CORRESPONDENCE

e-mail submissions to correspondence@lancet.com

Prevention of neurolathyrism during drought

Sir—In our Research Letter (Nov 29, p 1808),[1] we presented evidence that neurolathyrism in Ethiopia can be prevented if food aid baskets contain sufficient cereals to balance the deficiency of essential sulphur aminoacids in the staple diet of grass pea *(Lathyrus sativus)* in periods of drought and insufficient food supply.

In a Commentary on our Research Letter, Peter Spencer and Valerie Palmer[2] criticise the potential role of cereals in the grass pea diet and cite profusely from the conclusions of a paper by Teklehaimanot and colleagues,[3] which refers to a 1974 epidemiological survey by Dwivedi and Mishra in the Indian districts of Durg, Rajnandgaon, and Raipur. This paper states that, "The Indian staple ghotu, prepared by cooking a mixture of grass pea and rice . . . precipitated lathyrism more rapidly than chapatti, the unleavened bread form", suggesting that the addition of rice to the grass pea had had an adverse effect. However, reports on this survey are confusing. In a subsequent publication,[4] Dwivedi himself mentions that during this 1974 survey, there was "a shortage of rice in these drought affected areas, resulting in the consumption of large quantities of the only available pulse Khesari dal (*L sativus*) in the form of ghontu (a paste prepared by boiling *L sativus* flour in water)". The shortage of rice resulted from the failure of the monsoon rains, and this precipitated lathyrism much faster than normal in this rice-growing area.

The original paper by Dwivedi and Mishra,[5] however, mentions that "all the nine affected cases gave history of getting the disease about 20 days after consuming Ghotu containing mainly *Lathyrus* flour with small quantities of rice. Ghotu is prepared by cooking 3 parts of *Lathyrus* and 1 part of rice in water". This ratio is less than the "at least a third cereals" we recommended in our Research Letter. The advice to mix at least a third cereals with grass pea preparations thus remains valid.

Spencer and Palmer propose to reduce the neurotoxin level in the grass pea diet by soaking and rinsing the seeds with sufficient water. Soaking and rinsing seeds before cooking is a culinary practice that has been used for millennia, which has not prevented several neurolathyrism epidemics in the Indian subcontinent and Ethiopia during the previous century. Optimising this on a laboratory scale might indeed reduce the availability of water-soluble neurotoxin, together with other water-soluble metabolites such as vitamins. However, to advise the poorest of the poor on the Ethiopian highlands to use more water to rinse the seeds and then to discard this water when the land is parched and the crops wilted seems more cynical than practical.

We thank Ramesh Bhat of the National Institute of Nutrition, Hyderabad, India, for help with the original literature.

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2 Spencer PS, Palmer V. Lathyrism: aqueous leaching reduces grass-pea neurotoxicity. *Lancet* 2003, **362:** 1775–76.
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Sir—In their Commentary,[1] Peter Spencer and Valerie Palmer miss the real point of Haileyesus Getahun and colleagues' Research letter,[2] and instead give their own view on how neurolathyrism might be controlled.

The point made by Getahun and colleagues is that supplementation of grass pea with food-aid cereals has significantly reduced the risk of neurolathyrism, and that such supplementation could be used as a continued approach to further reducing the risks. Instead of highlighting this aspect, Spencer and Palmer suggest steeping the dehusked pulse in hot water and boiling as a simple means of control. I would like to point out that this simple procedure will never be acceptable at a household level. Pulses in particular are favoured for their taste and flavour. No one will be willing to throw away the soup made from it and eat only the solid pulse. Detoxifying 50–100 g of the pulse on a laboratory bench is no doubt very effective, but householders will pass it off as a joke.

