(Tetanus and Diphtheria Toxoids Adsorbed—For Adult Use, USP; Adult DT Toxoid). It is recommended for primary immunisation and re-immunisation of adults and older children without prior Schick testing. We report the use of this preparation on medical students, laboratory staff, and nurses.

Study and results

A total of 87 medical students received one dose—0.5 ml intramuscularly—of Adult DT Toxoid and samples of blood were taken from 60 of these, before and 12 days after inoculation. Many had received tetanus vaccine as adults, and most had probably received diphtheria and tetanus vaccine in childhood, but this information could not be confirmed with certainty. Side effects to the vaccine were acceptable and not severe enough to affect normal activity: two students had a painful, red arm and 11 others an itchy red arm; none were febrile. Serum antitoxin concentrations (table) were estimated by a slight modification of the method of Miyamura *et al*² for diphtheria, and by the method of the *European Pharmacopoeia*³ for tetanus.

Antitoxin levels before and after inoculation

Antitoxin IU/ml	Numbers of students	
	Pre-inoculation	Post-inoculation
<i>Diphtheria</i>		
<0.01	19	4
0.01-0.05	9	
0.05-0.15	15	
0.15-1.5	15	28
>1.5	2	28
<i>Tetanus</i>		
<0.01	8	1
0.01-0.03	2	
0.03-0.1	14	1
0.1-1.0	13	2
>1.0	23	56

Given that there is solid protection with a serum antitoxin concentration of 0.01 IU/ml or more, 19 of 60 students tested before immunisation had less than 0.01 IU/ml of diphtheria antitoxin, and eight had less than this concentration of tetanus antitoxin. After a single dose of vaccine the numbers failing to achieve this level of diphtheria antitoxin, and of tetanus antitoxin, were four and one, respectively.

Thirty-one members of staff of the Public Health Laboratory were Schick-tested, and six were susceptible. Three of these six responded to one dose of Adult DT Toxoid, but one required further immunisation. The two others, who were hypersensitive to tetanus toxoid, responded to a small dose (5 Lf) of purified diphtheria toxoid, with no side effects. A single dose of Adult DT Toxoid was also given to nurses in a children's hospital, without prior Schick testing, after contact with a case of diphtheria (Dr T N Stanbridge, personal communication). There were minimal side effects and none were off work, contrasting with severe reactions in nurses given 10 Lf doses of diphtheria vaccine during an outbreak of diphtheria in Manchester in 1971.⁴

Comment

Certain sections of the adult civilian community may require diphtheria immunisation. We have taken as examples medical students, sections of the nursing staff, and laboratory staff. Severe local and general reactions may follow the use of routine diphtheria prophylactics, particularly if hypersensitive subjects are not first excluded by Schick testing. Although toxoid-antitoxin floccules (Dip/Vac/TAF) has been widely used for immunising adults, it contains a little horse serum, which may cause sensitisation. The standard preparations of adsorbed diphtheria vaccine or plain diphtheria vaccine are clearly not optimal for adults, as even as little as 5 Lf of purified unadsorbed toxoid can cause severe reactions.⁵ The Adult DT Toxoid may be given without prior Schick testing, and, as most young adults have had primary diphtheria and tetanus immunisation at some time, one dose is often sufficient to produce immunity to diphtheria and tetanus with minimal side effects. If it is essential that the individual is known to be fully immune to diphtheria, the immune state may be checked by Schick testing about two weeks after immunisation, and further doses of vaccine given if required. Many young adults are fully immune to tetanus and some are hypersensitive to tetanus toxoid. For these a preparation of adsorbed diphtheria vaccine (1.5 Lf) without tetanus toxoid would be useful.

We recommend, therefore, that stocks of adsorbed diphtheria vaccine (1.5 Lf), and of adsorbed diphtheria-tetanus vaccine with 1.5 Lf of diphtheria toxoid and 7.5 Lf of tetanus toxoid, preferably

in individual doses, should be available for use within the National Health Service.

