Correspondence

Newly diagnosed cystic fibrosis in middle and later life

SIR,—In their study Drs B Hunt and DM Geddes (*Thorax* January 1985;**40**:23–6) make the diagnosis of cystic fibrosis (CF) on dubious grounds. CF is a generalised disease of exocrine glands. The diagnosis requires demonstration of exocrine gland abnormalities uniquely characteristic of the disease.

The sweat of children with CF is uniquely characteristic. A sweat Na or Cl concentration of greater than 60 mEq/l is diagnostic if there is also evidence of pulmonary disease or pancreatic disease or a family history of CF. Other causes of a positive result in the sweat test[1] are usually easy to rule out.

In adults the sweat test is less helpful. Na or Cl concentrations above 60 mEq/l are common in normal people.[2] A concentration below 50 mEq/l does, however, rule out CF. Pulmonary changes in CF are primarily the result of chronic infection and are not, by themselves, diagnostic.

Drs Hunt and Geddes put faith in the diagnostic significance of suppression of sweat Na concentration by fludrocortisone, as described by Hodson *et al.*[3] This paper presents a graph where two CF patients have no drop in sweat Na concentration after the steroid, while two control subjects show a marked suppression. The data on all patients, unfortunately, are much less impressive. The average suppression in controls is 26.3%, while that in CF patients is 8.7%. The average Na concentration, before steroid, in the controls was 43.2 mEq/l and that in the CF patients 103.0 mEq/l. The authors did not calculate the average drop in Na concentration. This is 11.4 mEq/l for the controls and 9.0 mEq/l for the CF patients. The difference between these numbers is not significant and is not of diagnostic importance.

The diagnosis of CF in an adult can be established. All exocrine glands are involved. Almost every CF male has total obstruction of the vas deferens. Eighty five per cent to 90% of all patients have virtually total obstruction of the pancreatic ducts. With a positive sweat test and pulmonary disease, the demonstration of either azoospermia or absent pancreatic enzymes confirms the diagnosis. Even the difficult case of a woman without malabsorption may be diagnosed. When the CF pancreas is only partially obstructed the pancreatic juice is still abnormal. The output of enzymes may be normal, but the outputs of water and bicarbonate are markedly, and diagnostically, reduced.[4,5] A duodenal drainage can establish the diagnosis.

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**This letter was sent to the authors, who reply below.

SIR,—Professor Gibson raises an important issue about the confidence of a diagnosis of cystic fibrosis (CF). Since biological events can be described only in terms of probability all diagnoses are more or less dubious. This is tacitly acknowledged by the words "almost," "virtually," "markedly," "usually" in Professor Gibson's letter. Fortunately it is possible to estimate the probability or doubt of the diagnosis of CF in the patients we described since the distribution of sweat sodium levels in the normal and CF population were determined by Hodson *et al* (his ref 3). The probabilities that each patient comes from the CF rather than the normal population are 170:1, 3:1, 29:1, 12:1, on the basis of the sweat sodium concentration alone. The compatible pulmonary disease, abnormality of pancreatic function, and high sweat sodium after fludrocortisone all considerably increase these probabilities.

The chance that all these patients do not have CF and all come from the normal population is less than 1:100 000 and we therefore stand by our conclusions.

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Serum concentrations of vitamin D metabolites in untreated tuberculosis

SIR,—We have read with interest the study carried out by Dr PDO Davies and colleagues (March 1985;**40**:187–90) on Indian patients with untreated tuberculosis, abnormal calcium metabolism and low serum 25-hydroxycalciferol (25-OH vit D) levels. These authors also underline the risk of iatrogenic vitamin D deficiency and osteomalacia occurring particularly in this population treated with antituberculous drugs. They therefore proposed prevention by supplementation with 1,25-dihydroxycalciferol ($1,25\text{-}(OH)_2$ vit D).

Nevertheless, high serum calcium concentrations have been found in 25% or more of patients with pulmonary tuberculosis where it is associated with vitamin D supplementation.[1] A study[2] on an anephric patient reports hypercalcaemia during clinically active tuberculosis; it was associated with an increase in serum $1,25\ (OH)_2$ vit D levels, which suggested an extrarenal 1α-hydroxylation of 25-(OH) vit D. We have recently been able to demonstrate in a 26 year old Haitian woman with active pulmonary tuberculosis and hypercalcaemia that this conversion could actually occur in vitro in alveolar macrophages recovered from bronchoalveolar lavage fluid. Our method was similar to the one described by Adams *et al*[3] in patients with hypercalcaemia during sarcoidosis.

