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,