Although different culinary methods of preparing a grass-pea meal based on regional and cultural backgrounds might have a role in the incidence of neurolathyrism, a point to remember is that for any boiled form of grass pea (porridge, soup, *ghotu*) most of the toxin will be in a solubilised form and thus available for absorption straight away. Absorption of toxins in bread or *chapati* made from the pulse will occur over a longer period. Our own findings[3] show that the neurotoxin in grass pea is indeed detoxified in human beings, in contrast to what happens in animals. Hence the form in which grass pea is presented to the system might well be an important point to consider in risk assessment.

Although we keep debating how to reduce the risk of neurolathyrism, what Getahun and colleagues have reported is that in Ethiopia, a cereal food-aid supplementation has really worked and is indeed a very practical solution.

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Schistosomiasis control

Sir—A lengthy policy article on schistosomiasis control (Dec 6, p 1932)[1] surely represents a sign of renewed interest in the control and research on this disease. However, we would like to complement the article with a few issues to clarify the current WHO policy and the commitment of the Schistosomiasis Control Initiative (SCI) to sustained control of morbidity due to schistosomiasis.

Jürg Utzinger and colleagues state that World Health Assembly (WHA) resolution 54.19 does not contain recommendations for preventive measures. We would like to point out that the resolution does recommend preventive measures. It urges WHO Member States "to promote access to safe water, sanitation and health education through intersectoral collaboration" and "to ensure that any development activity likely to favour the emergence or spread of parasitic diseases is accompanied by preventive measures to limit their impact".[2] WHO welcomes the international momentum in favour of provision of clean water and sanitation which will eventually lead to long-term transmission control, provided sufficient quantities of safe water are made available in transmission areas so that individual households will have safe water for daily activities other than their needs for drinking and cooking.

We believe, however, that regular chemotherapy is able to control morbidity even in the absence of sanitary improvements, and that it can be delivered in a sustainable way. Praziquantel is one the most potent anthelmintics on the market. It is now out of patent and can be purchased at a cost of less than US$0·20 to treat a child. Up to now, despite massive use in countries such as Egypt, and effective monitoring by an EU-funded concerted effort, efficacy in the field continues to be excellent.[3] The best way forward today is to make this drug available by use of existing systems and local resources. We therefore agree with Utzinger and colleagues that the main challenge in endemic countries is "the political will for use of local control resources".

The authors mention that all the controls in the 1980s in Africa have been abandoned and state that this underscores that dependence on chemotherapy alone is not sustainable. The work of the 1980s has showed that regular chemotherapy reverses morbidity and prevents irreversible sequelae in adulthood. However, the real reasons behind the failure to sustain these achievements could have been different. Schistosomiasis control was undertaken in a totally different regional and global context from that existing today. Expensive drugs were delivered through vertical structures driven mainly by bilateral donors. There was no sense of ownership by countries and communities. We therefore believe the real issue was related to sustainability of funding rather than the effect of chemotherapy.

We believe that the launch of the Partners for Parasite Control (PPC) after the 2001 WHA resolution has triggered momentum for the control of helminths and other parasitic diseases, and not solely schistosomiasis.[4] The main challenge will be to progressively build simple interventions into available delivery structures such as health services, schools, and communities, by use of local resources. The PPC today is an open platform, with no heavy or costly structure, and the SCI programme is an excellent example of a PPC partner initiative. The time could soon be opportune for a more formal alliance, but we wish this to be discussed in open fora where existing partners and new ones will clearly show what each is able to offer.