¹ Edsall, G, Altman, J S, and Gaspar, A J, *American Journal of Public Health*, 1954, **44**, 1537.
² Miyamura, K, *et al*, *Journal of Biological Standardization*, 1974, **4**, 203.
³ *European Pharmacopoeia*, volume II, p 274. Paris, Maisonneuve, 1971.
⁴ Butterworth, A, *et al*, *Lancet*, 1974, **2**, 1558.
⁵ Pappenheimer, A M, *jun, et al*, *American Journal of Hygiene*, 1950, **52**, 353.

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Increased prevalence of epilepsy in coeliac disease

Several neurological symptoms and disorders have been described in association with coeliac disease, including paraesthesiae, peripheral neuropathy, and myeloneuropathy.¹

In 30 patients with coeliac disease Morris *et al* described two who had fits—one grand mal and one myoclonic—giving a prevalence of epilepsy of 6%. Cooke and Smith² noted “attacks of unexplained loss of consciousness” in five out of 16 patients with coeliac disease, all of whom had other neurological conditions. The term epilepsy was not used. To our knowledge, an increased prevalence of epilepsy in coeliac disease has not been specifically recorded.

Patients, methods, and results

One hundred and eighty-five treated patients with coeliac disease were circulated with a questionnaire inquiring about the occurrence and frequency of faints, fits, blackouts, and other medical conditions. Altogether 165 patients returned the questionnaire and were eligible for inclusion in the survey. All patients with epileptic symptoms were interviewed by two of us (JML, RC) and reviewed by a consultant neurologist. The criterion for coeliac disease was taken as an original abnormal jejunal biopsy specimen of coeliac type and clinical response to gluten withdrawal. To determine the prevalence of epilepsy in a normal population in the area, 165 age- and sex-matched controls were randomly selected from a Southampton general practice. All controls were circulated with a similar questionnaire; 163 replied, and all those with symptoms suggestive of epilepsy were further investigated in the same way as the coeliac group.

Nine patients with coeliac disease who had admitted to having epileptic symptoms on the questionnaire were considered by the neurologist to have epilepsy (see table), giving a prevalence of 5.5%. Seven (five women and two men) were diagnosed as having temporal lobe epilepsy. No cases of epilepsy were found in the control group, in keeping with a national

Age and sex of epileptic patients

Case No	Age (years)	Sex	Type of epilepsy
1	30	M	Grand mal
2	58	M	“ “
3	33	M	Temporal lobe
4*	50	M	“ “
5*	63	F	“ “
6	47	F	“ “
7	17	F	“ “
8	36	F	“ “
9*	22	F	“ “

*Epilepsy improved by gluten withdrawal.

prevalence of epilepsy of 0.5%.³ The difference in the prevalence comparing the epilepsy between the two groups was significant ($P < 0.01$, χ^2 test).

Comment

This study has shown an increased prevalence of epilepsy, particularly temporal lobe epilepsy, among patients with coeliac disease. The possible reasons for this association are not clear and may well be multifactorial. These include genetic factors and calcium, magnesium, and vitamin deficiencies. Four patients had had low calcium and magnesium concentrations, but correction of these deficiencies some years before coeliac disease was diagnosed did not improve the control of their epilepsy in three out of the four. Similarly, correction of folate deficiency in eight out of nine patients did not improve their epileptic control. The improvement in epileptic control in three patients after starting a gluten-free diet may have been due to the correction of deficiencies both known and unknown, although improved anticonvulsant absorption may have played an important part. Selective immunoglobulin A deficiency has been reported in association with coeliac disease⁴ and familial epilepsy,⁵ but it was not present in any of our patients.

A large survey of epileptics⁶ showed that only 20% had temporal lobe epilepsy, which highlights the unusually high prevalence (77%) of this type in our series. This remains unexplained.

We think that the demonstrated association between epilepsy and coeliac disease raises important clinical implications in the management of both conditions. Greater awareness of the association should lead to the improved diagnosis of both epilepsy and coeliac disease.

We are grateful to Dr P Kennedy for his help in assessing the epileptics; to Dr G Salmon, Dr J Bamforth, and Professor Ralph Wright for allowing us to study patients under their care.

¹ Morris, J S, Ajdukiewicz, A B, and Read, A E, *Gut*, 1970, **11**, 549.

² Cooke, W T, and Smith, W T, *Brain*, 1966, **89**, 683.