We would like to suggest that treatment with 1,25-$(OH)_2$ vit D is likely to reveal hypercalcaemia in active tuberculosis and should therefore be given to these patients with great caution.

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2 Gkonos PJ, London R, Hendler ED. Hypercalcemia and elevated 1,25 dihydroxy-vitamin D levels in a patient with end stage renal disease and active tuberculosis. *N Engl J Med* 1984;**311**:1683–5.
3 Adams JS, Sharma OP, Galad MA, Singer FR. Metabolism of 25 hydroxyvitamin D3 by cultured pulmonary alveolar macrophages in sarcoidosis. *J Clin Invest* 1983;**72**:1856–60.

**This letter was sent to the authors, who reply below.

SIR,—We would like to thank Dr Cadranel and colleagues for their interest and comments. The paper by Abbasi *et al*[1] to which they refer showed transient hypercalcaemia in 22 of 79 patients on treatment for tuberculosis, all but one receiving vitamin D supplements. Patients were either white or black, presumably of negro descent, and no serum vitamin D measurements were made. The paper by Gkonos *et al*[2] refers to a single 34 year old black patient who developed tuberculosis while on $25(OH)D_3$ and calcium supplements for presumed renal osteomalacia. The sudden hypercalcaemia, fall in $25(OH)D_3$, and rise in $1,25(OH)_2D_3$ at the time is said to be related to extrarenal production of $1,25(OH)_2D_3$ in a manner analagous to that seen in sarcoidosis. Both studies took place in the USA. The study carried out by Cadranel *et al* suggests that conversion of 25 to $1,25(OH)_2D_3$ occurs in alveolar macrophages in tuberculosis.

We cite separate studies based in the UK[3,4] which show that antituberculous chemotherapy depresses serum vitamin D and we have shown similar results in patients under treatment in Cardiff.[5] We would like to make the following observations: (1) Hypercalcaemia in granulomatous disease appears to be the exception rather than the rule. (2) Both studies referred to by Cadranel *et al* took place in the USA, where sunlight, and consequent sensitivity to $25(OH)D_3$, may be more plentiful than in the UK. (3) A recent large study in which calcium levels were observed during antituberculous chemotherapy and which was carried out in the UK showed, if anything, evidence of hypocalcaemia.[6] (4) An increasing proportion of tuberculosis in the UK is seen in subjects of Indian subcontinent ethnic origin (that is originating from India, Pakistan, and Bangladesh), a population known to be generally deficient in vitamin D.

We would conclude that in "at risk" groups of patients in the UK a strong case can be made for vitamin D supplementation during antituberculous chemotherapy. Further studies are required, however, before supplementation can be recommended and practised and we would concur with Cadranel *et al* that careful patient selection and frequent monitoring of calcium levels would be needed if vitamin D supplementation is given. Vitamin D should be given to those who need it and not to those who do not.

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1 Abbasi AA, Chemplavil JK, Faram S, *et al.* Hypercalcemia in active pulmonary tuberculosis. *Ann Intern Med* 1979;**90**:324–8.
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6 Subcommittee of the Research Committee of the British Thoracic Association. A controlled trial of six months chemotherapy in pulmonary tuberculosis. *Br J Dis Chest* 1981;**75**:141–53.

Notices

Current clinical management of cystic fibrosis

An all day symposium on this subject will be held at the Royal Society of Medicine, London, on Friday 25 October 1985. Further information may be obtained from the honorary secretary of the Section of Paediatrics, Dr TJ David, Department of Child Health, Booth Hall Children's Hospital, Charlestown Road, Manchester M9 2AA.

Current concepts in pulmonary pathology

A postgraduate course on current concepts in pulmonary pathology will be held at the Massachusetts General Hospital, Boston, Massachusetts, from 21 to 25 October 1985. Further information may be obtained from the Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, Massachusetts 02115, USA.

Dr HM (Bill) Foreman Memorial Fund

The trustees of this fund invite applications for grants relating to study in respiratory disease. Limited funds are available for registered medical practitioners to assist in travelling to countries other than their own to study respiratory disease, and also for support of clinical research abroad. Intending applicants should write for further details to Dr BH Davies, Sully Hospital, Sully, South Glamorgan CF6 2YA.