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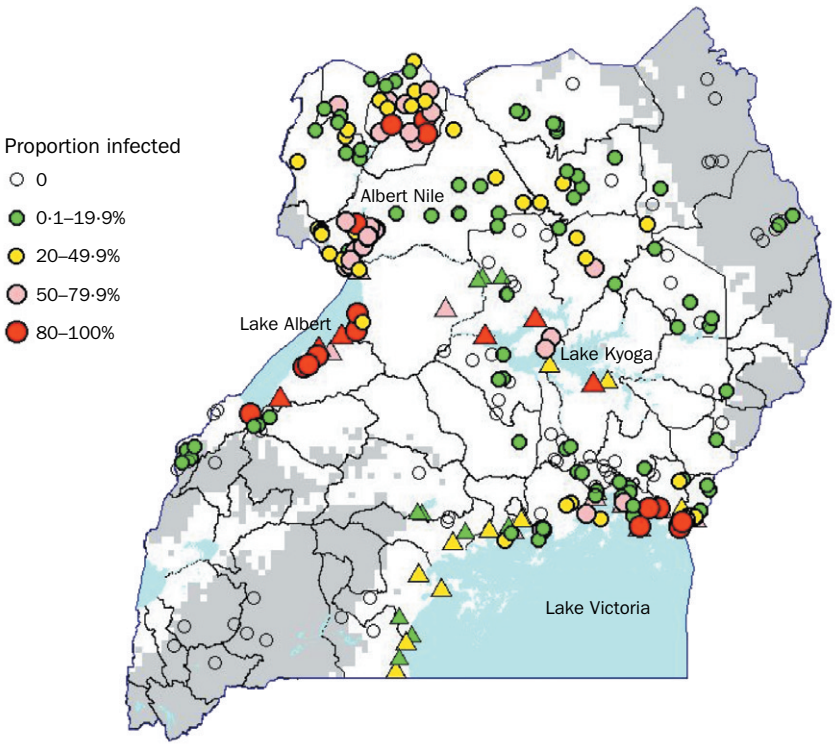
Sir—Jürg Utzinger and colleagues[1] discuss the design and implementation of large-scale schistosomiasis control under the auspices of the Schistosomiasis Control Initiative (SCI). A key issue identified by the authors was the rapid and accurate identification of endemic regions and of populations at risk. We would like to comment on these issues and highlight our experience in Uganda, the first country selected for SCI support.

Although schistosomiasis (mainly caused by *Schistosoma mansoni*) in Uganda is an important public health problem, the current epidemiological situation has not been fully described. Our first stage in targeting national control was to use geographic information systems (GIS) to map available epidemiological data collected with traditional parasitological methods.[2] The derived map, based on 23 627 individuals in 269 schools or communities, indicated a widespread occurrence of infection and a striking variability in infection prevalence (figure). The second stage was to overlay environmental data to identify ecological limits of transmission; no transmission occurred in communities where total annual rainfall was less than 900 mm and altitude was more than 1400 m, and these areas could be set aside without the need for further surveys. In the third stage, high spatial resolution Landsat satellite data were used to define lakes and large rivers. It was shown that prevalence consistently exceeded 50% (WHO's recommended threshold for mass treatment) in areas within 5 km of Lakes Victoria and Albert, and thus, it could be justified with relative certainty to provide populations in these areas with mass treatment. Outside these regions, however, there is a need to augment geographical information systems and remote sensing (GIS-RS) approaches with field-based mapping and surveillance methods.

Although simple, inexpensive school questionnaires can be used to screen communities for *S haematobium*, such approaches for *S mansoni* remain elusive and although costly, parasitological diagnosis is still the preferred option.[3] To reduce these associated costs, we have been exploring sequential sampling methods,[4] which aim to combine data collection and data analysis into a single process that relies on counting the number of infected individuals found and checking whether this exceeds a predetermined number of cases (ie, treatment threshold). For example, 20 individuals are examined and when any nine infected individuals are detected, sampling ceases and mass treatment is provided. Computer simulations of field data indicated that such a sampling plan had a sensitivity of 0·967 and a specificity of 0·973 in identifying communities with true prevalence of 50% or more. On this basis, rapid mapping is underway in Uganda with new, cheap portable microscopes for diagnosis, coupled



Distribution of intestinal schistosomiasis (*Schistosoma mansoni*) in Uganda
Circles indicate school survey prevalences and triangles represent community survey prevalences. Grey areas indicate areas where either altitude exceeds 1400 m or total annual rainfall is less than 900 mm.

with integrated global positioning systems and hand-held computer devices for data collection to determine the fine-scale distributions of schistosomiasis. Sensible application of such rapid, low-cost methods will help guide control efforts, driven by practical science, to achieve the maximum benefit to afflicted populations.