³ Research Committee of the College of General Practitioners, *British Medical Journal*, 1960, **2**, 416.

⁴ Crabbé, P A, and Heremans, J F, *Gut*, 1966, **7**, 119.

⁵ Fontana, A, et al, *Lancet*, 1976, **2**, 228.

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Haemodialysis-triggered asthma

Changes in respiratory function during haemodialysis using cellulose membranes include mild hypoxemia, variable hypocapnia, reduced carbon monoxide diffusing capacity, and increased lung closing volumes.¹ We describe a patient in whom haemodialysis was associated with severe asthma and leucopenia.

Case report

A 40-year-old housewife reached end-stage renal failure due to proliferative glomerulonephritis and began haemodialysis at home in 1972. She also had a three-year history of episodic attacks of dyspnoea, wheezing, and non-productive cough. She was a non-smoker and there was no personal or family history suggestive of atopy. Blood eosinophilia was absent and skin prick test results were negative to four common allergens; nevertheless, asthma had been triggered when she had taken salicylates, and intrinsic asthma had been diagnosed. Before dialysis her asthmatic symptoms had been mild and infrequent and usually associated with respiratory infection. Nevertheless, when dialysis began with a Cupraphane membrane (PM150) and a Meltec Multipoint 1 m² haemodialyser her asthma deteriorated. The

Peak expiratory flow rate changes during dialysis (mean $\pm$ SEM of ten studies done with each membrane) and neutrophil count (mean $\pm$ SEM of percentage of change of predialysis values of three studies done with each membrane).

usual pattern was that within an hour or so of starting haemodialysis the patient noticed chest tightness, dyspnoea, and wheezing, which became progressively worse as dialysis proceeded. On one occasion the FEV₁ changed from 1.82 to 0.97 litres and the FVC from 2.175 to 1.8 litres, after four hours' haemodialysis. She noticed that terminating dialysis early stopped the progression of symptoms but that she continued to wheeze for several hours after dialysis. Her general practitioner was frequently called on dialysis days to administer aminophylline and steroids. At no time had there been any clinical or radiological evidence of fluid overload or left ventricular failure. Treatment before and during dialysis with intravenous aminophylline and hydrocortisone or inhaled salbutamol and beclomethasone failed to prevent the dialysis-triggered attacks. Changing the osmotic pressure of her dialysate, changing the rate of ultrafiltration, and substituting Silastic for polyvinyl chloride lines were also ineffective. Substantial improvement followed a renal transplant in 1973 but her asthmatic symptoms reappeared when dialysis was started again after transplant rejection and nephrectomy in 1974. Some improvement was obtained with oral prednisone, 10 mg on dialysis days and 5 mg on other days, but dialysis was still frequently curtailed by dyspnoea.

Formalin used as a sterilising agent was suspected² to be responsible but inhalation of formalin vapour failed to produce any symptoms or change in peak expiratory flow rate. Dramatic improvement occurred when the Cupraphane membrane was substituted by a polyacrylonitrile membrane (Rhône-Poulenc, RP6 dialyser). The figure shows the progressive reduction in peak flow during haemodialysis with Cupraphane membrane (PM150) compared with that of polyacrylonitrile (PAN); changes in neutrophil count are also shown. When, unknown to the patient, she was again dialysed with a Cupraphane membrane a dramatic reduction in peak flow was once again seen. She is now dialysing again at home with a polyacrylonitrile membrane (RP6 dialyser), a Bellco double-headed single-needle dialysis blood pump, and a Lucas Mark II proportionating unit; for economic reasons the RP6 dialyser is re-used.³ She has been free from asthma for six months since using the RP6 and her prednisone has been reduced to steroid replacement dosage only.

Comment

Selective leucopenia affecting neutrophils and activation of complement occur during haemodialysis with cellulose membrane dialysers.¹ The leucopenia arises from sequestration of neutrophils in the pulmonary capillary bed.¹ There is evidence that complement is concerned in asthma, particularly when allergic factors are not prominent.⁴ Our patient's asthma triggered only by Cupraphane-membrane dialysis could be due to either activation of complement or pulmonary leucostasis with subsequent release of bronchoconstrictor