that an expensive treatment is ineffective or—if a new drug is a real advance—will at least let clinicians and managers make an informed decision on whether to use it. A cost-benefit analysis could be built into the original design, though care must be taken to avoid biased analysis.[10]

The Medicines Control Agency might initially—if the government does not wish it to pursue the goal of efficacy—license new drugs for use only in large scale randomised trials testing their role in clinical medicine, the cost of drugs and the trials being funded by NHS research funds and not the pharmaceutical companies. A further safeguard in research may be the introduction of a "middle man" between the drug company and clinical researcher. The present direct payment on a per caput basis and other arrangements for trials might be better handled by a funding body with strong representation from the drug industry. Pharmaceutical companies paying into a central pool could then be protected from the "avarice" of some clinicians, and clinicians in turn would be better protected from pressure from drug companies.

The present means of developing oncological (and many other) drugs is becoming increasingly unacceptable and outdated. Regulation of this market, together with more stringent use of clinical science, can only improve this situation for drug companies, clinicians, and patients. The rapid present moves towards common marketing policies in the European Community[4] and concern about drug development in the United States[11] present a challenge and should be regarded as a stimulus to change the present, and largely outdated, means of developing clinical drugs. Solutions will be difficult to arrive at but are more likely to be found if contentious issues are discussed openly.

We feel that many of the pharmaceutical companies deserve praise for their part in the advances that have been made and fully support the concept of a free market. In many respects, however, the current system puts them in an invidious position—hence the present unsatisfactory state of affairs.

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1 Kessler DA. Drug promotion and scientific exchange. The role of the clinical investigator. *N Engl J Med* 1991;**325**:201-3.
2 Schein PS. Presidential address: the plight of clinical cancer research. *J Clin Oncol* 1984;**2**:1433-9.
3 Wiggins SN. Costs of developing a new drug. Office Policy Analysis, Pharmaeutical Manufacturers Association, June 1987.
4 How drugs get to market. *Drug Ther Bull* 1990;**28**(26):101-4.
5 Association of the British Pharmaceutical Industry. *Guidelines on good clinical practice*. London: ABPI, 1988.
6 Gerlin L. Good clinical practice in clinical research. *Lancet* 1989;i:1008-9.
7 Doolittle RF. Biotechnology—the enormous cost of success. *N Engl J Med* 1991;**324**:1360-2.
8 Begg C, Berlin JA. Publication bias and dissemination of clinical research. *J Natl Cancer Inst* 1989;**81**:107-15.
9 Smith R. An NHS research strategy. Overdue but potential problems with implementation. *BMJ* 1991;**302**:1034-5.
10 Hillman AL, Eisenberg JM, Pauly MV, Bloom BS, Glick H, Kinosian B, *et al*. Avoiding bias in the conduct and reporting of cost-effectiveness research sponsored by pharmaceutical companies. *N Engl J Med* 1991;**324**:1362-5.
11 Marks PA, Bennett JC, Hanft RS, *et al*. *Institute of Medicine: resources for clinical investigation*. Washington, DC: Academic Press, 1988.

Off the rails

Train drivers and alcohol shouldn't mix

Several railway accidents have occurred recently in which it has been either proved or suspected that the ability of the drivers concerned was impaired by alcohol or other drugs. After a serious accident at Morpeth in 1984 the government committed itself to update the Railway Regulation Act of 1842. This made it an offence for a railway employee to be found "drunk" while employed conducting traffic on the railway or repairing and maintaining railway works. The government promised legislation to increase penalties and to include drugs other than alcohol. Meanwhile, remarks made by the coroner at the inquest on a disaster at Cannon Street have further stimulated the government to propose "more comprehensive drink and drugs provisions based closely on those in the Road Traffic Act of 1988," which replaced previous legislation.

A consultation paper[1] has now been published with less than a month allowed for comments on the proposals to repeal an act that has been in force for 150 years. The paper's flaws are many. Reference is made throughout to "drink or a drug"—evidence of parliament's continuing reluctance to accept alcohol as a drug. Far more important, however, is the government's decision to adopt the same limits of alcohol concentration for the train drivers' offence as are prescribed for drivers of motor vehicles. Nowhere in the paper is it recognised that the consequences of accidents caused by train drivers whose ability is impaired by alcohol can be far worse than those of accidents caused by drivers of motor vehicles. The fact that it will not be regarded as a criminal offence to drive a train with a blood alcohol concentration of up to 80 mg/100 ml should fill passengers with alarm. The limit should, of course, be zero.

The provisions for enforcement are even less satisfactory. A police officer, provided he or she is in uniform (and transport police are frequently on duty out of uniform), may request a breath specimen only if there is reasonable cause to suspect that the driver has alcohol in his body or has been involved in an accident. Experience with prosecutions under the same provisions in the road traffic acts has shown that counsel, under our adversarial and confrontational system of criminal justice, have frequently obtained acquittals for drivers proved to have had quite high alcohol concentrations by persuading courts that the police officer had no reasonable cause to suspect that the driver had alcohol in his body when the specimen was requested. Furthermore, the complex procedures under the road traffic acts for charging offenders and administering breath tests and the use and servicing of the relevant equipment concerned are entirely outside the experience of the transport police, a point that is not even mentioned in the paper.

