deaths due to Creutzfeldt-Jakob disease reported to the Office of Population Censuses and Surveys during the 15 years 1979-93 show a significant excess in 1992 ($\chi^2=11.67$, $P<0.01$) and the interval 1987-93 ($\chi^2=4.29$, $P<0.05$). The age adjusted mortality rose by 30%, from 0.6 to 0.8 deaths per million.

Deaths from Creutzfeldt-Jakob disease in the two intervals 1979-85 and 1987-93 can also, however, be viewed as two samples taken from a common distribution, with the earlier sample being less complete than the later. The difference between the two distributions of cumulative mortality was minimal ($\chi^2=0.151$, $df=16$, $P>0.999$), and a two by two analysis of the proportion of deaths below age 45 during the two intervals (8.8% and 11% respectively) did not show a significant difference ($\chi^2=0.261$, $df=1$, $P=0.61$). The rise in overall mortality to date is therefore more likely to be attributable to increased awareness of Creutzfeldt-Jakob disease than to an increased risk of death.

Standard survival modelling techniques² indicate that there is a small subpopulation susceptible to death due to Creutzfeldt-Jakob disease, whose relatively high mean age at death could potentially be reduced by exposure to a triggering agent derived from cattle. In particular, the mortality is well fit by a multistage (Weibull) mortality distribution³ in which mortality rises as the seventh power of age (for all ages) and the risk of death is restricted to about 70 per million of the general population, or about 3500 people. Figure 1 compares the distributions of theoretical and observed mortality in 1979-85 ($\chi^2=1.42$, $df=19$, $P>0.999$) and 1987-93 ($\chi^2=0.329$, $df=19$, $P>0.999$) and also shows the projected effect of a 50% increase in exposure to risk. Declining mortality after age 67 can be explained by the reduction in the number of susceptible people.

Fig 1—Probability distribution of mortality from Creutzfeldt-Jakob disease in England and Wales during 1979-85 and 1987-93, best fitting Weibull distribution, and hypothetical curve based on 50% increase in risk

The earlier age at onset noted in cases with identified polymorphisms⁴ may merely reflect the difficulties of genetic analysis and detection of familial associations in late onset cases. While bovine spongiform encephalopathy may represent a risk to these select people, there is no evidence that it has done so.

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- Gore SM. Bovine Creutzfeldt-Jakob disease? *BMJ* 1996;312:791-3. (30 March.)
- Neilson S, Robinson I. Reinterpreting mortality statistics: some uses of Gompertzian analysis in epidemiological research. *J Clin Epidemiol* 1993;46:1063-9.
- Doll R. The age distribution of cancer: implications for models of carcinogenesis. *Journal of the Royal Statistical Society* 1971;134:133-66.
- Brown P. Transmissible human spongiform encephalopathy (infectious cerebral amyloidosis): Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome and kuru. In: Calne D B, ed. *Neurodegenerative disease*. Philadelphia: W B Saunders, 1994:839-76.

Plasma lactate and blood cyanide in acute cyanide poisoning

Confounding factors should have been considered

EDITOR,—Frédéric J Baud and colleagues fail to consider the possibility of a confounding factor in their observed relation between plasma lactate and blood cyanide concentrations.¹ The patient with acute cyanide poisoning on whom they report had a cardiorespiratory arrest shortly after arriving in hospital, and resuscitation initially produced a very low arterial blood pressure. Further support was provided by a high dose adrenaline infusion. His condition improved with this treatment and infusion of hydroxycobalamin. Initial blood samples showed extremely high lactate concentrations, which were still raised at 10 hours.

The patient clearly had profound shock, including a period of circulatory standstill. In such circumstances, even in the absence of cyanide poisoning, blood lactate concentration will rise as a result of impaired tissue perfusion.² Inotropic support, while improving global haemodynamics (for example, normalising blood pressure), may not lead to resolution of lactic acidemia as there may be shunt across tissue beds, and oxygen use may not increase despite increases in oxygen delivery. In addition, if the liver is not perfused adequately lactate will not be cleared from the circulation. With improvement in global and regional perfusion, production of lactate will fall and clearance of lactate will increase, leading to a fall in plasma concentration. The data presented do not allow us to determine whether tissue perfusion was adequate during the first hours of treatment; the presence of high cyanide concentrations at tissue level produces a metabolic blockade, so that venous oxygen saturation is not a useful measure of global tissue perfusion.

