1893, 100 years after Jenner's pioneering cowpox experiments in the English countryside. My grandfather would have been gratified to learn that his method for purifying the lymph containing the virus had remained essentially the same for almost another century (surely a medical therapeutic record?). During this time one of the most loathsome of communicable diseases has been extirpated and is medical history. Those of us from the medical schools of St Thomas's and Westminster, where Monckton Copeman was student and pedagogue, have another reason to be proud.

P W MONCKTON COPEMAN

Department of Dermatology,
Westminster Hospital,
London SW1P 2AP

High-carbohydrate diets and insulin-dependent diabetics

SIR,—I read with interest the article "High-carbohydrate diets and insulin-dependent diabetics" by Dr R W Simpson and others (1 September, p 523).

It is possible that the improvement noted in the 24-hour blood glucose concentrations and the other parameters of diabetic control noted in the diabetics on the high-carbohydrate diet may have been due to a difference in the fibre content of the two diets. A valid conclusion on the beneficial effects of a high-carbohydrate diet in diabetics in this study could be drawn only if the fibre content of the two diets was known to be equal, as dietary fibre content is known to be relevant in diabetic control.

N M O'MULLANE

Royal Liverpool Hospital,
Liverpool L7 8XP

Pathogenetic mechanisms in legionnaires' disease

SIR,—Your recent leading article on legionnaires' disease (14 July, p 81) indicates an emerging picture of a multisystem disease that attacks the lungs and often involves several tissues and parts of the body. We, like others,¹ have suggested an endotoxin (or an endotoxin-like substance) as a possible pathogenetic mediator of these multiple changes.

Many described manifestations (for example, high fever, profound hypotension, propensity to acute renal failure, hepatic abnormalities, gastrointestinal disturbances, neurological disorders, thrombocytopenia, and sometimes disseminated intravascular coagulation) are characteristic also of endotoxin shock. On the other hand, from some recent work²⁻⁴ there is increasing evidence that *Legionella pneumophila* possesses some of the in-vivo and in-vitro biological properties associated with Gram-negative bacteria (that is, pyrogenic response, *Limulus* gelation, Shwartzman skin reaction) even if with different potency.⁵ There are difficulties in correlating the endotoxin content of Gram-negative organisms during infection with the pathological effects, but this does not mean that no correlation exists.⁶ Unfortunately, as in the case described by Edelstein *et al*,¹ despite the bacteraemia one cannot assume this correlation without endotoxin assay.

Further detailed investigations are necessary

to characterise more clearly the biochemical profile⁷ and the biological properties⁸ of the bacterium and to determine whether the endotoxin acts independently or collaborates with other bacterial products, so increasing the damage to the host. In this connection, some recent findings concerning an exotoxin activity⁹ offer a challenge for future research: a complex interaction between endotoxin and haemolysin (suggested as the pathogenetic mechanism in *Aeromonas* infection¹⁰) might trigger disease production. Solving the problem of bacterial products could lead to an assessment of the immunological aspects of the disease. Finally, new stratagems for increasing host defences may emerge from such researches—which could also result in the eventual development of a safe, active, and effective immunogenic procedure to protect against the disease.¹¹

DONATO FUMAROLA

Institute of Medical Microbiology,
Bari University School of Medicine,
Bari 70124, Italy

¹ Edelstein, P H, Meyer, R D, and Finegold, S M, *Lancet*, 1979, **1**, 750.

² Fumarola, D, *Bollettino dell'Istituto Sieroterapico Milanese*, 1978, **57**, 680.

³ Highsmith, A K, *et al*, *Current Microbiology*, 1978, **1**, 315.

⁴ Fumarola, D, *IRCS Medical Science*, 1979, **7**, 304.

⁵ Wong, K H, *et al*, *Annals of Internal Medicine*, 1979, **90**, 624.

⁶ Shands, J W, *jun*, *Microbiology*, 1975, **2**, 330.

⁷ Moss, C W, and Dees, S B, *Journal of Clinical Microbiology*, 1979, **9**, 648.

⁸ Fumarola, D, *Bollettino dell'Istituto Sieroterapico Milanese*, 1979, **58**, 100.

