Medical restrictions to driving form an important subject area because of the implications for both the individual and other road users. Many in the medical profession are not sufficiently well aware of the requirements of existing legislation. Undergraduate and postgraduate teaching on the subject have been suggested as mechanisms to increase awareness about restrictions. With only 36% of students recalling having had some teaching on driving restrictions and knowledge among this group being poor, there remains potential for improvement in this area.

SARA ORMEROD

M T E HEAFIELD

Birmingham Neurosciences Centre, Queen Elizabeth Hospital, Birmingham B15 2TH, UK


Comment

The prevalence of diabetes mellitus may be as high as 7.8% among patients with proven primary hyperparathyroidism, either as a result of the fact that, since both type 2 diabetes and primary hyperparathyroidism are age related, their prevalence in old age might be sufficiently high to result in their coexistence by pure chance, or because hypercalcaemia can be complicated by insulin resistance. Support for the latter theory comes from the case report of a 56 year old woman presenting simultaneously with type 2 diabetes and primary hyperparathyroidism, in whom parathyroidectomy resulted in reversal of glucose intolerance. This therapeutic “coup” was validated by the fact that, postoperatively, she sustained her hypercalcaemia and her hypercalciuria, and haemoglobin A1c (a measure of glycemic control) has been maintained at levels below 6.5% (39 mmol/mol) for over 3 years.

In the case presented here, an 81 year old woman with diabetes mellitus, a 56 year old woman with primary hyperparathyroidism, and a 46 year old woman with primary hyperparathyroidism and multiple myeloma, the converse is also true that treatment of metabolic crisis can occasionally prove to be equally beneficial for diabetic decompensation and for coexisting unsuspected endocrinopathy other than Addison’s disease. This is illustrated by an 81 year old woman admitted with diabetic decompensation characterised by a plasma glucose concentration of 35.1 mmol/l, urea 32.2 mmol/l, creatinine 164 mmol/l, and bicarbonate 24 mmol/l, in the presence of Enterococcus coli septicemia. By day 17, as a result of treatment with intravenous fluids, insulin infusion, and antibiotics, she was much improved, with random blood glucose of 3.1 mmol/l, urea 8.9 mmol/l, and creatinine 126 mmol/l, and she was subsequently discharged home. What had been overlooked, in the preoccupation with her diabetic status, was that plasma calcium concentrations on day 1 and on day 17 were 3.6 mmol/l and 2.64 mmol/l, respectively (unsolicited, therefore not perceived!), and that emergency treatment of diabetes, using large amounts of intravenous fluids, had been of equal benefit for diabetes and for coexisting hypercalcaemia. The latter, on subsequent investigation, proved to be attributable to primary hyperparathyroidism (characterised by a serum parathyroid hormone level of 75 pmol/l (reference range 11–55 pmol/l), the presence of a plasma calcium of 2.94 mmol/l, with concurrent plasma albumin of 30 g/l).

O M P JOLORIE

Department of Medicine for the Elderly, Tameside General Hospital, Fountain Street, Ashton under Lyne OL6 9WY, UK


BOOK REVIEWS

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


The fifth edition of Bedside Cardiology is a refreshing educational read to all training in cardiology as well as established consultants in cardiology and those with an interest in the subject. Dr Constant is Associate Clinical Professor at the State University of New York at Buffalo. He clearly is an expert clinician. This book has a unique style incorporating what the author calls the Socratic method of teaching. The information is presented very much as a question and answer format for programmed learning.

Cardiac diagnosis in recent years has tended to become more focused on accurate non-invasive investigations rather than an in-depth precocious clinical bedside diagnosis. This book would tend to redress that trend and focus the emphasis again on accurate examination. Anyone teaching medical students or postgraduate students would greatly enjoy their diagnostic acumen with a careful examination of this book. The author emphasises many important aspects of a clinical examination and educationally the discussion of false positive and false negative signs that every technology suffers from is particularly valuable.

I found this a highly educational and exciting book to read. The author has a style which attracts you to constantly read every section and it is very difficult to skim any section for fear of losing valuable information.

The chapters on the jugular venous pressure and arterial pulses are particularly educational.

This book is essential reading for all those involved in clinical cardiology, not only to enhance their own diagnostic acumen but also to refresh their knowledge, enabling them to become better teachers of the bedside manner of diagnosing and teaching cardiology.

