had a good initial response to tetracosactrin and those who did not, nor indeed between those with a low level of circulating plasma cortisol and those with a normal level. It is interesting, however, that the one patient who did show signs of a major complication during the attempted substitution had both a low level of plasma cortisol and a very poor response to tetracosactrin.

Another observation which we feel is worth making is that all our patients' asthma was well controlled on a maintenance dosage of prednisone before we attempted substitution with beclomethasone dipropionate. We have found that it is extremely difficult, if not impossible, to make this substitution if the asthma is not well controlled initially by corticosteroids administered other than by inhalation.—We are, etc.,

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Cholestyramine and Diabetic and Post-vagotomy Diarrhoea

SIR,—We wish to report four diabetic patients with intractable diarrhoea responding to oral cholestyramine, a resin which combines with bile acids to form insoluble complexes.

The first, a 37-year-old male diabetic with neuropathy and retinopathy, had had diarrhoea (8-20 stools daily) for 16 years. Pancreatic extracts, codeine phosphate, antispasmodics, diphenoxylate hydrochloride, and methylcellulose had little effect. Treatment with cholestyramine 4 g thrice daily with meals resulted in 1-2 solid stools daily. Diarrhoea recurred twice when cholestyramine was withdrawn, but restarting therapy resulted in relief. In the second patient, a 52-year-old man with neuropathy and diarrhoea unresponsive to other forms of therapy, solidification of the stools and reduction in frequency from 6-8 to one daily occurred when cholestyramine was given. Two other patients with intractable diarrhoea also responded to oral cholestyramine. In both cases withdrawal of cholestyramine caused a return of the diarrhoea, which was controlled again within 24-48 hours by restarting treatment.

The only known type of diarrhoea responding to cholestyramine is that following disease or resection of the terminal ileum,[1 2] when excess bile salts enter the colon, inhibit absorption of water and electrolytes, and disturb colonic activity.[3 4] Feeding bile salts induces diarrhoea[5 6] and since no ileal disease is demonstrable in diabetic diarrhoea, it is possible that excess bile is entering the gut at "inappropriate" times.

Diabetic diarrhoea is associated with neuropathy,[7] and the vagus, which supplies fibres to the biliary system, may be involved. Indeed post-vagotomy and diabetic diarrhoea have many features in common—watery stools, sometimes steatorrhoea, delayed gastric emptying, and disordered small-intestinal transit. Vagotomy may result in increased gall bladder volume and poor contraction.[8-10] Diabetics also have large-volume poorly contracting gall bladders[11] and a high incidence of gall stones occurs both following vagotomy and in diabetics.[12 13] Furthermore, there is no demonstrable disease of the gut and response to therapy is poor, though the incidence of post-vagotomy diarrhoea is reduced by preserving the coeliac and hepatic vagal branches.

Though bile flow is increased after vagotomy,[14] the concentration of bile salts in the postprandial aspirate is low,[15] suggesting that gall bladder contraction is out of phase with gastric emptying, resulting in poor admixture of bile and chyle. If gall bladder volume is greater than normal, increased amounts of bile salts might enter the small intestine, swamping its reabsorptive capacity and (deconjugated by bacteria) inducing "colonic" diarrhoea.

Both post-vagotomy and diabetic diarrhoea may therefore be related to excess bile salts entering the gut as a result of gall bladder dysfunction following severance or neuropathy of the vagus.—We are, etc.,

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Vaccination of Smallpox Contacts

SIR,—In his Milroy lecture on antiviral chemotherapy (4 August, p. 275) Dr. D. J. Bauer stated that "persons who have been in contact with smallpox infection are vaccinated routinely, but if they have not been vaccinated at some time in the past the development of immunity is too slow to protect them against developing the disease." With this latter phrase we disagree. It is generally accepted that successful vaccination within up to about 48 hours after exposure will usually protect contacts against smallpox whether they have been previously vaccinated or not. The earlier the vaccination after contact, the greater the chance of prevention of the disease, but vaccination even within three or four days of contact produces some measure of protection by modifying the disease. The reason for this protective effect is that the immunity which follows vaccination develops more rapidly than that following infection by smallpox virus. The efficacy of the vaccination of contacts (whether previously vaccinated or not) has been largely responsible for the nearly world-wide eradication of smallpox carried out by the World Health Organization and for the success of the epidemiological control methods which are used when smallpox is imported into this country.

In view of Dr. Bauer's statement we reviewed some of the literature on the protective effect of vaccination of contacts of variola major in Britain.[1-6] In general, the success of vaccination of contacts is indisputable, though there are some reports of failures in protection of up to 10% of contacts. Some of these failures appear to have been due to the fact that vaccination was done late in the incubation period and no one should be surprised that vaccination does not protect when done late in the first week of the incubation period. Other failures could be attributed to faulty technique during panic vaccination and low-titre lymph. However, we have no evidence to shake our belief in the protective value of immediate vaccination of contacts nor any data which support Dr. Bauer's statement that if contacts have not been vaccinated in the past, "the development of immunity is too slow to protect them against developing the disease." There is no evidence that there is anything better, apart from the concomitant use of antivaccinial immunoglobulin in close family and household contacts.—We are, etc.,

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Amyloidosis Complicating Actinomycosis

SIR,—In the discussion of the case of actinomycosis and amyloidosis that was the subject of the Clinicopathological Conference at the Royal College of Physicians of London in July (20 October, p. 149) the question was raised whether actinomycosis predisposes to amyloidosis. Since reporting a case of this association in 1956[1] I have been collecting material from cases of actinomycosis in connexion with a study of fungal infections. This series now includes 112 cases of visceral (including septicaemic) actinomycosis and 174 cases of faciocervical actinomycosis. In the visceral group 68 patients died with active actinomycosis; in 63 of these cases the infection (including its complications) was considered to be the cause of death; the other five patients died of unrelated causes. In the faciocervical group 19 died with active actinomycosis; in 17 the infection was the cause of death. In all the other cases in both groups the infection was considered to have been cured. All cases were characterized by sinus formation. No case of faciocervical actinomycosis was found to be associated with amyloidosis. In contrast, amyloidosis was found in 14 of the 112 cases of visceral actinomycosis; 12 of these were among the 63 patients whose death was attributed to the infection. The amyloid deposition was of only microscopic extent in five of these 12 cases; it was macroscopically evident in seven—six of these seven patients had symptoms that, in retrospect, were attributable to