Because of the extreme dangers posed by train drivers whose ability is impaired by alcohol police should be given absolute discretion to request a breath test on producing adequate identification, whether or not they are in uniform. Furthermore, the provision in the Road Traffic Act 1988 that in marginal cases the driver may opt to provide a sample of urine rather than of blood is hardly necessary in the case of professional train drivers and simply perpetuates a highly unscientific method of determining blood alcohol concentra-

tion. The provision that blood may not be required "if a medical practitioner is of the opinion that for medical reasons a specimen of blood cannot or should not be taken" should similarly be dropped.

What is almost beyond belief is that the provisions in the Road Traffic Act 1988 concerning the temporary detention of drivers whose tests give positive results are also to be applied to train drivers. It is proposed that the driver may be detained "until it appears to the constable that, were that person then on duty, he would not be committing an offence." In other words, as soon as the driver's breath alcohol concentration has fallen below 35 μg/l (broadly equivalent to 80 mg/100 ml blood) the police are powerless under the proposed legislation to stop him going back on duty and driving his train.

Unless substantial amendments can be made to the unsatisfactory provisions of this consultation paper it would be better for the proposed legislation to be postponed until the climate is right for a more sensible and scientific approach to the problem. Parliamentary time is at a premium, and if the legislation is approved it could take another 150 years before another opportunity arises to remedy its outstanding defects.

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1 Department of Transport. *Consultation paper on proposed railway drink and drugs legislation*. London: Department of Transport, 23 September, 1991.

Postoperative feeding

Time to rehabilitate the gut

Twenty five years after Dudrick pioneered total parenteral nutrition[1] sceptics have begun to question its efficacy. In that time few good studies have shown that total parenteral nutrition improves the outcome in surgical patients,[2,3] especially if feeding takes place for less than 10 days. A recent meta-analysis of 11 studies showed little, if any, clinically important benefit.[4] A more recent study suggested that although the incidence of serious non-infectious complications is lower in patients given total parenteral nutrition, the incidence of septic complications is substantially higher.[2] Only in severely malnourished patients—5% of the study population—did the benefits outweigh the risks.

Total parenteral nutrition is complicated by displacement of the catheter, sepsis, mechanical problems, and metabolic derangements, which each occur in 5-10% of cases.[5] The incidence of death due to complications is 0·2%. Many of the problems relate to the lipid component of the infusions. Intravenous fat emulsions replaced glucose as the main source of energy because of problems with overfeeding with glucose.[6] The benefits of fat emulsion were that it was a more concentrated source of energy, the fact that glucose intolerance and hyperglycaemia were less likely, a lower carbon dioxide load owing to its lower respiratory quotient, and its isotonicity (allowing some formulations to be given through peripheral veins).[7]

Although the newer preparations are safer than their very hazardous predecessors, reports of adverse effects continue. For example, the serum of some acutely ill patients may agglutinate intravenous Intralipid,[8] and several cases have been reported of fat accumulating in the pulmonary capillaries of neonates fed with Intralipid.[9,10] Giving neonates intravenous lipid emulsions increases by six times their risk of developing coagulase negative staphylococcal bacteraemia.[11] In adults serious complications and death are less likely if lipid free parenteral nutrition instead of standard parenteral nutrition is given preoperatively.[12] Intravenous fat has many immunosuppressive effects: intravenous long chain triglycerides reduce the functions of the reticuloendothelial system[13] and neutrophils[14] and the ratio of T helper to T suppressor cells.[15] Lipid emulsions in total parenteral nutrition are prone to peroxidation, and oxygen derived free radicals may damage tissue.[16] One report described intravenous Intralipid reducing the perfusion of skin, muscle, gut, and other organs.[17] Others describe various hepatobiliary abnormalities with total parenteral nutrition.[18,19]

Taken together, these problems with nutrition have turned attention back to the gut. Long considered dormant in critical illness, the gut has a very active role in modulating the clinical course of critically ill patients. Much evidence suggests that the bowel serves as a reservoir of pathogens - hence the importance of maintaining its function. If the normal gut barrier breaks down (with mucosal ischaemia probably being the main cause in the critically ill),[20] translocation of bacteria and endotoxin into the portal circulation may follow. Translocation plays a part in sepsis and shock,[21] and endotoxins and organisms that enter the bloodstream may initiate a hypermetabolic state which progresses to multiple organ failure.[22,23]

Like starvation, total parenteral nutrition causes considerable mucosal atrophy.[24,25] Current regimens for total parenteral nutrition lack glutamine, the main source of energy for the gastrointestinal mucosa.[26] Other important fuels are butyrate (produced by bacterial fermentation of the polysaccharides in dietary fibre) and ketone bodies. Total parenteral nutrition not only lacks fibre but also, because of its glucose content, suppresses the formation of ketone bodies. It also promotes bacterial translocation from the gut[27]: thus current nutritional support in the intensive care unit often leads to iatrogenic starvation of the bowel and prejudices the bowel's barrier function.

Conversely, enteral nutrition, if it includes glutamine and fibre, maintains mucosal integrity, reduces bacterial translocation,[23,26,28] and enhances the autoregulation of blood flow to the gut.[29] Furthermore, a multicentre trial has shown that postoperative enteral nutrition significantly reduces septic complications when compared with total parenteral nutrition.[23,30]

Before giving anything by mouth or nasogastric tube after surgery surgeons have traditionally relied on the return of bowel sounds or passage of flatus as evidence of a functioning gastrointestinal tract. What these signs mean, however, is the return to normal function of the stomach and colon. Work in the 1960s showed that small intestinal motility and function are maintained in the immediate postoperative period and that "normal post-op ileus" affects only the stomach and colon.[31,32] Provided that the stomach is bypassed, feeding may be initiated in the immediate postoperative period through