

and may be dangerous for elderly patients. The widespread use of second and third generation cephalosporins in elderly patients has been linked to an increased incidence of *Clostridium difficile* colitis with substantial morbidity and mortality.

Brown and Lerner's article was published shortly after the Standing Medical Advisory Committee's report from the UK Department of Health⁴ and the House of Lords select committee report.⁵ Both reports address the issue of antibiotic resistance in the UK and the need for rational and controlled antibiotic prescribing. It is therefore disappointing that the seminar did not address this important issue and may exacerbate the resistance problem in the UK by making some inappropriate recommendations.

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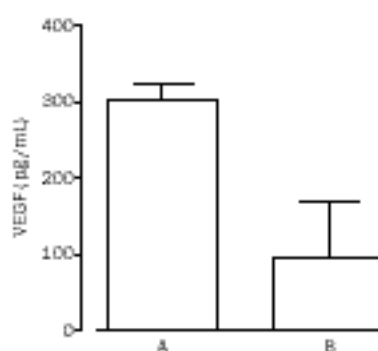
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- 1 Brown P, Lerner S. Community-acquired pneumonia. *Lancet* 1998; **352**: 1295-302.
- 2 Felmingham D, Robbins MJ, Tesfaslassie Y, Harding I, Shrimpton S, Gruneberg RN. Antimicrobial susceptibility of community acquired lower respiratory tract bacterial pathogens isolated in the UK during the 1995-1996 cold season. *J Antimicrob Chemother* 1998; **41**: 411-15.
- 3 Johnson AP, Speller DC, George RC, Warner M, Domingue G, Efstratiou A. Prevalence of antibiotic resistance and serotypes in pneumococci in England and Wales: results of observational surveys in 1990 and 1995. *BMJ* 1996; **312**: 1454-56.
- 4 Standing Medical Advisory Committee Subgroup on Antimicrobial Resistance. The path of least resistance. London: Department of Health, 1998.
- 5 House of Lords select committee on science and technology. Resistance to antibiotics and other antimicrobial agents. London: Stationery Office, 1998.

Space flight and growth factors

Sir—Hans-Christian Gunga and colleagues (Feb 6, p 470)¹ report the measurement of haemopoietic growth factors and vascular endothelial growth factor (VEGF) in the serum of a cosmonaut before, during, and after a space flight. Serum VEGF concentrations increased early in the flight, which was attributed to intravascular fluid shifts under microgravity.

We have measured more than 1000 serum and plasma samples for VEGF with a commercially available ELISA,



Serum concentrations of VEGF

Serum concentrations of VEGF in patients (65) with platelet counts of 100-200×10⁹/L (column A) are significantly higher than those of patients (83) with platelet counts of 30-99×10⁹/L (column B; p<0.0001). SEM error bars are shown.

and recorded a striking correlation between peripheral blood platelet counts and VEGF concentrations in serum ($r=0.8$; $p<0.001$). VEGF serum concentrations were substantially lower in thrombocytopenic patients, suggesting that platelets are the predominant source of VEGF in serum samples (figure). Moreover, people subjected to microgravity developed thrombocytopenia.^{2,3} Therefore, the fall in VEGF concentration in the cosmonaut's serum is likely to be the result of a lowered platelet count during the space flight and not a result of intravascular fluid shifts. This assumption is supported by slightly raised serum concentrations of thrombopoietin in the cosmonaut while he was in space. Thrombopoietin is constantly produced by the liver and kidney and its plasmatic clearance occurs by binding to the thrombopoietin receptor on megakaryocytes and platelets.⁴ Therefore, a lowered platelet count during space flight may result in raised thrombopoietin concentration and lower VEGF concentration in human serum.

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- 1 Gunga HC, Kirsch K, Roecker L, Jelkmann W. Haemopoietic, thrombopoietic, and vascular endothelial growth factor in space. *Lancet* 1999; **353**: 470.
- 2 Kalandarova MP. Changes in hematologic indicators in personnel testing during 370-day anti-orthostatic hypokinesia. *Kosm Biol Aviakosm Med* 1991; **25**: 15-18.
- 3 Davis TA, Wiesmann W, Kidwell W, et al. Effect of spaceflight on human stem cell hematopoiesis: suppression of erythropoiesis and myelopoiesis. *J Leukoc Biol* 1996; **60**: 69-76.
- 4 Cohen-Solal K, Debili N, Vainchenker W, Wendling F. Thrombopoietin (Mpl-ligand) and the regulation of platelet production. *Thromb Haemost* 1997; **78**: 37-41.

Vitamin B12 deficiency and nitrous oxide

Sir—Phillip Lee and colleagues (March 13, p 554)¹ highlight the danger of giving nitrous oxide to patients who may have unrecognised vitamin B12 deficiency. The number of patients reported to develop neurological problems is now into double figures.^{2,3} However, the worrying aspect of this report, from an anaesthetist's point of view, is that nitrous oxide was given for only 65 min. Since many operations last considerably longer than 1 h the implication is that are putting a substantial number of patients at risk.

How can we best manage patients with potential vitamin B12 deficiency who are about to undergo a general anaesthetic? Haemoglobin and mean corpuscular volume do not accurately reflect vitamin B12 concentrations.^{4,5} The investigators comment that serum vitamin B12 concentrations would have been helpful in the case described, but even this test is not entirely sensitive. Measurements of serum methylmalonic acid and total homocysteine are required to confidently rule out a deficiency in total body stores.⁵ Furthermore, screening every patient would be impractical, whereas limiting testing to vegetarians and those already known to have a disorder associated with vitamin B12 deficiency would inevitably mean missing some cases.

Nitrous oxide is certainly not essential for general anaesthesia; therefore, the safest answer is not to use it. However, if anaesthetists wish to use nitrous oxide, an alternative approach is perhaps to give vitamin B12 to all patients perioperatively for everything but the shortest of procedures.

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- 1 Lee P, Smith I, Piesowicz A, Brenton D. Spastic paraparesis after anaesthesia. *Lancet* 1999; **353**: 554.
- 2 Rosener M, Dichgans J. Severe combined degeneration of the spinal cord after nitrous oxide anaesthesia in a vegetarian. *J Neurol Neurosurg Psychiatry* 1996; **60**: 354.
- 3 Takacs J. N20-induzierte akute funikulare Myelose bei latentem Vitamin-B12-Mangel. *Anesthesiol Intensivmed Notfallmed Schmerzther* 1996; **31**: 525-28.
- 4 Broin SD, Kelleher BP, McCann SR, Ryder RJW, Scott JM. The value of the erythrocyte indices as a screening procedure in predicting nutritional deficiencies. *Clin Lab Haematol* 1990; **12**: 247-55.
- 5 Lindenbaum J, Healton EB, Savage DG, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anaemia or macrocytosis. *N Engl J Med* 1988; **318**: 1720-28.