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Plea to restore public funding for vaccine development

Sir—The article by the new Director General of the WHO (Dec 20/27, p 2083)[1] will lift the hearts of many in the developing world because of its thrust "to take the organization back to its core values".

I write from India where the WHO, in the recent past, had developed an unsavoury reputation. I am looking here only at the issues surrounding vaccinations. The WHO and the Global Alliance for Vaccines and Immunization (GAVI) have been bullying the government to include newer (and expensive) vaccines such as hepatitis B vaccine and the *Haemophilus influenzae* type b (Hib) vaccine into the routine programme of immunisation in the country. Reliable data from India suggest only a very small number die of hepatocellular carcinoma.[2] Similarly, for Hib, the incidence of invasive disease in India is remarkably low.[3]

The argument blatantly used to try to make the vaccine universal is that the price of the vaccine can come down if its uptake can be increased. Data from overseas[4] are misleadingly extrapolated to the Indian population to convince the government to underwrite the vaccination programme. For example, it is suggested that 193 000–261 000 people die of hepatocellular carcinoma due to hepatitis B,[5] although data from well maintained, population-based registries in India, project a figure of just 5000 deaths.[2]

I have been keen to know how the figure of 193 000–261 000 deaths from hepatocellular carcinoma in India each year was arrived at. The underlying calculation is fascinatingly simple. Beasley has reported that 25% of male hepatitis B carriers in Taiwan die of the disease.[4] The same report says death among women carriers is a fourth of this, but that is disregarded. If 4% of the population in India are carriers, then extrapolating Taiwan figures for death, 1% of all deaths in India must be due to hepatitis B. In a population of one billion, 1% of deaths is uncannily close to 193 000 and 261 000.

In effect, poor countries are being asked to use vaccines they do not need, so that the price of vaccines is reduced in the west.

Publicly funded organisations, such as university research departments, have been squeezed out of the field of basic research in areas of public health, including vaccine development, and we have become dependent on vaccine manufacturers for further research into newer vaccines. With them as partners for projects like GAVI, the thrust has been to increase uptake of vaccines whether needed or otherwise. Vaccine manufacturers thus ensure good returns per dollar expended on philanthropy. This, I feel, needs to be reversed and universities and similar public institutions must be funded to be able to do essential vaccine development so we can move out from the stranglehold of vaccine manufacturers.

I hope the new Director General will be able to influence this and find the fund for his many projects. He certainly has the goodwill and good wishes of all of us.

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Anopheles funestus in Sahel: new evidence from Niger

Sir—The Sahel is one of the African zones most exposed to climate change. Because of the obligatory aquatic phase of malaria mosquitoes, rainfall is thought to have a large effect on malaria prevalence, and drought seems to be associated with fewer mosquito bites. The disappearance of one the most dangerous African vectors, *Anopheles funestus*, from the Sahelian zone was imputed to the drought that has lasted three decades.[1] In 1999, its comeback in Sahelian Senegal was suspected of being linked with the local development of irrigation systems.[2]

We did a study in Niger during the 2003 rainy season to assess malaria vector presence and abundance across a south–north transect containing isohyet curves of 800–100 mm, corresponding to the most variable rainfall zone. 14 villages were sampled in the Soudanian, Sahelian, and Saharan regions.

Members of *Anopheles gambiae* complex were found in all three zones, as expected. However, *A funestus* was also found in eight of the villages: all four of those in the Soudanian region and four of six in the Sahelian zone. This distribution is similar to that seen in the 1960s, but more recent studies have failed to show it. Irrigation is limited to the Niger valley and could not explain the comeback of *A funestus* in these regions.