These confounding factors blur the picture. While it is entirely reasonable to suspect a causal association between the time course of the lactic acidemia and that of the blood cyanide concentrations, the contribution to raised plasma lactate concentrations of cardiac arrest, shock, and subsequent inotropic support may be considerable. Similar observations in a patient who did not suffer cardiac arrest might be even more illuminating.

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- Baud FJ, Borron SW, Bavoux E, Astier A, Hoffman JR. Relation between plasma lactate and blood cyanide concentrations in acute cyanide poisoning. *BMJ* 1996;312:26-7. (6 January.)
- Pregel AW, Linder KH, Ensinger H, Grunert A. Plasma catecholamine concentrations after successful resuscitation in patients. *Crit Care Med* 1992;20:609-14.

Authors' reply

EDITOR,—We agree with T M Cook's analysis of the factors resulting in lactic acidosis in acute cyanide poisoning but not with the conclusion. We would like to focus our reply on the mechanisms of lactic acidosis induced by cyanide in mammals.

At a cellular level, short term exposure of cultured cells to cyanide rapidly induces a dramatic intracellular acidosis associated with increased lactate concentration. The blockade of cellular respiration through the inhibition of cytochrome aa3 by cyanide is considered to be the basic causative mechanism accounting for the increased production of lactate through the anaerobic pathway. Even in the case of intracellular acidosis it has now been shown that mechanisms other than increased production of lactate occur.¹

In mammals, however, numerous additional disturbances induced by cyanide eventually result

in the onset of severe lactic acidosis.^{2,3} We suggest that, as well as the blockade of cellular respiration, these disturbances should not be excluded, as proposed by Cook, but rather taken into account in any attempt to explain the basic mechanisms of lactic acidosis induced by cyanide in mammals. Acute cyanide poisoning induces sustained seizures, endogenous catecholamine release, increased blood glucose concentrations, and cardiovascular shock, which are all known to be associated with increased plasma lactate concentrations. As Cook points out, supportive treatment with an infusion of β mimetic agent is an additional cause of increased production of lactate. Furthermore, liver failure either through low cardiac output or through a direct effect of cyanide should result in a decrease in clearance of lactate from blood. These factors figure in previous reports of lactic acidosis in both experimental models and acute cyanide poisoning in humans. In rats the induction of lactic acidosis was recently shown to depend critically on the dose of cyanide.²

In conclusion, lactic acidosis induced by cyanide in mammals should be considered to be the result of numerous mechanisms at both cellular and organic levels whose respective contributions have not been assessed. Our case report suggests that, even in such a complex clinical setting, some relation seems to exist between plasma lactate and blood cyanide concentrations.

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- Madhu EU, Borowitz JL, Isom GE. Cyanide-induced alteration of cytosolic pH: involvement of cellular hydrogen ion handling processes. *Toxicol Appl Pharmacol* 1990;106:201-8.
- Salkowski AA, Penney DG. Metabolic, cardiovascular, and neurologic aspects of acute cyanide poisoning in the rat. *Toxicol Lett* 1995;75:19-27.
- Isom GE, Borowitz JL. Modification of cyanide toxicodynamics: mechanistic based antidote development. *Toxicol Lett* 1995;82/83:795-9.

Vocational training schemes in south London have been improved

EDITOR,—Course organisers for vocational training schemes in general practice in south London have spent the past three years developing initiatives to deal with the problems described by Tess Harris and colleagues.¹ The four training schemes in south London (Guy's, King's, Lewisham, and St Thomas's) have cooperated to form the South London Organisation of Vocational Training Schemes; we have been supported by Lambeth, Southwark and Lewisham Health Commission and have obtained funding for educational initiatives.

The dearth of trainers, especially now that we are appointing more registrars in general practice, is more than compensated by the trainers' enthusiasm and skill and the quality of training that they offer to those who want to work in the inner city.

