Q_{10} biosynthesis and lead to myotoxic effects. Coenzyme Q_{10} status should, therefore, be monitored in patients taking statins and the possibility of coenzyme Q_{10} supplementation should be considered.

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1 Farmer JA. Learning from the cerivastatin experience. *Lancet* 2001; **358:** 1383–84.
2 Bliznakov EG, Wilkins DJ. Biochemical and clinical consequences of inhibiting coenzyme Q_{10} biosynthesis by lipid lowering HMG-CoA reductase inhibitors (statins): a critical overview. *Adv Therapy* 1998; **15:** 218–28.
3 Ogasahaa S, Engel AG, Frens D, et al. Muscle coenzyme Q deficiency in familial mitochondrial encephalomyopathy. *Proc Natl Acad Sci USA* 1989; **86:** 2379–82.
4 Sobreira C, Hirano M, Shanske S, et al. Mitochondrial encephalomyopathy with coenzyme (Q_{10}) deficiency. *Neurology* 1997; **48:** 1238–43.
5 Aberg F, Appelkvist EL, Broijersen A, et al. Gemfibrozil-induced decrease in serum ubiquinone and alpha and gamma-tocopherol levels in men with combined hyperlipidaemia. *Eur J Invest* 1998; **28:** 235–42.

Re-emergence of ebola haemorrhagic fever in Gabon

Sir—On Nov 16, 2001, a woman arrived at the Mékambo Hospital from Medemba village, about 30 km south of Mékambo, Gabon. She was admitted with symptoms of high fever, asthenia, arthralgia, diarrhoea, and vomiting, and died 4 days later. Just before she died, evidence of blood was noted in her faeces and mouth.

This woman was the fifth person in Medemba, all in the same family, to have such symptoms in less than 2 weeks. The other deceased family members had remained in the village. The first died on Oct 28. On Nov 26, a sixth member of the same family was admitted to Mékambo Hospital with the same symptoms. He died on Dec 1. On Nov 27, a nurse from the hospital, who had taken care of the woman, became ill and died in Makokou General Hospital on Dec 4, after developing similar symptoms.

The symptoms and the within-family transmission of the disease suggested ebola haemorrhagic fever. Dead great apes (about 20 gorillas and four chimpanzees) have also been found by hunters near Medemba and neighbouring villages.

On Dec 7, sera from the last two cases who died were sent to the Centre International de Recherches Médicales de Franceville (CIRMF) for testing by ebola antigen virus capture ELISA assay and IgG ELISA assay. Reverse transcriptase PCR to detect ebola viral RNA was also done on 200 µL of each serum sample.[1] The two sera had high titres (>256) of virus antigen and contained ebola virus RNA. These results confirm ebola virus infection. No IgG to ebola viral antigens was detected, but this finding is consistent with previous results, showing that fatal cases of ebola infection do not develop specific IgG.[2] The outbreak of ebola haemorrhagic fever was officially declared on Dec 8, 2001.

To characterise this new strain, we extracted viral RNA from the two sera. The first strands of cDNA from the L-gene were synthesised and amplified by a DNA thermal cycler 9700.[1] Analysis of the sequenced PCR products (420 bp) showed only four synonymous substitutions compared with Mayinga-76 (DR Congo, 1976), Kikwit-95 (DR Congo, 1995), and Gabon-94 sequences. This strain is, therefore, new (Mekambo-01) and belongs to the Zaire subtype. The genetic diversity of this 420 bp sequence between Mekambo-01 and Gabon-94 strains is 0·95%. Molecular characterisation of the glycoprotein and the nucleoprotein genes is in progress at CIRMF.

On Dec 20, 2001, the outbreak was still continuing, and national (Gabonese public health authorities and army medical services, and CIRMF) and international (WHO, Médecins Sans Frontières, and Institut Pasteur-Mérieux de Lyon) teams are trying to contain it. This is the fourth outbreak of ebola in Gabon in 6 years, the last one ending in May, 1997,[3] and for the fourth time, the outbreak happened in the same area of Gabon (Ogooué-Ivindo province). The virus, therefore, circulates at a high concentration in this area. The reservoir for the ebola virus is still unknown and this situation reinforces the need to search for it in this densely contaminated area.

