Although *H influenzae* may be found in the sputum of children with cystic fibrosis, we were surprised that *Staphylococcus aureus* was not also isolated. Furthermore, *C albicans* is an unusual finding in children's sputum unless they have been receiving long term antibiotic treatment.

Diarrhoea and failure to thrive are common presenting features in children with symptomatic HIV infection.[2] In our child the diarrhoea was not malabsorptive and did not respond to pancreatic replacement treatment. Organisms which may be suspected in this situation are protozoans such as cryptosporidium, microsporidia, and *Isospora belli*. A search should also be made for atypical mycobacteria, cytomegalovirus, and herpes simplex virus, any of which may cause a malabsorptive picture. Our patient had no evidence of any of these organisms or any evidence of neoplasia.

With the incidence of cystic fibrosis in the community of 1 in 2000 it would not be surprising that a child with clear evidence of cystic fibrosis responding to standard treatment should be found to be HIV positive (personal communication, Dr J Mok, consultant paediatrician, City Hospital, Edinburgh). Although initially HIV positive this child has since become HIV negative, therefore suggesting clearing of maternal HIV antibody.

Measuring immunoreactive trypsin is not helpful as a diagnostic aid beyond the neonatal period, and gene probe analysis would not have been useful as there was no family history of cystic fibrosis. We think that there is little doubt that our patient had not got cystic fibrosis.

We therefore suggest that children presenting with symptoms suggestive of cystic fibrosis but with atypical features such as unexpected bacteriological results, failure to respond to treatment, or hyperglobulinaemia should have both their sweat test result validated by a fludrocortisone suppression test and their HIV state checked. If the HIV test result is positive it will, as in our family, allow rationalisation of treatment and counselling for the family.

References

1 Lobeck CC, McSherry MS. Response of sweat electrolyte concentrations to 9 alpha-fluorohydrocortisone in patients with cystic fibrosis and their families. *J Pediatr* 1963;62:393-8.
2 Pahwa S, Kaplan M, Fikrig S, *et al*. Spectrum of human T cell lymphotropic virus type III in children. *JAMA* 1986;255:2299-305.

(Accepted 20 October 1987)

SHORT REPORTS

Cervical adenocarcinoma and oral contraceptives

Two recent papers from the United States reported a twofold to threefold increase in the incidence of invasive adenocarcinoma of the uterine cervix in women under the age of 35 between 1973 and 1982.[1,2] This was not seen in older women or in squamous carcinoma of the cervix, which in the United States has been decreasing in women at all ages. Peters *et al* suggested that the increase in the incidence of adenocarcinoma might reflect the use of oral contraceptives by young women.[1] Cervical changes, particularly "microglandular hyperplasia," within the endocervix of women with a history of oral contraceptive or hormone use have been reported,[3] and Dallenbach-Hellweg reported on a series of 23 women with invasive adenocarcinoma of the cervix in whom the prevalence of oral contraceptive use was unusually high.[4] We report comparable English data on the incidence of cervical cancer.

Methods and results

Annual numbers of registrations of cervical cancer from 1968 to 1982 were obtained from the South Thames, Oxford, and West Midlands cancer registries. Cases were divided into adenocarcinoma (including adenosquamous carcinoma), squamous cell carcinoma, and "unknown and unspecified" cancer. Non-epithelial tumours were omitted. Incidences were calculated in three age groups (20-34, 35-54, and 55 and over) and for three five year periods (1968-72, 1973-7, and 1978-82). Within each age group the incidences were standardised for age by the indirect method using five year age groups; the 1968-82 rates for South Thames were taken as standard.

The table shows that the incidence of adenocarcinoma of the cervix in women under the age of 35 increased from 2·4 to 6·6/million between 1968-72 and 1978-82. The incidences of squamous and unclassified carcinomas also increased.

Standardised incidences of invasive cervical cancer (numbers of cases/million) by histological type and time period from three English regional cancer registries

	Age (years)					
	20-34		35-54		≥55	
Histological type and time period	Incidence (and No of cases)	% Of all cervical cancers*	Incidence (and No of cases)	% Of all cervical cancers*	Incidence (and No of cases)	% Of all cervical cancers*
Adenocarcinoma:						
1968-72	2·4 (16)	5·7	22·9 (194)	8·9	28·9 (287)	10·8
1973-7	4·7 (34)	7·4	22·1 (183)	10·7	28·8 (287)	10·9
1978-82	6·6 (52)	7·6	20·0 (161)	10·5	26·7 (277)	10·7
Squamous cell carcinoma:						
1968-72	34·6 (233)	81·9	205·3 (1744)	80·0	190·7 (1947)	71·3
1973-7	54·0 (386)	84·5	164·3 (1362)	79·5	190·0 (1903)	71·9
1978-82	69·9 (549)	79·9	148·3 (1192)	78·2	183·1 (1898)	73·4
Unknown and unspecified carcinomas:						
1968-72	5·3 (36)	12·4	28·5 (243)	11·1	47·7 (463)	17·9
1973-7	5·2 (37)	8·1	20·2 (167)	9·8	45·5 (446)	17·2
1978-82	10·9 (84)	12·5	21·5 (173)	11·3	39·5 (411)	15·8

*Based on incidences.