D J COLTART
Consultant Cardiologist/Clinical Director, Cardiothoracic Unit, St Thomas’s Hospital, London, UK


I recommend this new short soft backed immunology textbook to both medical students and to those studying for their respective collegiate examinations. A major advantage of the format of this book is that it allows one to find essential pockets of information that in many other immunology books are disseminated throughout the text and hence difficult to extract. The key notes at the start of each chapter are good revision/overview statements. This is not a clinical immunology book, but it does apply basic mechanisms to clinical situations in the applied chapters. The 120 multiple choice questions at the end of the book will be particularly welcomed by candidates for collegiate examinations as there is a lack of quality published multiple choice questions in the field of immunology.

At £14.95 this book is a worthy investment for those interested in expanding their knowledge of immunology.

R J POWELL
Clinical Immunology Unit, Queen’s Medical Centre, Nottingham, UK


The 12th edition of this book is a mine of information. The sections on history and intensive care medicine will be missed, but it does allow the sections to be easily portable again. The book having been read once, will be used to revise, and subsequently to refer to and time again.

The trainee anaesthetist will obviously need to undertake wider reading. For example, the section on acid-base balance is excellent from which to revise, but perhaps difficult to learn from. The synopsis has justifiably strict criteria for accepting patients for daycase surgery, but some anaesthetists may not be so strict. In further reading the anaesthetists will be assisted by the excellent references at the end of each chapter.

The chapter on obstetric anaesthesia is most comprehensive. The section on regional anaesthesia is a great reference section with clear unequivocal descriptions of techniques. The brief final section on statistics is most helpful.

The chapter on rare diseases will be of great use when the anaesthetist is confronted with a patient only an hour or two before an operation, who is suffering from a rare condition.

Lee’s Synopsis of Anaesthesia is a textbook to have at hand and will prove invaluable to those in training, those recently trained, and those anaesthetists old enough to have been examined by J Alfred Lee himself. I can well remember being asked to tell him all I knew about Di Vinyl Ether!

N W KING
Consultant Anaesthetist, Leicester General Hospital, UK


The stated aim of this book is to be a “must for all of you who are involved in promoting physical activity and advising people who are interested in exercise”. Its target audience is diverse and includes specialists in sports medicine, general practitioners, sports scientists, and trainers. Individual chapters cover most aspects of exercise and range from a general overview of the methods of promoting physical activity in primary care to the specific problems of altered reproductive function in endurance athletes and the physiologic adaptations of altitude training. There are excellent chapters on exercise and diabetes and exercise and hypertension, with a chapter concentrating on the important interaction between exercise and psychological well being. Concise summaries are provided for all chapters and the most important learning points are highlighted in boxes. Multiple choice questions are also provided at the end of each chapter which allow the reader to test their knowledge. The book is well referenced and up to date, but deficiencies in the literature are acknowledged by the authors.

Anyone with an interest in sports medicine will find something in this book in support of them. It is well written and provides a concise yet comprehensive overview of the benefits and hazards of exercise.

R ROBINSON
Glenfield NHS Trust, Leicester, UK


The first section comprises three chapters. The first chapter is a brief historical history of the origins of a united Europe, the administrative bodies, how legislation is passed, and the implications for healthcare professionals. Chapter 2 focuses on the differences between EU member states by region: English speaking countries (UK and Republic of Ireland), Benelux countries (Belgium, the Netherlands, and Luxembourg), French speaking countries (France, Belgium, Switzerland (although not part of the European economic area), and Luxembourg), German speaking countries (Germany, Austria, Switzerland, and Luxembourg), Norden (Denmark, Finland, Iceland, Norway and Sweden), and Southern Europe (Spain, Portugal, Italy, and Greece). The organisation of healthcare systems, education and clinical training, terms and conditions of employment, practical differences in the workplace, recognised qualifications and examination grades, culture, and ethics are all outlined. In the third chapter the practical points of moving abroad are covered including two valuable checklists of the costs of moving abroad and planning a move.

The second section comprises details relevant to the 19 individual countries, including the United Kingdom. Obviously this book should be in every medical library. But would it be a worthwhile investment for someone who is going to work in Europe, especially as they will usually only be working in one country? The first section, of 43 pages, provides such a wealth of general information and advice that specific information provided about the country to which you intend to move and the others is so interesting, that the answer is “Yes.”

Oh, and whatever you do, ensure that you have the necessary qualifications, or can acquire the recognised equivalents abroad, such that you can return to your home country—comprehensive recognition of qualifications throughout Europe is not yet with us.

