much screening after vaccination, probably by single radial haemolysis. Recognition of the limitations of this otherwise cheap, quick, and effective method would avoid reports suggesting failure of vaccines leading to unnecessary revaccination.

Subjects, methods, and results

Thirty young adults (20 men, 10 women) with no detectable antibodies against rubella were successfully vaccinated with RA27/3 (Almevax, Wellcome Medical Division). IgG was estimated by single radial haemolysis, enhanced single radial haemolysis,² and Rubazyme (Abbott Laboratories Ltd); combined IgG and IgM by haemagglutination inhibition; and IgM by three commercially available methods: Rubazyme M (Abbott Laboratories Ltd) and Rubenz M1 and M11 (Northumbria Biologicals Ltd). Eighty four specimens were obtained 17-107 days after vaccination.

Ten specimens were collected within three weeks of vaccination. Eight showed IgM but none significant IgG antibodies. Nevertheless, compared with pre-vaccination serum samples nine showed a positive Rubazyme diagnostic ratio, suggesting seroconversion. IgM was invariably detected at 3-6 weeks; haemagglutination inhibition consistently detected antibody from four weeks, Rubazyme from six, but single radial haemolysis from only seven onwards (table). Before

Detection of rubella antibodies in 84 specimens after vaccination from 30 vaccinees. (Blocks showing 100% positives represent optimum period for detection by each method)

No of specimens showing detectable rubella antibodies							
		IgM		Combined IgG and IgM		IgG	
Days after vaccination	No of specimens*	Rubenz M1 (no longer available)	Rubenz M11	Rubazyme M	Haemagglutination inhibition	Rubazyme	Single radial haemolysis
17-21	10	6	6	8	6		
22-28	7				6	3	4
29-35	6	100%	100%	100%	†	6	5
36-42	13	9	↓	†		11	6
43-49	9	5	7	†			7
50-56	8	8	8	7			
57-63	3	0	0	0	100%		
64-70	8	6	6	5		100%	
71-77	4	1	3	2†			100%
78-84	8	5	5	4††			
>84	8	4	5	7	↓	↓	↓
Total	84	57	66	69	79	68	61

*30 specimens from vaccinees before vaccination.

†Each mark means one sample was not tested because insufficient serum was available.

seven weeks Rubazyme detected antibodies in nine samples that gave no zones by single radial haemolysis. By enhanced single radial haemolysis seven of these produced zones similar in size to that of a 15 IU/ml control. Two samples taken 36-42 days after vaccination were negative by Rubazyme and gave no zones by single radial haemolysis and only small zones by enhanced single radial haemolysis. These showed slow IgG conversion as subsequent specimens were positive by all methods.

After vaccination Rubenz M1 detected IgM less than Rubazyme M and Rubenz M11, which detected similar numbers but not always the same samples. IgM was still detected by at least one method in six of eight specimens taken over 12 weeks after vaccination. Eight vaccinees gave nine specimens 9½-21 months after vaccination. IgM was present at 9½ months in one of the "slow responders" but had disappeared by 12½ months. The seven others were negative.

Comment

Although haemagglutination inhibition gave early results, the method is time consuming for mass screening, and non-specific inhibitors are a problem. Rubazyme also gave early results but would be expensive for large numbers. For a single, quick result, however, haemagglutination inhibition or enzyme linked immunosorbent assay could be advocated after 3-4 weeks. By single radial haemolysis zones of varying sizes and clarity became apparent from 22 days onwards, but all samples produced zones at least as large as that of standard serum containing 15 IU/ml only after seven weeks. Mortimer *et al* reported a delayed response by single radial haemolysis after Cendehill vaccine,³ and we found a similar delay after Almevax. Enhanced single radial haemolysis can increase sensitivity, but we recommend that Edinburgh schoolgirls be screened two months after vaccination. The slow rather than inadequate single radial haemolysis response in some people was shown by the development of haemolysis zones beyond the 15 IU/ml control in subsequent specimens.