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1 Leroy EM, Baize S, Lu C-Y, et al. Diagnosis of Ebola haemorrhagic fever by RT-PCR in an epidemic setting. *J Med Virol* 2000; **60:** 463–67.
2 Baize S, Leroy EM, Georges-Courbot M-C, et al. Defective humoral responses and extensive intravascular apoptosis are associated with fatal outcome in Ebola virus-infected patients. *Nat Med* 1999; **5:** 1–5.
3 Georges AJ, Leroy EM, Renaut AA, et al. Ebola hemorrhagic fever outbreaks in Gabon, 1994–1997: epidemiologic and health control issues. *J Infect Dis* 1999; **179** (suppl 1)**:** S65–75.

Transplantation in chronic myeloid leukaemia

Sir—The European Group for Blood and Marrow Transplantation (EBMT) has done a survey on transplant numbers in Europe every year since 1990. Information is obtained according to indication, donor type, and stem cell source for the preceding year. These surveys, which are published regularly, cover more than 95% of all transplants in Europe and provide a synopsis of current practice and trends.[1]

Data from the 2000 survey point to a new phenomenon. So far, chronic myeloid leukemia (CML) has been the leading indication for allogeneic transplants, with an annual increase of about 100 transplants per year. In 2000, however, the number fell by about 150 transplants, corresponding to a reduction of about 10%. This change took place despite a continuing rise in overall transplant activity. Even more striking was the decline in autologous transplants for CML with less than 50% of numbers in 2000 compared with 1999.

The decline in CML transplant numbers coincides with the introduction of imatinib, a disease-specific tyrosine kinase inhibitor. Phase I data, published in spring, 2001, document its clinical efficacy.[2] This compound will change current strategies in CML treatment and alter wider cancer treatment. The decline in transplants preceded the first publication of clinical data in this field by a year, which is a notable observation. For such a disease as CML, long-term observations are essential for final assessments of treatment strategies, and transplants are the only therapeutic approach with the potential for cure.

A similar change in transplant activity was noted a few years ago with autologous transplants for breast cancer. Numbers rose substantially from 1993, then declined in 1998. The increase and decrease began about 1–2 years before the key publications appeared.[3] Moreover, the debate on the usefulness of transplants in breast cancer is still not settled.

Such changes in transplantation activity for specific indications within a short period are of interest. Decisions in the respective institutions for breast cancer and CML seem to have been affected more by expectation than by evidence-based medicine criteria, and followed stock-market patterns—anticipation drives decisions.

These changes arose in an area of

advanced medicine at its highest scientific and technological level. It might be time to integrate into medical decision making some of the motives that drive decisions at the stock exchange. Anticipatory decisions are not bad or necessarily based on rational criteria, but physicians and patients should be aware of them. Hopefully, the results for CML will meet the expectations.

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1 Gratwohl A, Passweg J, Baldomero H, Urbano-Ispizua A. Hematopoietic stem cell transplantation activity in Europe. *Bone Marrow Transplant* 2001; **27:** 899–916.
2 Goldman JM, Melo JV. Targeting the BCR-AbL tyrosine kinase in chronic myeloid leukemia. *N Engl J Med* 2001; **344:** 1084–86.
3 Stadtmauer EA, O'Neill A, Goldstein LJ, et al. Conventional-dose chemotherapy compared with high-dose chemotherapy plus autologous hematopoietic stem-cell transplantation for metastatic breast cancer. *N Engl J Med* 2000; **342:** 1069–76.

On prion disease and form

Sir—There is a notion called formative causation, in which morphogenic fields play a causal part in the development and maintenance of the forms of systems at all levels of complexity (both internal structure and external form).[1]

Three-dimensional form can be learned by molecules, seen, for example, when a new crystalline structure is grown. A new substance can take a long time to develop its crystalline structure, but after it has been achieved once, it becomes easier. If a solution of the substance to be crystallised is seeded with microcrystals of the ultimate form, the process is accelerated.