We have used funding provided for educational initiatives within the London Implementation Zone to purchase protected time for education. We have provided more variety, flexibility, and community focus for hospital based training in general practice. We have created innovative

posts that address problems of inner cities—for example, homelessness and drug misuse. We have been able to extend training based in general practice within the three year scheme when necessary.² Research by the South London Organisation of Vocational Training Schemes has shown that many registrars do not feel ready to enter general practice after vocational training (C Vaughan, personal communication). We provide a fourth year of training in the form of a vocational training associate scheme, which addresses registrars' further learning needs while giving them time to gain experience and confidence in practice. This initiative, in its second year, has also been able to support 34 local practices under stress.

These changes have allowed us to recruit a full complement of high quality registrars to our schemes and increase the number of locally trained doctors becoming principals in south London. The training issues have become too complex to be solved by appending general practice training to hospital training. We look forward to the results of the evaluation of our innovations. These results will inform the debate about developing excellent training for general practice that will supply highly trained general practitioners for inner cities into the next century.

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- 1 Harris T, Silver T, Rink E, Hilton S. Vocational training for general practice in inner London. Is there a dearth? And if so what's to be done? *BMJ* 1996;312:97-101. (13 January.)
2 Savage R, Kiernan E, Ruben A. Registrar training for general practice: a pilot of eighteen months of hospital posts and eighteen months in general practice. *Br J Gen Pract* (in press).

Florence Nightingale's fever

EDITOR,—No one doubts that Florence Nightingale's illness was at least partly the consequence of her attack of "Crimean fever" in 1855. There have been many suggestions about the causal organism for this fever, and *Brucella melitensis* is as convincing as any,¹ though Miss Nightingale herself claimed that the fever was typhus.²

What has intrigued historians is why she stayed in bed, or on a couch, for over 20 years. The short answer is that this was the treatment prescribed and that she acquiesced. The reason for the apparent long term illness has interested scholars for years. While lecturing in North America on "Florence Nightingale and the nursing legacy"³ I met Dr Byron Marshal Hyde in Ottawa; he is an authority on myalgic encephalomyelitis and is convinced that it was the basis of Miss Nightingale's invalidism. I thought that the volume of work that she undertook from her bed made this unlikely.

On the same tour I was shown a paper claiming that Miss Nightingale's malady was due to lead poisoning incurred as a child in Derbyshire,⁴ that she had been "a sickly child," and that she had said that she had been unable to write until she was 11. Knowing Miss Nightingale's propensity to exaggerate and that examples of her letters as a young child exist, I regard this with suspicion. Another, and more bizarre, suggestion said to emanate from Canada was that Miss Nightingale contracted syphilis in the Crimea.

Cook, her official biographer, consulted doctors and thought that "though she worked like Hercules she suffered from dilatation of the heart and neurasthenia."⁵ Smith, who did not like his subject and was bent on destroying her reputation, saw her as a malingerer.⁶ Pickering, in his book about

eminent Victorians who "took to their beds" and then led creative lives, saw a psychosomatic element.⁷

There is a strong case for suggesting that once she became bedridden Miss Nightingale manipulated her illness and those around her to get work done. A series of "last letters" concentrated minds wonderfully. Anyone who has spent long periods with her letters will conclude that she was inclined to dramatise everything, including her illness. Dramatisation often, however, paid dividends in pursuit of a cause such as the reform of army welfare, medical statistics, the poor law, midwifery, hospital architecture, and nursing.

The conclusion must be that, like so much Victorian illness, Miss Nightingale's was multifaceted and compounded by the advice and treatment of the day.

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- 1 Young DAB. Florence Nightingale's fever. *BMJ* 1995;311: 1711-4. (23-30 December.)
2 Baly ME. *As Miss Nightingale said*. . . . London: Scutari, 1991:36.
3 Baly ME. *Florence Nightingale and the nursing legacy*. London: Routledge, 1986.
4 Ference HM. Of Nightingale lead at Lea in Derbyshire. *Nightingale Society* 1988;1(winter).
5 Cook E. *The life of Florence Nightingale*. Vol 1. London: Macmillan, 1913:483.
6 Smith FB. *Florence Nightingale—reputation and power*. London: Croom Helm, 1983.
7 Pickering G. *The creative malady*. London: Allen and Unwin, 1974.