Adenocarcinoma as a proportion of all cervical cancers increased from 5·7% to 7·6% in this age group.

In women aged 35-54 the incidences of both squamous carcinoma and adenocarcinoma declined, although the proportion of cervical adenocarcinomas rose slightly from 8·9% to 10·5%. In women aged over 55 the incidence of both squamous carcinoma and adenocarcinoma declined slightly, and the relative proportion of each histological type changed little.

Comment

As in the United States, there has been a pronounced increase in the incidence of adenocarcinoma in young English women, which cannot be explained by more accurate classification of previously unspecified cancer. In England squamous cell cancer has also increased but to a lesser extent.

These data thus give limited support to the suggestion that the two histological types may have different aetiologies. Our rates of adenocarcinoma, however, were based on small numbers, and the differential increase in the rates for the two histological types was not significant. Interpretation of these incidences is also complicated by the fact that it is more difficult to detect adenocarcinoma than squamous carcinoma by cervical screening. In the two American studies adenocarcinoma as a proportion of all cervical cancers in young women was 10·3%[1] and 13·6%[2] in 1979-82; these compare with our figure of 7·6% and may reflect the success of the screening programme in the United States.

There has been only one epidemiological study comparing the characteristics of patients with the two histological types of cancer,[5] and we are currently conducting a case-control study of carcinoma of the cervix in young women to address this issue directly.

We thank the Oxford, Thames, and West Midlands cancer registries for supplying the data, and Cynthia Taylor and Sybil Farrell for computing and secretarial help. The Institute of Cancer Research receives support from the Cancer Research Campaign and the Medical Research Council.

1 Peters RK, Chao A, Mack TM, Bernstein L, Henderson BE. Increased frequency of adenocarcinoma of the uterine cervix in young women in Los Angeles County. *JNCI* 1986;76:423-8.
2 Schwartz SM, Weiss NS. Increased incidence of adenocarcinoma of the cervix in young women in the United States. *Am J Epidemiol* 1986;124:1045-7.
3 Mingeot R, Fievez C. Endocervical changes with the use of synthetic steroids. *Obstet Gynecol* 1974;44:53-9.
4 Dallenbach-Hellweg G. On the origin and histological structure of adenocarcinoma of the endocervix in women under 50 years of age. *Pathol Res Pract* 1984;179:38-50.
5 Silcocks PBS, Thornton-Jones H, Murphy M. Squamous and adenocarcinoma of the uterine cervix: a comparison using routine data. *Br J Cancer* 1987;55:321-5.

(Accepted 3 September 1987)

Section of Epidemiology, Institute of Cancer Research, Sutton, Surrey SM2 5PX
CLAIR CHILVERS, MSC, senior staff scientist

Department of Community Medicine and General Practice, Gibson Laboratories, Radcliffe Infirmary, Oxford
DAVID MANT, MB, senior registrar

Imperial Cancer Research Fund's Cancer Epidemiology Unit, Radcliffe Infirmary, Oxford
M C PIKE, PHD, director

Correspondence to: Clair Chilvers.

Proteoglycan concentration in synovial fluid: predictor of future cartilage destruction in rheumatoid arthritis?

The proteoglycans of the cartilage matrix are degraded early in the course of inflammatory joint diseases, and the fragments are liberated into the synovial fluid. These fragments can be measured in synovial fluid by an enzyme linked immunosorbent assay (ELISA).[1] This assay was used to show differences in proteoglycan metabolism among diseases and also that synovial fluid proteoglycan concentrations vary considerably among patients with rheumatoid arthritis.[2] This might indicate heterogeneity of the disease process and possibly predict the degree of progression of the disease and future joint destruction. We therefore studied a group of patients with rheumatoid arthritis from whom synovial fluid that had been aspirated 10 years previously was available, to see if the proteoglycan concentration at that time could be correlated with the degree of joint destruction later.