Rubella IgM was detected in six of eight cases more than 84 days after

vaccination and in one after the tenth month. Mortimer *et al* also detected IgM in 35 of 36 cases at 77 days by anti μ capture radioimmunoassay, and O'Shea *et al* reported low concentrations of IgM two, three, and even four years after Cendehill vaccine.⁴ IgM clearly persists in some people, which may cause problems in interpreting results.⁵

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Osteopathic manipulation resulting in damage to spinal cord

Three cases are described in which osteopathic manipulation resulted in acute spinal cord injury that required surgery.

Case reports

Case 1—A 56 year old engineer presented to this hospital in August 1984. He had been treated 14 years previously with manipulation for neck pain. Two months before admission, while working under his car, he had experienced pain and Lhermitte's sign in all four limbs. He then developed difficulty in fine finger manipulation and suffered some weakness of both legs. His symptoms worsened with osteopathic manipulation of both cervical and lumbar spines, but the osteopath was unconcerned by this. On admission to hospital he had severe spastic tetraparesis and was unable to walk. Myelography showed compression of the cervical cord, and he underwent anterior cervical discectomy with fusion (Cloward's procedure) at the C3/4 and C5/6 levels with good result. Six weeks after his operation he was walking well.

Case 2—A 70 year old retired printing manager presented to this hospital in August 1984. In 1978 he had had osteopathic treatment for low back pain. Two months before admission, after lifting a heavy weight, he had experienced more low back pain and left sided sciatica and had received osteopathic manipulation of both the lumbar and cervical spine. The sciatica resolved immediately, but he became unsteady and developed difficulty in fine finger movements. On admission he was unable to walk unaided and had a spastic tetraparesis. Myelography showed an extremely narrow spinal canal that required emergency cervical decompression. Subsequently, he was able to walk unaided.

Case 3—A 64 year old man was admitted to this hospital in January 1985 with a six week history of right lower limb and neck pain. A month before admission he had undergone cervical manipulation that had caused excruciating neck pain. Since that time he had been unable to move his head. On admission the patient was cachectic and clearly in severe pain. Neck movement was impossible. He had a mild tetraparesis and some bilateral sensory loss in his fingers. Plain cervical spine radiographs and computed tomography—myelography showed complete destruction of the C2 vertebral body with an anterior extradural mass from the clivus to the body of C3. Chest radiographs suggested a carcinoma of the bronchus. Transoral odontoidectomy and posterior fixation stabilised his neurological state, but he remained in poor condition because of underlying carcinomatosis.

Comment

In case 2, apart from a stiff neck, the patient had no clear neurological symptoms, though neurological examination may have resulted in findings consistent with cervical myelopathy. After manipulation by an osteopath, registered with the British Society of Osteopathy, the patient developed severe neurological problems. In the two other cases there were pre-existing neurological symptoms, and manipulation was undertaken by respectable

non-registered osteopaths. In the third case this almost certainly resulted in acute vertebral body collapse.

In the United Kingdom there has been a recent upsurge of interest in "alternative" treatment for spinal spondylotic disease. In 1984 a case was reported from the United States in which chiropractic manipulation exacerbated a myelopathy.¹ In the past 55 years there have been periodic reports of manipulation causing spinal problems with the most serious results affecting the cervical spine.²⁻⁵ There are virtually no published scientific reports that document the beneficial effects of manipulative treatment, though where the spinal cord and its roots are near compression forced flexion and extension might compromise on a mechanical or vascular basis either acutely or insidiously with repeated manipulation. In the three cases reported patients were unwilling to give details of their treatment let alone complain.

During the past 12 months of the five cases of "traumatic" subacute cervical cord compression that required surgery at the Maida Vale branch of the National Hospital for Nervous Diseases, three were caused by spinal manipulation. The medicolegal implications of doctor to osteopath referrals are self evident.

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Liver enzyme abnormalities after insulin induced hypoglycaemic coma

Multiple liver enzyme abnormalities are often noted in diabetic ketoacidosis.¹ We show that pronounced enzyme abnormalities may be associated with severe acute hypoglycaemia.