⁹ Baine, W B, *et al*, *Journal of Clinical Microbiology*, 1979, **9**, 453.

¹⁰ Rigney, M M, Zilinsky, J W, and Rouf, M A, *Current Microbiology*, 1978, **1**, 175.

¹¹ Wong, H K, *et al*, *Seventy-ninth Annual Meeting of the American Society for Microbiology* (Los Angeles, 1979), abstract E(H)3, p 78.

Gastric and duodenal ulceration after burns

SIR,—Without sufficiently differentiating between ulceration of the stomach and of the duodenum after burns, your leading article (1 September, p 512) states that the condition is common. We would agree that superficial gastric erosions commonly occur in the early days after burn injuries but these rarely give rise to serious complications. The dangerous lesions are the deeply penetrating ulcers of the duodenum and these alone should be termed Curling's ulcers. It is difficult to know the incidence of this ulcer in patients who survive burn injuries, but what we can say with certainty is that the number of patients who show clinical evidence of Curling's ulceration during life is very small indeed.

In an extensive inquiry in this country in 1974¹ we found that only 18 examples of severe gastroduodenal haemorrhage had occurred during the treatment of over 32 000 children and adults in 13 centres treating major burns. An extensive search of the literature showed that in reports of over 14 000 patients treated in Denmark, Sweden, Italy, and Czechoslovakia the incidence of alimentary haemorrhage was 0.2%.

You contrast these low European figures with the much higher incidence of haemorrhage and perforation (11.7%) reported from the United States Army Burns Centre in Texas and consider this difference to be unexplained. It is worth noting that the centre does not admit children or women² and it seems likely that it admits a highly selected population of severely burned men, so perhaps this very

high figure is not representative of burned patients in general.

There is at least one other possible reason for the difference in incidence in this country and in the United States. In Britain it is general policy to give relatively large volumes of colloid during early fluid replacement, whereas in the USA the policy is to give large volumes of electrolyte solution with little or no colloid. This latter type of management is often associated with low blood volumes and a high haematocrit and blood viscosity.³ These are conditions likely to be associated with poor blood flow in the visceral microcirculation, which must increase the likelihood of gastroduodenal ulceration.⁴

IAN F K MUIR

PETER F JONES

Royal Aberdeen Children's Hospital,
Aberdeen AB9 2YS

¹ Muir, I F K, and Jones, P F, *British Journal of Surgery*, 1976, **63**, 60.

² McAlhany, J C, Czaja, A J, and Rosenthal, A, in *Burns—A Team Approach*, ed C P Artz, J A Moncrief, and B A Pruitt, p 513. Philadelphia, Saunders, 1979.

³ Moyer, C A, and Butcher, N R, *Burns, Shock and Plasma Volume Regulation*, p 262. St Louis, Mosby, 1967.

⁴ Friesen, S R, *Surgery*, 1950, **28**, 123.

Offspring of phenylketonuric parents

SIR,—Professor D Kutter and Dr J Thoma in their paper "Management of maternal phenylketonuria" (PKU) (28 July, p 272) raise an interesting problem, if I understand the figures from their world literature review correctly. Fourteen homozygous offspring from 62 pregnancies (if that is what they mean), on the assumption that the homozygous parents chose mates at random, would imply a carrier rate of nearly one in 2.2, which is clearly absurd as this would give an incidence of PKU in the general population of about one in 20.

There are at least three other possible explanations (separately or in combination) for their review figures: (a) The literature has under-reported cases of PKU parents producing normal (heterozygous) offspring. (b) Assortative mating has occurred, possibly on the basis of olfactory discrimination, or (as with the deaf) by meeting in select social groups such as clinics. (c) Incest has occurred at least in some cases.

The first possibility is highly likely unless all the review cases were selected before the birth of the offspring. The second possibility is more speculative. The third possibility is not as improbable as one might at first suspect, particularly in the case of dull or mentally handicapped mothers. Although hard evidence on this point is difficult to come by, I suspect that incest between fathers and mentally handicapped daughters (and perhaps also brothers and mentally handicapped sisters) is not rare. As in the case of child abuse, objective possibilities may be overlooked because of naive assumptions about family behaviour.

