SHORT REPORTS

Value of booster immunisation with influenza vaccine in patients undergoing haemodialysis

The public health authorities of most Western countries recommend annual influenza vaccination for some patients, including those with end stage renal disease.¹ Patients on haemodialysis, however, show impaired antibody responses after a single influenza vaccination, which may result in insufficient protection.² These patients also respond poorly to hepatitis B vaccine, but a booster immunisation will produce protective antibody titres.³ In a large group of patients on haemodialysis we therefore attempted to induce adequate protection against influenza by performing a booster vaccination.

Patients, methods, and results

Ninety eight patients in a stable condition who were undergoing long term intermittent haemodialysis took part. They were aged 17 to 76 (median 57) years and had been undergoing haemodialysis for one month to 13 years (median two years). None had received steroids or immunosuppressive drugs for at least six months. Twenty nine healthy volunteers aged 19 to 69 (median 27) years served as controls. A commercially available trivalent split virus vaccine (Alorbat, Asta Werken, Bielefeld, Federal Republic of Germany) containing 15 µg haemagglutinin of A/Philippines/2/82 (H₃N₂), A/Chile/1/83 (H₁N₁), and B/USSR/100/83 was administered by intramuscular injection in the upper arm on day 0 and day 30 (booster immunisation). Serum was obtained on days 0, 30, and 60. The study took place in the autumn of 1985. Antibody titres were determined twice in paired sera by the haemagglutination inhibition technique, and geometric mean titres were calculated. A fourfold or more rise in titre was considered to be a satisfactory response, and protection was defined by titres of ≥ 100 against influenza A and ≥ 200 against either treated influenza B.⁴

Before vaccination geometric mean titres against the three virus strains did not differ between the groups (table). After the first injection the patients undergoing dialysis had significantly lower geometric mean titres than the controls for all viruses tested ($p < 0.001$, Wilcoxon rank test). Booster vaccination did not influence the final titres reached.

Among the initially unprotected patients and controls significantly fewer of the patients showed a more than fourfold rise in titre against the three viruses (H₃N₂ and B $p < 0.05$, H₁N₁ $p < 0.001$; χ^2 test) after the first injection (table). Booster immunisation produced greater than fourfold rises in titres against H₃N₂, H₁N₁, and B in, respectively, a further 14%, 8%, and 0% of the patients and 5%, 8%, and 4% of the controls. The seroconversion rate to protective titres against H₃N₂ and B was also significantly lower among the patients after the first injection than among the controls ($p < 0.001$, χ^2 test). Booster immunisation increased the seroconversion rate among the patients but not significantly so. Together the first and second vaccinations induced adequate protective antibody titres in 81 (83%) of the patients for H₃N₂, 37 (38%) for H₁N₁, and 47 (48%) for B. The statistical significance of the results measured as geometric mean titres, more than fourfold rises in titres, and seroconversion rates was maintained when controls were compared with age and sex matched patients undergoing dialysis.

Comment

In patients undergoing haemodialysis vaccination with an influenza vaccine was significantly less effective than in the controls for all three

Effects of first injection and booster vaccination with influenza vaccine on mean log geometric mean titre against influenza viruses H₃N₂, H₁N₁, and B in patients undergoing haemodialysis and controls, and greater than fourfold rises in titres and seroconversion rates to protective titres in individuals with unprotective prevaccination titres

	Patients (n=98)			Controls (n=29)		
	H ₃ N ₂	H ₁ N ₁	B	H ₃ N ₂	H ₁ N ₁	B
Mean log geometric mean titre:						
Before first injection	1.10	1.07	1.28	1.14	1.12	1.14
After first injection	2.21	1.66	2.05	2.93	2.39	2.63
After booster vaccination	2.30	1.68	2.05	3.01	2.47	2.62
No (%) with non-protective titres before vaccination	71 (72)	88 (90)	82 (84)	20 (69)	25 (86)	25 (86)
No (%) with $\geq$ fourfold rise in titre:						
After first injection	49 (69)	39 (44)	47 (57)	19 (95)	21 (84)	20 (80)
After second injection	59 (83)	46 (52)	47 (57)	20 (100)	23 (92)	21 (84)
Seroconversion rate (No (%)):						
After first injection	47 (66)	22 (25)	22 (27)	17 (85)	21 (84)	19 (76)
After booster vaccination	54 (76)	27 (31)	31 (38)	18 (90)	22 (88)	20 (80)

viruses. The better conversion rate to protective titres against H₃N₂ in the patients can be explained by a "priming" effect, as the H₃N₂ strains have circulated for over 10 years and have caused several epidemics in the Netherlands. Booster immunisation only marginally improved the efficacy of vaccination against the three influenza viruses in both the patients and the controls. Only a small minority of the 98 patients developed protective titres as a result of the second immunisation: seven for H₃N₂, five for H₁N₁, and nine for B. Therefore we cannot recommend a booster immunisation with influenza vaccine in patients undergoing dialysis. Prophylactic amantadine therapy, which protects against influenza A viruses but not against influenza B, may be considered for these patients if an epidemic is imminent.⁵

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Neuropathy of the feet due to running on cold surfaces

After running a race in bare feet on a day when the temperature was below freezing several runners presented to hospital with injuries to their feet. Such injuries have not been reported before.

Patients and findings

In February 1986, 160 runners took part in a sponsored five mile run; all had to run in bare feet. The participants were members of a karate club, and most of them had run in bare feet on previous occasions without any problems. The course was along paths in a park in Leicester; at the start of the race the ambient temperature was -5°C and the ground temperature -9°C (United Kingdom Meteorological Office, personal communication). All the runners finished the event without any problems. Shortly afterwards, however, 25 participants presented to the accident and emergency department with almost identical injuries to their feet.