Although a global decrease in rainfall is still evident, groundwater levels are increasing in several areas of the Sahel.[3] The clearing of natural wooded savannah and increases in cultivated areas have modified surface characteristics such that they tend to enhance water run-off. Temporary ponds are linked with groundwater recharge, and are now more numerous than they used to be and are present for longer. Many vectors are adapted to such breeding sites, which could lead to increase vector density. The greatest abundance of *A funestus* we found was in the Sahelian zone, in a village where this hydrological process is known to take place.

Although the whole Sahel zone should not be concerned by the described hydrological process, the striking effect of local or subregional factors on transmission should be taken into account in malaria transmission models. At a time when transgenic mosquitoes are making the headlines in entomological malaria research, we would be wise to remember the interactions between anopheline populations and environmental factors.

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Taenia asiatica intermediate hosts

Sir—In their Rapid review (Dec 6, p 1918),[1] Akira Ito and colleagues conclude that human beings are probably excluded from the list of potential intermediate hosts for the tapeworm *Taenia asiatica* because they are not included in the list of intermediate hosts for its sister species *Taenia saginata*. This point is of great relevance to human health because if the eggs of *T asiatica* are infective for human beings, the carriers of adult *T saginata*-like specimens could also be involved in the production of human cysticercosis.[2]

Ito and colleagues' conclusion is a possibility, but that prediction logically should also be valid for whatever other hosts are not included in the list of *T saginata* intermediate hosts. For example, since pigs and wild boar are not included in this list, we should be able to predict that cysticercosis caused by *T asiatica* does not occur in these two hosts either. However, pigs and wild boar are precisely the naturally infected hosts of *T asiatica*.

It would be more appropriate to predict that, due to the clear tropism of the larval stage of *T asiatica* in its intermediate host, neurocysticercosis caused by this species is unlikely in human beings. But in the context of the differential diagnosis of human liver lesions compatible with the larval development of cestodes, *T asiatica* should be included, particularly in Asian countries where the parasite is already known to exist.[3]

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Addressing internet reference loss

Sir—We write to draw your attention to the growing problem of the loss of access to internet citations.[1–4] The internet has revolutionised access to information, and, not surprisingly, readers of medical journals are increasingly referred to the internet for information unavailable elsewhere.[2]

Since recent research shows that more than one in eight internet citations in high-impact medical and scientific journals become extinct in about 2 years,[2] concern about whether referenced electronic information will be accessible in the future is justified. Furthermore, even if internet addresses yield information, a reader cannot be assured that the accessed electronic information is unchanged from the original referenced by the authors.

Although *The Lancet* does request inclusion of accession dates in internet references, additional measures are needed to better preserve electronic citations. Two additional guidelines would help fulfil this need: requiring authors to submit all referenced internet information to the Internet Archive (www.archive.org), and to keep hard copies of all such referenced information until available on this archive (about 6 months).

The Internet Archive, a non-profit internet library that preserves digital information at no cost to the author, reader, journal, or publisher, provides a promising first step towards solving problems incurred by broken internet links and altered electronic information in scientific publications.[5] Through use of the Alexa web crawler, the archive's WayBack Machine allows for the storage and retrieval of electronic information located at a given internet address (uniform resource locator [URL]) as it appeared on a specific date. A collaborative effort by authors and journals to submit all cited article URLs to the Internet Archive will better ensure access to electronic

references now and for years to come.

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Viral hepatitis C

Sir—We enjoyed the Seminar by Thierry Poynard and colleagues (Dec 20/27, p 2095),[1] but were disappointed that space permitted only a cursory comment about orthotopic liver transplantation (OLT) in the management of patients with chronic hepatitis C virus (HCV) liver disease. As Poynard and colleagues indicated, HCV-mediated cirrhosis is currently the primary indication for OLT in the USA and Europe: during 2002, almost 40% of US patients undergoing OLT had end-stage chronic HCV liver disease.[2]

However, a huge imbalance exists between the number of patients listed for OLT with end-stage chronic HCV liver disease and the very limited availability of donor organs. Moreover, the technique of adult living donor liver transplantation (265 cases in USA during 2002) cannot be expected to make up this shortfall at the current rate.[3] Therefore, alternative therapeutic strategies that could reduce or delay requirement for OLT in this group of patients are required.