The four PKU fathers producing three homozygous offspring are, despite the small numbers, most interesting. The mates are obviously identified and therefore their genotype should be known. If, as expected, they are heterozygous and are not blood relatives, then selective reporting or assortative mating (or both) must be operating. Only prospective studies can determine the true incidence of PKU offspring of PKU parents,

and even then assortative mating may be involved.

None of this, of course, contradicts the recommendation to examine potential partners of PKU homozygotes for the carrier state in order to give genetic counselling.

JACK BAVIN

Twynver Unit,
Coney Hill Hospital,
Gloucester GL4 7QJ

*We sent a copy of this letter to Professor Kutter, whose reply is printed below.—ED, BMJ.

SIR,—Since the publication of my previous letter I have been able to complete the list of patients with phenylketonuria who have progeny. I have found reports on 75 patients (71 female and four male) of which 17 have one or more homozygous PKU offspring (14 mothers and three fathers). This would correspond to a carrier frequency of about 1:4. We have checked for the possible mechanisms proposed by Dr Bavin: so far as we can conclude from the different case reports there is no evidence for selective mating. In one of the cases incest is quite possible; in a second it cannot be excluded. In four cases there exists evidence of very remote consanguinity. Even if we exclude these six cases from our calculation we still find a carrier frequency which is very far from the 1:50 generally accepted.

I think that the carrier frequency is really much higher than we admit and that the 1:50 frequency, which is based on the homozygote detection in screening for PKU, is incorrect. There are several reports of increased reproductive casualties in PKU carrier women. This may mean that there is a higher quota of carrier marriages but that a large proportion of homozygous PKU pregnancies do not yield live births.

Carrier tests always compare parents of PKU children with a "normal" population. The possibility is not excluded that this "normal" sample contains a larger proportion of carriers and that the overlap between the two populations which is found by all the authors really does not exist.

I think at any rate that the problem is worth further investigation and I would welcome any suggestions.

D KUTTER

Luxembourg

Psychiatric symptoms and hallucinogenic compounds

SIR,—I was interested to read of the case of persistent panic attacks following the eating of psilocybin mushrooms described by Mr C Benjamin (19 May, p 1319). Like Dr D Jacobs (7 July, p 49), I have seen a number of cases in which persistent panic attacks followed the taking of cannabis and LSD. I would like to describe one such case and how it was treated.

The patient was a 23-year-old woman who had a three-year history of panic attacks which were precipitated by a particularly bad LSD "trip." During this trip what the patient experienced was horrific. Apart from the usual visual distortions associated with LSD she experienced herself being continuously raped by seven men. This sexual "assault" was truly brutal and over the period of six hours while the trip lasted she felt her body being continuously violated. The trip itself took place at home in the presence of her parents and sister. The experienced sexual

molestation could therefore have had no basis whatever in reality.

The panic attacks consisted of episodes of acute anxiety with palpitations, dryness of the mouth, hyperventilation, depersonalisation, derealisation, and a feeling of being about to go insane. Like those Dr Jacobs described, the attacks were unrelated to any particular situation and just seemed to come out of the blue. Treatment was based on the hypothesis that the patient had undergone what to her was a real traumatic experience, even though it was in fact a hallucinogenic one. Treatment consisted of sessions of abreactive psychotherapy. In these the patient was encouraged to relive her experience by talking about it in as much detail as possible. During such sessions she became extremely frightened and ended up screaming and crying. After only three such abreactions the panic attacks disappeared completely and they have not returned in the year and a half that she has been followed up since then.

Phobic anxiety with panic attacks has long been known to follow frightening real-life experiences.¹ Could it be that a frightening hallucinogenic experience may also produce this effect?

AIDAN MCGENNIS

St Brendan's Hospital,
Dublin 7

¹ Marks, I M, *Archives of General Psychiatry*, 1970, 23, 542.

SIR,—I read the short report on persistent psychiatric symptoms associated with the consumption of psilocybin mushrooms (19 May, p 1319) with interest as at the time I had under my care a patient with experience of eating "magic mushrooms" (as he referred to them), whose history may be of interest to some of your readers.