PHILIP D WELLSBY
Consultant Physician, Western General Hospital, Edinburgh, UK
**CD-ROM REVIEW**

**Blood Pressure Measurement.** Produced by the British Hypertension Society. BMJ Publishing Group; £47.00. ISBN 0727-913743.****

This CD-ROM specifies on its outside cover, in some detail, the minimum system requirements. These will not be met by all equipment currently in use in medical libraries nor by bottom of the range home computing. The technical qualities of the CD-ROM are excellent. It is easy to read, the sound production is clear (perhaps a little loud for use in library computer rooms), and it is user friendly. The content reflects current British Hypertension Society (BHS) guidelines and includes, in addition to historical notes, relevant explanation of different techniques used in incorporating ambulatory blood pressure measurement, measurement in special populations, and finally the rudiments of equipment evaluation.

The main features are detailed instructions in the technique of blood pressure measurement, pointing out common pitfalls and self testing sequences of falling mercury and Korotkov sounds. The anticipated audience ranges from junior nurses to senior physicians whose digit preferences and habitual methodological errors need ironing out. The material presented is up to date and lends itself to use in learning and assessment tutorials geared to the level of the learner group. The failure of the BHS measurement group to come up with unequivocal recommendations for standard sphygmomanometer cuff bladder dimensions will limit the shelf life of the BHS production and limits this reviewer's value for money verdict to a recommendation of purchase by institutions rather than individuals.

J E F POHL
Consultant Cardiologist,
Leicester General Hospital, Leicester, UK

**DIARY**

**Falk Symposia**

1–2 October 2000: Non-neoplastic diseases of the anorectum—an interdisciplinary approach (Freiburg, Germany)

3–4 October 2000: Immunosuppression in inflammatory bowel diseases—standards, news, and future trends (Freiburg, Germany)

12–13 October 2000: Biology of bile acids in health and disease (Den Haag, The Netherlands)

4 November 2000: Chronic inflammatory bowel diseases—progress and controversies at the turn of the century (Bucharest, Romania)

Details: Falk Foundation eV–Congress Division, Leinenweberstr 5, PO Box 6529, D-79041 Freiburg, Germany (tel: +49 (0) 761 130340, fax: +49 (0) 761 1303459, email: symposia@falkfoundation.de).

**Ninth International Symposium on celiac disease**

10–13 August 2000: Hunt Valley, MD, USA

Details: Althea Pusateri, Program Coordinator, University of Maryland School of Medicine, 655 W Baltimore Street, Baltimore, MD 21201, USA (tel: +1 410 706 3957, fax: +1 410 706 3103, web site: http://www.celiaccenter.org).

**Royal College of Physicians of Edinburgh**

2–15 September 2000: Healthcare for older people—the UK experience (course)

7–8 October 2000: Stroke treatment and service delivery (consensus conference)

Details: Education, Audit, and Research Department, Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh EH2 1JQ, UK (tel: +44 (0) 131 225 7324, fax: +44 (0) 131 220 4393, web site: www.rcpe.ac.uk).

**Royal College of Physicians of Edinburgh/Scottish Intercollegiate Guidelines Network**

3 November 2000: Symposium on clinical effectiveness, clinical guidelines and clinical standards

Details: Mrs Anne Fairbairn, Coordinator for Research and EBM, Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh EH2 1JQ, UK (email: a.fairbairn@rcpe.ac.uk).

**3rd Teupitz Colloquium**

17–20 September 2000: Basic Research in Endocrine Dermatology

Details: Professor Dr Ch C Zouboulis, Department of Dermatology, University Medical Center Benjamin Franklin, Free University of Berlin, Hindenburgdamm 30, 12200 Berlin, Germany (tel: +49 30 84 45 28 08, fax: +49 30 84 45 42 62, email: zoubbere@zedat.fu-berlin.de).

**St Mark’s Hospital & Academic Institute**

16–18 October 2000: Frontiers in colorectal disease (lecture course)

Details: The Administrator, St Mark’s Academic Institute, St Mark’s Hospital, Northwick Park, Harrow, Middlesex HA1 3UJ (tel: +44 (0) 20 8235 4046/8, fax: +44 (0) 20 8235 4039, email: e.power@ic.ac.uk; web site: www.stmarkshospital.org.uk).

**CORRECTION**

Iron deficiency anaemia—a clinical challenge

We regret that an error occurred in the above editorial by Wurm and Wicks in the April issue (2000;76:193–4). In referring to a related paper in the same issue by Willoughby and Laitner (2000;76:218–22) the name of Dr Laitner was inadvertently misspelt. Our apologies to Dr Laitner.