treatment can promote prostatic carcinoma in the elderly. The pathogenesis of hypogonadism in patients with peripheral vascular disease is probably related to atherosclerosis of the testicular and renal arteries and the aorta.

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1 Lerich R. Des obliterations arterielles hautes comme cause d'une insufficiance circulatoire des membres inferieurs. *Bull Soc Chirurgie* 1923;**49**:1404.
2 Michal V. Arterial disease as a cause of impotence. *J Clin Endocrinol Metab* 1982;**11**:725-48.
3 Virag R, Bouilly P, Feydman D. Is impotence an arterial disorder? A study of arterial risk factors in 440 impotent men. *Lancet* 1985;i:181-4.
4 Wheeler MJ, Luther F. Development of testosterone radioimmunoassay for routine use. In: Hunter WM, Corrie JET, eds. *Immunoassay for clinical chemistry*. Edinburgh: Churchill Livingstone, 1983:113-6.
5 Hammond GL, Langley MS, Robinson PA. A liquid phase immunoradiometric assay (IRMA) for human sex hormone binding globulin (SHBG). *J Steroid Biochem* 1985;**23**:451-60.

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Mortality from leukaemia among relatives of patients with cystic fibrosis

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Cystic fibrosis is an inherited autosomal recessive disease, the gene for which has been localised on chromosome 7.[1] As part of a systematic clinical and molecular genetic study of families of patients with cystic fibrosis in Wales we obtained data on the prevalence of other diseases. We report here our findings on mortality from leukaemia.

Patients, methods, and results

Altogether 130 families of patients with cystic fibrosis were studied. No bias was exercised by selection of patients, who were seen when they attended for routine clinical follow up. Cystic fibrosis had been diagnosed after typical clinical features were seen and at least one sweat test gave a positive result. Detailed family histories were obtained, including vital state, all diseases, and causes of death. Diagnoses of leukaemia were verified from original haematological data.

We studied 149 patients, 260 parents, 119 siblings without cystic fibrosis, 57 half siblings without cystic fibrosis, 743 aunts and uncles, and 518 grandparents. Information was incomplete for 7% of aunts and uncles and 9% of grandparents; they were assigned according to the age distribution of the appropriate group. All relatives who had leukaemia had died.

The expected numbers of deaths from leukaemia were calculated by reference to age specific mortalities for England and Wales using age specific person years at risk in each of the six groups of relatives. These figures were then compared with the observed number of deaths with an exact binomial probability test. As a check comparisons were made for mortalities from all causes.

Seven relatives of patients with cystic fibrosis had died from leukaemia: two parents (one mother aged 37, who had had acute myelomonocytic leukaemia; and one father aged 42, acute promyelocytic); one half sibling without cystic fibrosis (a girl aged 2, acute lymphoblastic); one aunt (aged 55, acute myeloid); one uncle (aged 3½, acute lymphoblastic); and two grandfathers (one aged 73, acute myeloid; and one aged 78, acute myelomonocytic). These patients with leukaemia were from different families, apart from the younger grandfather and aunt, who were father and daughter. The cystic fibrosis carrier state was known for the two parents (obligatory carriers) but not for the other patients with leukaemia. The affected half sibling showed no visible abnormality of chromosome 7.

The table shows the expected and observed numbers of deaths from leukaemia. Overall these were 2·19 and 7 ($p=0·007$), and for parents only they were 0·18 and 2 ($p=0·014$). Mortality from all causes among relatives generally agreed with predicted rates, whereas patients with cystic fibrosis showed the expected increase ($p=0·001$).

Expected and observed numbers of deaths from leukaemia among patients with cystic fibrosis and their relatives

Relationship	No of subjects studied	No of deaths expected*	No of deaths observed
Patient	149	0·030	
Parent	260	0·181†	2†
Sibling without cystic fibrosis	119	0·030	
Half sibling without cystic fibrosis	57	0·011	1
Aunt or uncle	743	0·584	2
Grandparent	518	1·353	2
	1846	2·189‡	7‡

*Expected according to age distribution, age specific person years at risk, and age specific mortality from leukaemia in England and Wales 1979-85 (Office of Population Censuses and Surveys).
†$p=0·014$.
‡$p=0·007$.

Comment

In this study leukaemia was not found among the patients with cystic fibrosis, though such cases have been recorded.[2] The cystic fibrosis gene and the met-oncogene are closely linked on the long arm of chromosome 7, being mapped to bands 7q31 and 7q21-31 respectively.[3] This region is associated with non-random chromosomal deletions, which have been observed in some patients with acute non-lymphocytic leukaemia.[3]

Chromosomal studies in the myelodysplastic syndrome and acute non-lymphocytic leukaemia have shown variable changes due to monosomy 7 or partial deletions of the long arm of 7; the met-proto-oncogene is within this deleted segment.[4] Additionally, 7q32 has been classified as one of the most common fragile sites.[5]

We suggest that a gene linked closely to the cystic fibrosis gene, possibly the met-oncogene, may predispose those who carry the cystic fibrosis gene to develop leukaemia. Further somatic events may be necessary for leukaemic transformation. Although only seven deaths due to leukaemia occurred, this was significant. It will be important to know if other centres can confirm this finding.

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1 White R, Woodward S, Leppert M, *et al*. A closely linked genetic marker for cystic fibrosis. *Nature* 1985;**318**:382-4.
2 Biggs B, Vaughan W, Sanger W, Purtilo D. Cystic fibrosis complicated by acute leukaemia. *Cancer* 1986;**57**:2441-3.
3 Dean M, Park M, Le Beau M, *et al*. The human met oncogene is related to tyrosine kinase oncogenes. *Nature* 1985;**318**:385-8.
4 Kere J, Ruutu T, De la Chapelle A, *et al*. Monosomy 7 in granulocytes and monocytes in myelodysplastic syndrome. *N Engl J Med* 1987;**316**:499-503.
5 Tsui L. Genetic markers on chromosome 7. *J Med Genet* 1988;**25**:294-306

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