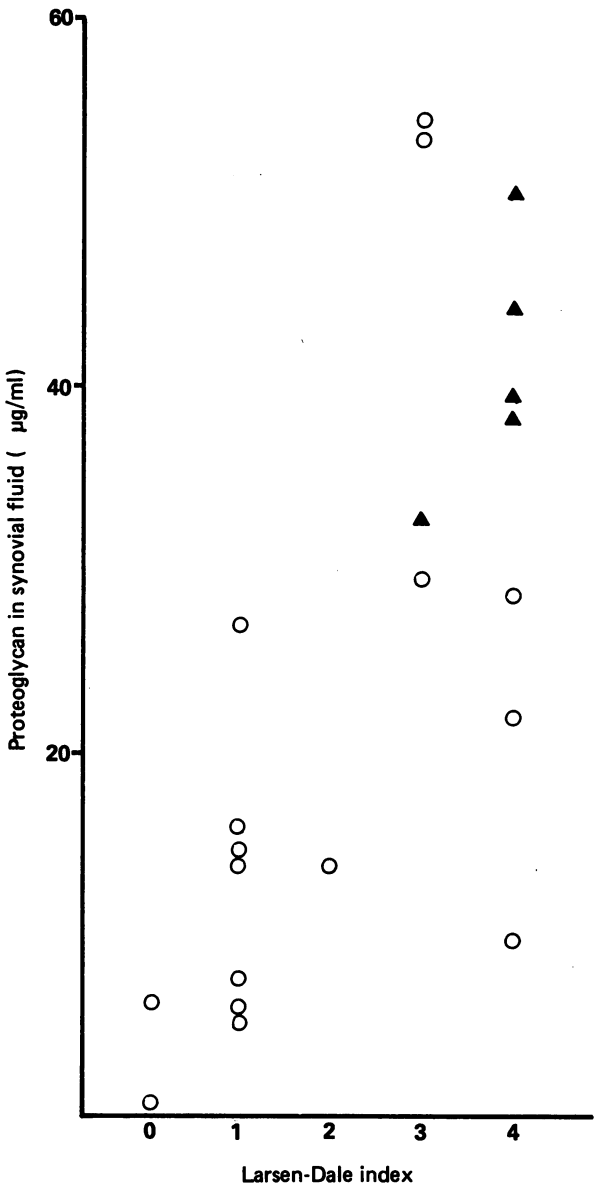
Patients, methods, and results

Thirty one specimens of knee joint synovial fluid from patients with classical or definite rheumatoid arthritis[3] were selected from a batch of specimens collected in 1976-7. Radiographs of the knee joints were assessed according to the Larsen-Dale index,[4] which measures destruction on a six grade scale: where 0 denotes a normal joint and 5 the most extensive disease of cartilage and bone. The knee joints looked well preserved radiologically at the time of aspiration (Larsen-Dale index 0-1). Intra-articular glucocorticoid injections had not been given for three months before aspiration. At follow up during 1985-6, 21 of the 31 patients (16 women and five men) were re-examined radiographically. Five patients had died, three refused examination, and two could not be traced. Five of the 21 patients had had an arthroplasty and for them the last radiographic examination before operation (1984-5) was used. All radiographs were assessed by the same radiologist.

All knee joints were aspirated to dryness. The synovial fluid was collected in sterile tubes containing edetic acid 5 mmol/l, centrifuged at 1800 *g* for 20 minutes, and then stored at −80°C before ELISA, as described.[1]

Correlations were calculated by Spearman's rank order correlation coefficient. A p value of $\leq 0{\cdot}05$ was considered to be significant.

The knee joints with the highest synovial fluid proteoglycan concentrations a decade previously had developed the most advanced joint destruction ($r_s=0{\cdot}70$, $p<0{\cdot}002$) (figure). The total amount of proteoglycans, calculated by multiplying the concentration by the aspirated volume of joint fluid, also correlated with radiological progression ($r_s=0{\cdot}58$, $p<0{\cdot}01$; data not shown). The median age of the 21 patients was 54 years (range 25-77 years) and the median duration of disease was 11 years (range 0·3-30 years) at the outset of the study. Seventeen of the patients had a positive Waaler-Rose test result.



Proteoglycan concentrations in knee joint synovial fluids (collected 1976-7) and current (1985-6) degree of joint destruction measured radiographically in 21 patients ($r_s=0{\cdot}70$, $p<0{\cdot}002$). Triangles denote patients who have had reconstructive arthroplasty.

Comment

Permanent progressive destruction of joints is a feature of rheumatoid arthritis but there is pronounced variability among patients, the reasons for which are poorly understood.

This report is the first to correlate release of a defined cartilage matrix component and later joint destruction. The results are promising and their relevance is supported by the finding of little spontaneous variation of