Patients, methods, and results

Three women with type I diabetes mellitus suffered a total of 12 episodes of severe hypoglycaemia between 1979 and 1984. In two patients (cases 1 and 2) the episodes were self induced, but in the third patient they were the result of gastroparesis. At the time of the initial episodes the patients were aged 28, 32, and 33 years and had been diabetic for eight, 12, and 20 years respectively. None of the patients was receiving drugs other than insulin. One patient (case 3) had chronic complications, including background retinopathy and peripheral and autonomic neuropathy.

Serum glucose concentrations were measured on a Beckman autoanalyser, and Ketostix (Ames Co) was used to detect urinary and serum ketones. Serum bilirubin concentration and aspartate aminotransferase, alanine amino-

transferase, alkaline phosphatase, and creatine phosphokinase activities were measured on a Technicon autoanalyser.

The table shows the liver enzyme values recorded after the 12 episodes of severe hypoglycaemia (serum glucose concentration <1.1 mmol/l; <19.8 mg/100 ml). Alanine aminotransferase activity increased on all occasions, aspartate aminotransferase activity increased in nine episodes, and alkaline phosphatase activity increased in eight. Peak alanine aminotransferase and aspartate aminotransferase activities were recorded immediately after the acute episode and thereafter there was a gradual decline, normal values being reached in all cases within 10 days. There was no increase in serum bilirubin concentration or creatinine phosphokinase activity. Serum phosphate concentration was abnormally low in four episodes and serum potassium concentration in two. No patient had ketonuria or ketonaemia.

Screening for toxic chemicals (including alcohol) and hepatitis was carried out with negative results in all cases. The three patients had normal electrocardiograms. Liver biopsy was performed in case 1 three days after the initial episode of severe hypoglycaemia. At that stage the serum glucose concentration was between 11.1 and 16.6 mmol/l (200 and 300 mg/100 ml), though alanine aminotransferase and aspartate aminotransferase activities were still raised. The histological appearances were essentially normal except for very mild fatty change. Periodic acid Schiff staining showed normal glycogen stores.

The three patients were also studied after five admissions for diabetic ketoacidosis, and twice a mild increase of alkaline phosphatase activity (<0.2 IU/ml) was observed. Alanine aminotransferase and aspartate aminotransferase activities, however, remained normal.

Comment

Mild liver enzyme abnormalities are not uncommon among diabetic patients² but the pronounced increases that we observed after acute insulin induced hypoglycaemia have not been reported. The enzyme changes varied between the episodes and among the patients. The high values attained make it unlikely that a change in clearance of these enzymes was implicated. Since the highest enzyme activities were recorded in association with prolonged unconsciousness these differences may be related to the severity or duration of the hypoglycaemic insult. Other factors including the prevailing insulin concentration, nutritional state, and coexisting hypoxia or hypotension may also play a part. Hypoxia at the outset of the hypoglycaemic episode, secondary to unconsciousness with or without convulsions, remains a potential cause of liver damage.³ Possibly also hypoglycaemia may lead to changes in hepatic blood supply and consequently to hepatic necrosis, as described in a case of diabetic ketoacidosis.⁴ On the other hand, severe hypoglycaemia may be a direct cause of liver damage. We speculate that an acute increase in liver glycogen may lead to the release of liver enzymes.

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Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (AP) activities immediately after episodes of insulin induced hypoglycaemic coma. [Normal values in square brackets]

Case No	Date	Coma <1 hour			Date	Coma >1 hour*		
		ALT (IU/ml) [<45]	AST (IU/ml) [<36]	AP (IU/ml) [30-120]		ALT (IU/ml) [<45]	AST (IU/ml) [<36]	AP (IU/ml) [30-120]
1	Nov 1979	56	89	72	June 1979	637	1386	185
					Dec 1980	594	957	85
2	Aug 1979*	71	65	125	June 1981*	237	150	155
	Oct 1979	153	30	144				
3	March 1980	66	29	146	Feb 1980	56	34	180
	Sept 1980	62	39	105	Jan 1981*	200	159	139
					Nov 1982	269	487	105
					Sept 1984	972	1056	244

*Duration of unconsciousness varied between two and 36 hours.
*Episode accompanied by seizure activity.