All the patients complained of severe pain in their feet, which had developed shortly after they finished the race. On examination the weightbearing surfaces of the soles of their feet were bright red and deeply ingrained with dirt. The areas affected resembled partial thickness burns. Large tense blisters were also found in several patients; debridement of these showed partial thickness skin loss (figure).

Comment

Most of the patients had taken part in similar runs before but never on a freezing day. In the past they had experienced pain in their feet during the run and on finding blistering had stopped. On this particular day pain had been absent during the event and the skin damage had not become apparent until some time afterwards.

Partial thickness loss of skin on feet.

Although this problem has not been described before in runners, experimental and clinical studies have shown that nerve conduction is altered by cooling. Ungley *et al* looked at the symptoms experienced by naval staff during the second world war after immersion of their feet in cold sea water: all the subjects reported loss of sensation.¹ Sinclair *et al* showed that cooling of the legs results in, firstly, cold feet, then pain, then loss of sensation to touch.² In a more recent study Basbaum cooled the sciatic nerve of a rat and found that a reduction in the temperature of the nerve to 5°C resulted in a total block in conduction, which recovered on warming.³

It is likely that because of the low ground temperature (−9°C) the runners reported on here developed temporary neuropathy of the feet, lost all sensation, and were able to continue running despite the severity of their injuries. This indicates the dangers of running on cold surfaces without adequate footwear.

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Occult chlamydial ophthalmia in men with non-gonococcal urethritis

Chlamydial ophthalmia in adults usually results from autoinoculation with genital secretion containing *Chlamydia trachomatis* (D-K).^{1,2} Little is known about the relation between occult chlamydial ophthalmia and overt genitourinary infections. The recent introduction of fluorescein labelled monoclonal antibody allows rapid and reliable identification of chlamydia in conjunctival smears.³ We used this method in a prospective study to evaluate the prevalence of chlamydia in the eye in men with urethritis associated with chlamydia.

Patients, methods, and results

Informed consent to ophthalmological assessment was given by 60 out of 67 men with non-gonococcal urethritis who presented consecutively to the department of genitourinary medicine. The patients' eyes were examined by slit lamp for conjunctival papillae and follicles, corneal staining, and opacities. Papillae and follicles in both eyes were graded on a four point scale.⁴

Topical amethocaine 1% was instilled in both eyes, and after five minutes conjunctival scrapings were taken with a scalpel blade, smeared on to a microscope slide, and fixed with methanol. Smears were stained with Orion Chlamyset

fluorescein labelled monoclonal antibody and the fluorescent chlamydial inclusion bodies counted. *C. trachomatis* was isolated from urethral swabs by inoculation on to McCoy cell monolayers treated with idoxuridine. The data were analysed by χ^2 (with Yates's correction), Student's *t* test, and analysis of variance (one way).

Eight of the 60 men had asymptomatic chlamydial ophthalmia; none had punctate keratitis, pannus, or tarsal scarring. Conjunctival smears showed five to 10 inclusion bodies in five men and 10-50 in the remaining three. Six of the eight men had evidence of genital infection associated with chlamydia as indicated by isolation of chlamydia either in the man or in his consort. There were no significant demographic or clinical differences between those who had chlamydia in the eye and those who did not (table). The eye disease was apparently cured by conventional treatment with oral triple tetracycline (tetracycline, chlortetracycline, and demeclocycline; Deteclo) for two weeks.

Epidemiological and clinical features of men with non-gonococcal urethritis

	With chlamydial eye infection (n=8)	Without chlamydial eye infection (n=52)	Significance test used*
<i>Demographic features</i>			
Mean (SD) age (years)	25.9 (3.8)	24.6 (5.5)	Student's <i>t</i> test
No (%) white	5 (63)	47 (90)	
No (%) with previous episodes of sexually transmitted disease	3 (38)	21 (40)	χ^2
No (%) who had taken oral antibiotics in previous month	1 (13)	7 (13)	χ^2
<i>Clinical features</i>			
No (%) with urethritis associated with chlamydia	2 (25)	14 (27)	χ^2
Mean (SD) duration of urethral symptoms (days)	11.6 (7.6)	11.7 (8.0)	Student's <i>t</i> test
Mean (SD) papillary score† [range]	1.9 (1.6) [0-4]	2.3 (2.4) [0-8]	
Mean (SD) follicular score† [range]	1.63 (1.1) [0-3]	2.4 (2.3) [0-8]	

*All differences in variables between groups not significant.

†Sum of grades of papillae or follicles on upper and lower eyelids in both eyes (0=none, 1=mild, 2=moderate, 3=severe; maximum score=12).

Comment

Asymptomatic chlamydial eye infection in men with non-gonococcal urethritis has not been described previously; indeed, in Sweden a study of cultures failed to identify any cases of chlamydial eye infection in 855 unselected patients attending a clinic for sexually transmitted diseases, even though 18.6% had genital chlamydia.⁵ In our study those patients who had chlamydia in the eye had few inclusion bodies. We postulate that the technique of conjunctival scraping combined with use of a specific monoclonal antibody to detect *C. trachomatis* is more sensitive than smears and conventional tissue culture. The minor conjunctival changes seen, predominantly papillae and follicles, were common and did not distinguish clinically between those who did and did not have chlamydial eye infection. This parallels the well recognised occult nature of chlamydial infection of the genital tract.

This study shows that chlamydial eye disease may be asymptomatic and is not uncommon in men with non-gonococcal urethritis. Further studies are necessary to document the clinical course of this condition and its response to concurrent treatment of urethritis associated with chlamydia.

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