SHORT REPORTS

Respiratory Function in Rheumatoid Arthritis

In 1948 Ellman and Ball drew attention to the pulmonary manifestations of rheumatoid arthritis.[1] Nevertheless, until recently little attention has been paid to the possibility of pulmonary dysfunction in an appreciable proportion of patients, despite a normal chest *x*-ray result.[2 3] The reported incidence of pulmonary involvement in rheumatoid arthritis shows considerable variation, ranging from 1·6% using radiological methods of detection alone,[4] to 47% using respiratory function tests in addition to radiology.[2]

This investigation set out to study respiratory function with particular attention to diffusing capacity for carbon monoxide (DCco) in patients with rheumatoid arthritis and a normal chest *x*-ray film.

Patients, Methods, and Results

A total of 85 patients (59 female, 26 male) fulfilling the American Rheumatism Association criteria for "classical" or "definite" rheumatoid arthritis were investigated. Those with abnormal chest *x*-ray films, anaemia, heart disease, or exposure to potentially harmful dusts were excluded. The duration of the rheumatoid disease was established, a detailed history taken, and a full clinical examination made. Radiological erosions were recorded and note made of past and present medication. Each patient had a chest *x*-ray examination, full blood count, E.S.R., antibody screen and the following respiratory function tests: spirometry; lung volumes; and gas transfer (DCco). Sixteen of the patients had significant airways obstruction and were included in the study but grouped separately to allow for comparison. The results were compared with the predicted values and matched healthy controls.

The mean difference in the observed and predicted DCco (ΔDCco) in the male and female control subjects was not significant and was not significantly different from zero. There was a significant difference in ΔDCco for the rheumatoid arthritic group, $P<0.001$ the difference between the male and female groups also being significant ($P<0.02$) (see table). The inclusion of those patients with airways obstruction was justified because the diffusing capacity in the groups with and without airways obstruction was not significantly different. Lung volumes were not significantly affected.

Observed minus Predicted DCco (ΔDCco) *for Patients with and without Airways Obstruction, Controls, and Patients with R.A.*

Group	Mean ΔDCco	Standard Deviation (S.D.)	Standard Error of the Mean (S.E.M.)
Control (29)	0·98	3·13	0·58
R.A. male (26)	−5·51	5·83	1·14
R.A. female (59)	−2·48	3·95	0·51
No airways obstruction (71) ..	−3·34	4·96	0·59
Airways obstruction (16) ..	−3·71	3·96	1·02

A decreased DCco correlated significantly only with smoking (correlation coefficient—0·48 $P<0.02$) and the Rose Waaler and latex scores ($\log_2$ titre in women (—0·48, $P<0.001$ and —0·42, $P<0.001$)). The diffusing capacity was reduced by more than 20% in 44·7 % of cases and exceeded 2 standard deviations below predicted in 18·4 %. In the male patients the mean Rose Waaler and latex scores were higher but failed to show significant correlation with ΔDCco. There was no correlation with the titre of antinuclear factor, nor was any particular antibody distribution associated with an impaired diffusing capacity.

Discussion

Significantly lower values of DCco were found in the patients with rheumatoid arthritis, compared with the predicted values and the control group. As other factors had been carefully excluded, probably this observation represents a pulmonary manifestation of rheumatoid arthritis. Though we did not obtain material for histological examination, Frank *et al.* found changes compatible with early fibrosing alveolitis in all seven of their cases subjected to biopsy, of which at least two had a normal chest *x*-ray film.[2] It is, therefore, tempting to speculate that similar changes may be present in our patients. The equivocal antibody findings were not surprising, as if damage were immunologically mediated it may be by an immune-complex or cell-mediated mechanism not necessarily depending on the factors measured.

We were unable to confirm the suggestion by others[5] of a relation between pulmonary manifestations in rheumatoid arthritis and treatment with gold or steroids, and we found no relation with penicillamine medication.

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Spongioform Myelinopathy in Premature Infants

Hexachlorophane (HCP) has recently been the subject of a restriction order under the 1968 Medicines Act, prompted by observations on the cutaneous absorption of HCP in newborn infants and by animal experiments showing that HCP may induce spongioform myelinopathy even after cutaneous application.[1] Nevertheless, because no deaths or toxic signs have been attributed to HCP under normal conditions of clinical practice, 3% preparations continue to be available under medical supervision.

We report here the isolation of considerable quantities of HCP from formalin-stored brain tissue from one of two premature infants with spongioform myelinopathy. Neuropathological findings have already been described.[2]

Patients and Methods

Both babies were girls and were born after 26 weeks gestation. The first weighed 980 g and needed intubation at birth but was well for the first 10 days, apart from jaundice, maximal on the third day 2·3 μmol/l (bilirubin 14 mg/100 ml). Reflex activity and E.E.G. were normal. Apnoeic attacks began at 10 days, increased in frequency, and on the 24th day she became apnoeic and did not respond to treatment. A pneumothorax was found at necropsy.

Microscopic examination showed vacuolation in myelin of globus pallidus, brainstem, and spinal cord, but not in unmyelinated white or in grey matter. There was a generalized poverty of myelin compared with sections from other infants of the same gestation but of shorter survival time (half to four days) without vacuolation. The topographic distribution of myelinization was probably normal for age.

The second baby weighed 900 g. She was given resuscitation at birth and was satisfactory until apnoeic attacks started on the second day. These increased in severity, requiring periods of ventilation. At 72 hours serum bilirubin was 205 μmol/l (12 mg/100 ml). Reflex activity on first and third days was normal. Fatal pulmonary haemorrhage occurred on the sixth day. Necropsy showed a small cerebral intraventricular haemorrhage. Microscopic changes in the brain and spinal cord were similar to the first case except that myelin poverty was less marked.

In both cases HCP in 3% detergent solution was applied daily with a swab to the face, napkin area, and umbilicus.

Formalin-stored samples of cerebral tissue and spinal cord were extracted by a method similar to that of Browning *et al.*[3] Using an electron capture detector only 0·147 nmol/g (0·06 μg/g) of HCP was found in cerebral tissue from case 1 but 1·60 nmol/g (0·65 μg/g) from case 2. Similar amounts were found in the spinal cord. No HCP was present in the formalin used to store the tissue. The low level in case 1 was confirmed with the flame ionization detector, but in case 2 impurities with a similar retention time obscured the results.

Discussion

Even the lowest estimate of the HCP content of brain from case 2 is in the range found in experiments with monkeys in which spongioform myelinopathy was induced by 5 mg/kg injected daily for over a month