This patient, a 26-year-old bachelor, was admitted to hospital informally in February 1979. His parents, with whom he was living, had noticed a change in him over the previous month in that he had become vegetarian, had taken to staying up all night reading the Bible, and had become preoccupied with "the evil in the world." He told them that he found himself "in tune with nature" and was planning the world-wide conscription of an "environmental army" to sort out the problems of the world (for example, pollution, armed conflict).

On admission he showed no sign of self-neglect and was well orientated and co-operative, with no evidence of clouding of consciousness. He gave his history spontaneously, but with no marked pressure of speech, although his conversation was disjointed. He said that he felt ecstatically happy and felt able to solve all the problems of the world as he had been imbued with Messianic powers following a vision of "a crown of thorns coming down"—and that he was in telepathic communication with other people, felt possessed by a divine spirit, and had experienced a sensation of everyone being able to hear his thoughts. He seemed to have experienced hallucinatory voices talking about him in the third person. He was considered to show mild formal thought disorder and a diagnosis of schizoaffective psychosis was made.

He was described by his parents as being an extraverted, sociable, warm, generous, energetic, cheerful, and popular young man, if rather impulsive; and he appeared to have been making a success of his own business. He had, however, a past psychiatric history inasmuch as he had taken an overdose four years previously following a broken engagement, but this had not led to his receiving psychiatric treatment. There is no family history of psychiatric illness. It turned out that for some years he had experimented with a variety of illicit drugs, including cocaine, amphetamines, pot, and lysergic acid; but that over the two years prior to his admission he had taken only pot and occasional amphetamine tablets. He had taken neither of these, however, since the autumn of

1978, when he had for the first time on a number of occasions consumed dried "magic mushrooms," whose description left little room for doubt that they were *Psilocybe semilanceata*, which is found in profusion in the area. He told me that he understood they contained psilocybin and described the immediate effects as heightened awareness, perceptual distortion, and visual hallucinosis. He responded to treatment with haloperidol and was discharged five weeks after admission, since which he has had a few brief depressive bouts but no further psychotic experiences.

One cannot be sure what part, if any, the ingestion of mushrooms played in the aetiology of this illness, although he had previously consumed LSD without any long-lasting or delayed effects and had given that up about two years previously. He had, however, persisted with amphetamines in small quantity and pot until six months prior to the illness. However, it may be that his illness represents a delayed effect of the consumption of these "mushrooms" in a person possibly made more susceptible by the abuse of other drugs.

N S DAVIES

North Wales Hospital,
Denbigh, Clwyd LL16 5SS

The grumbling appendix

SIR,—Mr I Lewis (a September, p 552) says that acute appendicitis normally presents with midepigastria pain and not with umbilical pain. This is at variance with my experience, but I am also interested to know how he would explain this. The appendix lies distally in the alimentary tract to the point at which the small bowel attaches to the umbilicus by the vitellointestinal duct. Pain from Meckel's diverticulum must therefore on an embryological basis be referred to the umbilicus; the appendix, being distal, should not logically have pain any higher than this and might in fact be expected to have a very slightly lower distribution.

I hope that not all cases of chronic appendicitis will be dismissed. Although the diagnosis should be made with great reluctance there are nevertheless some patients with a stricture and a trapped faecalith who experience severe pain that is relieved by the operation; and there are certainly others with lesser signs whose pain goes—presumably owing to the subsidence of the swollen glands Mr Lewis describes to the patients.

GEORGE WATTS

General Hospital,
Birmingham B4 6NH

Disinfection with glutaraldehyde

SIR,—Dr R M G Boucher (18 August, p 444) describes advantages in the use of non-ionic potentiated acid formulations of glutaraldehyde. He dismisses many of the recent developments which have taken place with alkaline glutaraldehyde formulations. He neglects to point out that under normal conditions at room temperature the potentiated acid variety, unlike the alkaline solutions, is not recommended for use as a chemical sterilising solution.¹

The instability of glutaraldehyde solutions is known to be a consequence of aldehyde polymerisation, the rate of which has been shown to increase with both increasing pH and increasing temperature.² Studies with the original Cidex formulation have demonstrated an approximately 44% reduction in free glutaraldehyde content after storage at room