Combination antiviral therapy (currently pegylated interferon alfa and ribavirin) has been examined almost exclusively in patients with compensated, stable, chronic HCV liver disease, including patients with biopsy-proven cirrhosis without clinical evidence of liver disease. Concern about liver decompensation or even liver failure based on experience gained from treating patients with chronic hepatitis B virus liver disease with interferon alfa, persuaded physicians that combination antiviral therapy for patients with decompensated chronic HCV liver disease should be avoided. Furthermore, possible induction or exacerbation of neutropenia and thrombocytopenia that might result in systemic sepsis or haemorrhage, respectively, among such patients have been major treatment deterrents.[4] Although the number of adverse events recorded in this study of only 15 treated patients was 23, just two of these had significant clinical consequences (infections).[4] Nevertheless, the study was halted.

Despite this sentiment, we believe that combination antiviral therapy for patients with decompensated, but stable, chronic HCV liver disease should be considered seriously for several reasons. First, viral eradication could lead to remission of liver disease, thereby obviating requirement for OLT. Second, sustained viral clearance could limit disease progression and the emergence of hepatocellular cancer. Third, pre-OLT viral eradication is highly desirable given the extent to which reinfection and subsequent allograft failure have become major problems among immunosuppressed patients. Antiviral therapy has been shown to be feasible and potentially effective in this group.

A low accelerated dose regimen of interferon alfa and ribavirin has been studied in patients with decompensated chronic HCV liver disease.[5] Both drugs were started at half the standard treatment doses and then advanced in step-wise fashion as tolerated, first interferon alfa, followed 2 weeks later by ribavirin. Almost 40% of patients cleared viral RNA, and 22% had sustained viral clearance. 20% of patients stopped treatment, either because of symptoms (15%) or laboratory abnormalities.

Therefore, we wish to qualify Poynard and colleagues' statement that "liver transplantation is the primary treatment option for patients with decompensated cirrhosis", and advocate that combination antiviral therapy should be considered in patients with decompensated, but stable, chronic HCV liver disease, not least the many individuals listed for OLT.

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Sir—In their Seminar on viral hepatitis C, Thierry Poynard and colleagues[1] do not discuss the appropriateness of vaccinating patients with hepatitis C virus (HCV) against hepatitis A virus (HAV).

Superinfection with HAV in patients with underlying chronic HCV infection can result in severe acute or even fulminant hepatitis.[2] Hepatitis A vaccine, which has been shown to be both safe and effective in patients with HCV infection, could prevent such poor outcomes.[3]

Although the vaccination of all patients with chronic hepatitis C against HAV might not be cost-effective in areas with a low incidence of HAV infection,[4] such vaccination should be recommended in individuals with HCV infection who have evidence of chronic liver disease.[5]

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Eponymous but anonymous: who was Dr Siewert?

Sir—100 years ago, on Feb 8 1904, the *Berliner klinische Wochenschrift* published a description, by Dr A K Siewert, of the patient "A.W" who since birth had the unusual combination of symptoms of bronchiectasis and *situs inversus totalis*.[1] This was the first description of what has since become known as Kartagener's syndrome,[2] immotile cilia syndrome, or primary ciliary dyskinesia. Siewert's 1904 paper has been much cited in recent years, and the disorder is often now referred to as Siewert's syndrome or Siewert-Kartagener syndrome.

The begetters of eponymous disorders are usually well known, with websites such as http://www.whonamedit.com providing detailed biographies. Siewert, however, is an exception, with even minimal biographical information apparently being unavailable. I cannot find his date of birth or death, his nationality, the university where he qualified, or even the meaning of his initials. My own research has found that when Siewert published his 1904 paper,[1] he was working in K E Wagner's clinic in Kiev, in the Ukraine, and in the same year he also published a paper on cardiovascular physiology from J Laudenbach's laboratory in Kiev's St Vladimir University (now National Taras Shevchenko University).[3] He was still in Wagner's clinic in 1912, as a *Privatdozent*, when he published a paper on biochemical changes in urine after meat-eating.[4] He survived World War I, and in 1922 published a further paper on cardiology from Kiev.[5] After this time, the trail runs cold. Perhaps this centennial year could provide the impetus for the publication of further biographical details about this eponymous but anonymous physician.