Men's health: don't blame the victims

EDITOR,—Sian Griffiths highlights some discrepancies between men's and women's health.¹ She states that men are less able than women to recognise physical and emotional distress, apparently because of "society's expectations," and that when men are ill they are less likely to consult their general practitioners. The subtitle of her editorial implies that this is because of men's "unwillingness to seek medical help." This is blaming the victim. An editorial about, say, sexual assault on women and their unwillingness to seek medical help would have highlighted aspects of the health service that put these women off. Yet Griffiths ignores health professionals' attitudes that may contribute to men not seeking help. In child health, fathers' concerns and feelings and the concomitant psychological and health consequences often seem to be ignored by health professionals. The professionals say that "every mother is concerned for her child" and talk of "a mother's worst nightmare" and the effects of rearing children on the health of the mothers. Some recent examples reflect this.

- A specialist counsellor said that counselling men was often difficult because they did not express their feelings; she believed that this was the men's fault
- A distressed father who was not coping with his first baby when his wife returned to work was greeted by unnecessary comments at (mothers') support groups such as, "We don't often get fathers here"
- A discussion on the health and emotional needs of parents of young babies focused exclusively on mothers. When I raised the needs of fathers someone commented, "We can check their prostates," to much guffawing from colleagues.

In the week after this last comment I met a 21 year old father who had a criminal record and was in an alcohol rehabilitation programme run by a charity, a father with postnatal distress, and the family of a 25 year old man who had committed suicide; none of the men had received support

from the health service. Increases of 78% in the suicide rate among men aged 14 to 24 and of 33% among men aged 14 to 44 between 1980 and 1990² show that many men have felt marginalised by the health service. Unsafe attitudes like these mean that half the population of Britain is being denied equitable health care.

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- 1 Griffiths S. Men's health. *BMJ* 1996;312:69-70. (13 January.)
2 Hawkton K. By their own young hand. *BMJ* 1992;304:1000.

Ethnic differences in outcome of serum screening for Down's syndrome

Differences in median values may account for differences in false positive rates

EDITOR,—Lucy Gilbert and colleagues report that serum screening for Down's syndrome had a higher false positive rate in women of Indian Asian origin than in white women.¹ They speculate that racial differences in the median concentrations of the biochemical markers used may explain this finding. Evidence from our laboratory indicates that this is at least part of the reason.

Samples from Indian Asian ethnic groups account for 25-30% of those received by our laboratory for assessment of the risk of Down's syndrome. Between October 1992 and December 1994 the false positive rate for the Asian population (7.6%) was considerably higher than that for the white population (4.2%). Medians specific to ethnic groups were therefore determined by log linear regression (weighted) for 15-20 weeks' gestation. They were based on 5837 samples obtained during the second trimester (1765 from Asian and 4072 from white women), which were assayed for α fetoprotein and intact human chorionic gonadotrophin (Wallac Delfia kits). Gestational ages were determined by ultrasonography in all cases. The median α fetoprotein concentration was not appreciably different between the two groups, but the median human chorionic gonadotrophin concentration was higher in the Asian than the white women at all gestational ages in the range 15-20 weeks (table 1).

Table 1—Median concentrations of human chorionic gonadotrophin in Asian and white women at 15-20 weeks' gestation

Gestation (weeks)	Median human chorionic gonadotrophin (kU/l)	
	Asian women	White women
15	29.3	25.0
16	25.2	21.8
17	21.7	19.0
18	18.7	16.6
19	16.1	14.4
20	13.9	12.6

Our findings show that if median concentrations of human chorionic gonadotrophin were derived from a mixed population of Asian and white women this would result in the use of inappropriately low median values for Asian women and inappropriately high values for white women. The bias would be particularly pronounced for Asian women owing to the greater contribution made to the median values by the larger white population. This would lead to the higher false positive rates that we and Gilbert and colleagues observed in Asian women. Amniocentesis might be offered inappropriately to Asian patients while being denied when appropriate to a section of the white population.