Influenza vaccination in adults with cystic fibrosis

E L C Ong, D Bilton, J Abbott, A K Webb,
R A McCartney, E O Caul

**Regional Department of
Infectious Diseases and
Tropical Medicine,
Monsall Hospital,
Manchester M10 8WR**
E L C Ong, MRCP, senior
registrar

**Adult Cystic Fibrosis Unit,
Monsall Hospital,
Manchester M10 8WR**
D Bilton, MRCP, research
fellow
J Abbott, PHD, research
fellow
A K Webb, FRCP, consultant

**Regional Public Health and
District Virology
Laboratory, Bristol**
BS2 8EL
R A McCartney, FIMLS,
senior chief medical laboratory
scientific officer
E O Caul, PHD, honorary
consultant

Correspondence to:
Dr Webb.

BMJ 1991;303:557

Respiratory viruses, particularly influenza viruses, cause infective respiratory exacerbations and deterioration of pulmonary function in patients with cystic fibrosis.^{1,2} Moreover, these patients have an increased risk of dying from influenza or its complications.³ Patients may, however, fear vaccination because of the flu-like side effects. We report a two year study of the clinical effect and antibody response after influenza vaccination in adults with cystic fibrosis and healthy volunteers.

Subjects, methods, and results

During October to December 1988, 30 patients from the adult cystic fibrosis unit at Monsall Hospital and 22 healthy volunteers were vaccinated intramuscularly with 0.5 ml inactivated influenza vaccine (split virion) containing A/Sichuan/2/76 (H₃N₂) 15 µg haemagglutinating activity, A/Singapore/6/86(H₁N₁) 15 µg haemagglutinating activity, and B/Beijing/1/87 (MFV-JECT FLU, Merieux). During October to December 1989 a further 22 patients were similarly vaccinated. Informed consent was given by all subjects and the study approved by the ethics committee.

Daily score charts of peak expiratory flow, temperature, headache, nausea, cough, and pain at the site of injection were recorded for 14 days after vaccination by the subjects themselves. Antibody response was measured by single radial haemolysis.⁴ Paired serum samples were examined, the first sample taken before vaccination and the second three weeks afterwards. An increase of ≥1 mm in zone diameter between the samples indicated a serological response. Zone diameters of ≥5.5 mm against influenza A H₃N₂ and influenza B and ≥6.5 mm against influenza A H₁N₁ confer increased protection as manifested by lower infection rates than seen with lower antibody levels.⁵

In October and November 1989, before revaccination of the 22 patients available from the 30 vaccinated in 1988 (four had died, the remainder refused), blood was tested for antibodies to A/Taiwan(H₁N₁), A/Mississippi(H₃N₂), and A/Sichuan(H₃N₂). The second group of 22 patients in 1989 were also tested for these antibodies before and after vaccination. Daily score charts were omitted in this group. Data from score charts were analysed by one way analysis of variance with repeated measures. Independent and paired *t* tests were used in analysing the number of responders to the vaccine.

Score charts of the 30 patients (16 men, 14 women, mean age 24) and 22 volunteers (14 women, eight men, mean age 44) studied in 1988 showed no differences in temperature, headache, nausea, cough, or pain. Patients showed a significant increase in peak expiratory flow over the first five days (*F* (4, 112)=3.19; *p*<0.05). None had an infective pulmonary exacerbation during the 14 day study period. Twenty five (83%) patients and 16 (73%) controls had a significant serological response (>1 mm increase in zone diameter between paired samples) to all three vaccine strains (*p*<0.001). Thirteen patients (43%) and four controls (18%) had intermediate and high antibody responses to all three strains. Overall, more patients with cystic fibrosis showed a greater increase in antibody levels than controls.

Of the 22 patients vaccinated in 1988 who were studied again in 1989 before their second vaccination, 18 had intermediate to high antibody titres to A/Mississippi(H₃N₂), seven to A/Sichuan(H₃N₂), and 15 to A/Taiwan(H₁N₁). These levels are associated with increased protection.⁵ The 22 additional patients (12 men, 10 women, mean age 23) studied in 1989 had antibody responses to all three strains of influenza A that were similar to those studied in 1988.

Comment

These patients showed a greater increase in antibody response than the controls. One year later intermediate and high antibody levels were maintained by 82%, 32%, and 68% of patients vaccinated in 1988 to A/Mississippi(H₃N₂), A/Sichuan(H₃N₂), and A/Taiwan(H₁N₁). These levels were not significantly different from the post-vaccination state in 1988. The vaccine was well tolerated. The most common side effect in the patients was pain at the injection site, but this was not more frequent than in controls. No infective pulmonary exacerbation was recorded.

Doctors caring for adults with cystic fibrosis should maintain an active annual influenza vaccination programme.

We thank Dr J St Clair Roberts, of Merieux UK, for help with the study.

A table showing the antibody levels in patients and controls before and after vaccination may be obtained from AKW.

- 1 Wang EEL, Prober GC, Manson B, Corey M, Levison H. Association of respiratory viral infections with pulmonary deterioration in patients with cystic fibrosis. *N Engl J Med* 1984;311:1653-8.
- 2 Ong ELC, Ellis ME, Webb AK, Neal KR, Dodd M, Caul EO, et al. Infective respiratory exacerbations in young adults with cystic fibrosis: role of viruses and atypical microorganisms. *Thorax* 1989;44:739-42.
- 3 Eickhoff TC, Sherman IL, Serfling RE. Observations on excess mortality associated with epidemic influenza. *JAMA* 1961;176:776-82.
- 4 Grilli EA, Smith AJ. The use of a radial haemolysis test for neuroaminidase antibodies in the diagnosis of influenza A infection. *Journal of Hygiene (Cambridge)* 1983;91:147-56.
- 5 Davies JR, Grilli EA. Natural or vaccine-induced antibody as a predictor of immunity in the face of natural challenge with influenza viruses. *Epidemiol Infect* 1989;102:325-33.

(Accepted 7 June 1991)

ONE HUNDRED YEARS AGO

From time to time complaints reach us that some village parsons seem to regret the divorce between theology and physic, and we occasionally hear of them forsaking the medicines of the soul for those of the *Pharmacopœia*. A complaint is before us just now from a member of our profession, who states that in a certain village near the city in which he practises the clergyman prescribes and dispenses medicines for his parishioners, and even attends them in their sickness at their own homes, although he has not a medical degree and has not therefore duly qualified himself for the purpose. Our correspondent ventured respectfully to remonstrate with the cleric,

who wrote him to the effect that he did not think there was a single member of the city hospital staff, past or present, who would support him in that remonstrance. We are confident that the staff of the hospital in question would not support the rector in his amateur doctoring—a practice which can but be dangerous to the patients thus experimented with. He would probably be unwilling to lend his pulpit to any doctor who had a fancy for usurping his functions, and it might be well that he should restrict himself to the practice of the profession which he has studied.

(*British Medical Journal* 1891;iii:1056)