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A shoddy town named Batley

Sir—Batley, 8 miles south of Leeds in England's Yorkshire moors, provided me a locum job and the warmth of a hospital in the winter of 1952. It also allowed me to observe one of the last reminders of the industrial revolution as described by Dickens.

I took the appointment not knowing that Batley's factories wove the cheapest variety of woollen fabrics, termed "shoddy", using discarded wool. I could hardly imagine that there still existed such a town in the mid-20th century, in stark contrast even to bombed-out London and Birmingham.

In mid-winter, the hospital enjoyed brilliant sunshine on the snow-covered moors on either side of the narrow valley, reminiscent of Wuthering Heights. Nearby were the manor houses of the mill owners, flaunting Rolls-Royces in their porches.

The town in the valley was, however, permanently enveloped in a thick blanket of smog spewed from the factory chimneys. The narrow valley was paved with cobbled stones with workers' houses interspersed between the factories. A stream flowing through the valley provided water for the manufacture of the shoddy. Excess water due to rainfall or melting snow would enter the dwellings over their thresholds.

The common meeting place of those who lived in the vale and on the hilltop was the hospital. A discernible difference between the well suited elite and the ill-clad, but well nourished, workers denoted the economic disparity of society even after two centuries of democracy. While the affluent sought medical help in nearby Leeds, the Batley General Hospital, recently transferred to the National Health Service, provided adequate medical care to the workers, as well as a few days of respite from their gloom—a benefit provided by the recently elected labour party.

The workers' plight, despite the wealth derived from the industrial revolution and the colonies over 250 years, was revealed by the gross manifestation of rickets described only in older textbooks of medicine. A doctor trained in the 1940s could never dream of observing this—severe bowed legs, knock knees, massive bossing of the head, "rickety rosary", and dental caries were seen in almost every second person over the age of 40 years. Its elimination by vitamin-enriched butter was an equally dramatic manifestation of a medical solution to what was essentially a socioeconomic problem.

I hope that as a result of the "trickle down" effect of post-war western affluence and the labour government, the Batley of my days no longer exists.

The medicalisation of sociocultural and economic problems of the need-based countries comprising 80% of the present world's population has proved counterproductive. This is partly due to a technomanagerial and medicalised approach to health care imposed by international agencies like the WHO, UNICEF, and World Bank while ignoring their underlying economic exploitation.

An invariable "trickle up" effect is seen internationally and within these countries where an imitative urban industrial form of growth prevails. "Health for all" can only be based on a new socioeconomic order encompassing cooperation, justice, and equity.

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Geddes JR, Carney SM, Davies C, et al. Relapse prevention in antidepressant drug treatment in depressive disorders: a systematic review. Lancet *2003;* ***361:*** *653–61.*—In this Article (Feb 22), the Conflict of interest statement (p 660) should have noted that Guy Goodwin has acted as a consultant to Eli Lilly, Lundbeck, Pierre Farbre Medicament, and SmithKlein Beecham, and that David Kupfer has acted as a consultant to Novartis and is on advisory boards of Pfizer, Eli Lilly, and ForestLaboratories. Furthermore, the Acknowledgments section should have included that the research was supported in part by the National Institute of Mental Health Grant MH-30915 (Kupfer and Frank).

Vivekananthan DP, Penn MS, Sapp SK, Hsu A, Topol EJ. Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomised trials. Lancet *2003;* ***361:*** *2017–23.*—In this Article (June 14), in table 1 (p 2018), the number of controls in the PHS trial should be "11 035".