The difference between PrP^{C} and the prion form of the protein $PrPS^{C}$ is in the tertiary protein structure. The normal tightly folded α structures become more loosely bound in β sheets, then more and more of the PrP^{C} molecules transform into PrP^{SC} molecules until they disturb the function of the affected brain cells.

The reproduction of the prion molecules, therefore, seems not to be a gene-regulated event but one of an alternative formative causation that, within the cellular environment, has other molecules saying "me too".

The juxtaposition of PrP^{SC} to the PrP^{C} molecules might take a long time to alter the tertiary structure. Imitation might be the means of reproduction. If this is the case, we have a new form of disease.

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1 Sheldrake R. A new science of life. London: Blond and Briggs, 1988.

Strengthening research capacity

Sir—In your Oct 27 editorial[1] you highlight crucial issues about research capacity development in the less-developed world. We agree that, in Africa, greater acceptance of the notion that health research is a prerequisite of development, and not a luxury of affluent societies, is crucial to bridging the gap between research and policy. Existing solid scientific evidence about prevention, diagnosis, and treatment, should be the basis for health policy, and where such evidence is lacking we must invest in research.

Less than 10% of the global spending on health research is devoted to less-developed countries, which shoulder 90% of the global disease burden.[2] With the need to achieve so much with so little, every step must be taken to avoid duplication while maintaining a level of enthusiasm necessary for accomplishing such an enormous task. More research is needed in less-developed countries, but we must also realise that research already done in these parts of the world is under-represented in major databases. The efforts of the Cochrane Collaboration in unearthing previously unknown controlled trials done in these countries by hand searching indexed and non-indexed journals is to be commended.[3]

We believe that an indispensable first step in investing in new research in less-developed countries, as elsewhere, should be a systematic synthesis of relevant existing research. This search should identify areas in which new evidence is needed, and thus chart methods and rational paths for further research. Without such systematic synthesis, the limited resources made available for health research[2] will continue to be squandered on ill-conceived studies, and avoidable confusion will continue to result from failure to set new studies in the context of other relevant research. Examples abound where failure to systematically review research evidence has resulted in untold and avoidable suffering.[4]

Systematic reviews can be done with fewer financial and human resources and faster than other types of research. Such cost-effective research is certainly needed in the less-developed world, whose inhabitants deserve the best possible care that resources permit. Given that evidence-based health care offers the best chance of reaping maximum benefits from limited resources, there is need for funding agencies to provide resources for the preparation and maintenance of systematic reviews of existing research evidence relevant to the less-developed world, as a scientific and ethical requirement, before investing in new research.

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1 *The Lancet*. Strengthening research capacity's weakest link. *Lancet* 2001; **358:** 1381.
2 Global Forum for Health Research. 10/90 report on health research 2000. www.globalforumhealth.org/pages/index.asp (accessed on Jan 15, 2002).
3 Pienaar E. The African trials register: providing Africa with the best evidence. 9th International Cochrane Colloquium, Lyon, France, Oct 9–13, 2001.
4 Chalmers I. Foreword. In: Egger M, Davey Smith G, Altman DG, eds. Systematic reviews in health care: meta-analysis in context. London: *BMJ* Books, 2000.

Global issues in medical education

Sir—We believe that all medical undergraduates should learn about health and health care in a global perspective. Bateman and colleagues (Nov 3, p 1539)[1] describe examples of optional courses in three European countries. Elective courses preach to the converted, improving the knowledge of students who already recognise the effect that globalisation will have on their future practice.

Women, students with previous experience in less-developed countries, and members of political or voluntary organisations are more likely to support teaching on global health issues.[2] There might, therefore, be an inverse care law[3] under which medical students with the greatest teaching needs are least likely to attend courses from which they would benefit.

The University of Bristol has included global health topics as part of the core curriculum since 1999. The international health course is the longest established and one of the few compulsory global health courses in a UK medical school and is taught as a