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Ciliary function in Young's syndrome

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The association of recurrent sinopulmonary infection and azoospermia (Young's syndrome) was first described in 1970[1] but excited little interest until recently. The coexistence of male infertility, recurrent respiratory infection, and impaired mucociliary clearance[2] is reminiscent of primary ciliary dyskinesia; but in the latter condition sperm counts are usually normal while motility is diminished.[3] Three recent reports[4–6] commented on the similarity between Young's syndrome and primary ciliary dyskinesia, but on the basis of limited studies of ciliary ultrastructure tentatively concluded that Young's syndrome was unlikely to be caused by a ciliary abnormality.

This study reports a quantitative assessment of upper airway mucociliary clearance and ciliary ultrastructure in Young's syndrome. Because normal ciliary ultrastructure does not exclude the possibility of a functional defect,[7] ciliary motility was also studied.

Methods

Fifteen patients with azoospermia and recurrent respiratory infections were studied. Twelve had undergone surgical exploration of the scrotum and had typical findings at operation.[2] Of the three patients who had not undergone surgery, cystic fibrosis had been excluded in two by normal sweat test results and the third was known to have normal spermatogenesis from testicular biopsy. Further clinical details are given in the table.

All subjects had nasal mucociliary clearance measured by the saccharin test.[8] A small particle of saccharin was placed on the inferior nasal turbinate and the time taken for it to be transported to the pharynx and cause a sweet taste noted. In normal subjects nasal mucociliary clearance takes under 30 minutes. Nasal cilia were obtained by brushing the inferior turbinate with a cytology brush, suspending the cells in tissue culture medium, and measuring ciliary beat frequency at 37°C by a photometric technique.[9] Twenty randomly recorded readings for each subject (n = 11) were made. Brushings of nasal cilia were also fixed in 2·5% glutaraldehyde for subsequent transmission electron microscopy[10] (n = 12). Nasal mucociliary clearance was compared with normal values for male non-smokers (n = 25) by the Mann-Whitney U test, and ciliary beat frequency was compared with that of 16 healthy controls by the unpaired *t* test. The percentages of compound cilia and microtubular abnormalities and the numbers of inner and outer dynein arms present were compared by the Mann-Whitney U test with values obtained from 14 normal subjects.

Results

The mean nasal mucociliary clearance for patients with Young's syndrome was 30·6 minutes for the eight subjects with measurable clearance (range 7–50 minutes). In the seven

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Clinical details of 15 patients with Young's syndrome

Patient No	*Age (y)*	*Nasal disease*	*Sinus radiograph*	*Surgery (epididymo-vasostomy)*	*Chest radiograph*
1	39	AR, PR, polyps	MT	+	Bronchiectasis RML, RLL, LLL
2	35	PR, AWO	MT	+	R sided pneumonectomy
3	36	AR	MT	+	Bronchiectasis L, RML, LLL
4	33	PR	MT	+	LLL lobectomy
5	40	AR	N	+	N
6	49	O	MT	+	LLL lobectomy
7	57	AWO, A	MT	ND	Bronchiectasis LLL
8	28	A, SMR	N	+	Bronchiectasis LLL
9	27	Nil	ND	ND	Bronchiectasis RLL, LLL
10	37	PR, SMR	MT	+	Bronchiectasis LLL
11	44	A	MT	ND	RLL, LLL lobectomies
12	41	AWO	MT	+	Bronchiectasis RLL
13	31	AR	MT	Exploration only	N
14	38	O	MT	+	Bronchiectasis RML, RLL, LLL
15	30	O	MT	+	N

AR—anterior rhinorrhoea; PR—posterior rhinorrhoea; O—obstruction; AWO—antral washout; A—antrostomies; SMR—submucous resection; MT—mucosal thickening; N—normal; ND—not done; RML—right middle lobe; L—lingula; RLL—right lower lobe; LLL—left lower lobe.

remaining patients clearance was prolonged beyond one hour. The mean nasal mucociliary clearance differed significantly from that in the control group (mean value 11·7 minutes; $p < 0·001$). The mean ciliary beat frequency for the patients with Young's syndrome (12·8 (SD 1·0) Hz) did not differ significantly from the mean control values of ciliary beat frequency (13·6 (1·2) Hz).

Ultrastructure was examined in an average of 204 cilia from each patient (range 98–414). The mean percentage (range) of microtubular and compound cilia was 2·5 (0–7·9) and 4·1 (0·3–9·6) in patients with Young's syndrome and 2·6 (0–10·2) and 2·3 (0–9·6) in control subjects. The mean numbers of inner and outer dynein arms were 6·2 (4·4–7·1) and 8·4 (7·9–8·8) in patients with Young's syndrome and 6·4 (5·0–7·8) and 8·4 (7·9–8·8) in control subjects. None of the differences between patients with Young's syndrome and control subjects was significant. The mean number of perfect ciliary cross sections examined was 18·7 a subject.

In one subject a small mucosal sample of epididymis was obtained at the time of vasoepididymostomy. Of 93 epididymal cilia, 91 contained dynein arms. Microtubular disarrangement was seen in 22 of 175 cilia examined, of which 19 had missing or displaced microtubules.

Discussion

This study reports the finding of defective mucociliary clearance in the upper respiratory tract of patients with Young's syndrome, a finding described previously only in the lung. Nasal mucociliary clearance was prolonged in most patients, including two with minimal symptoms and no radiological evidence of sinusitis. As some delay in nasal mucociliary clearance may occur in patients with sinusitis[8] it is unclear whether this is in some way related to the aetiology of Young's syndrome or a secondary phenomenon. Ciliary beat frequency was not significantly reduced in the patients with Young's syndrome and the pattern of beating was also normal. Bronchial cilia were not examined in this study but a generalised ciliary defect would be apparent in nasal cilia.[3]

Electron microscopy of bronchial cilia from four patients with Young's syndrome was said to exclude a diagnosis of immotile cilia syndrome,[5] although further details were not given. Two other reports[2 11] described the presence of dynein arms in bronchial cilia in two and three cases respectively. We here present the results of electron microscopy in 12 patients and, having used quantitative techniques, confirm normal ciliary ultrastructure. More importantly, perhaps, in vitro ciliary motility was also found to be normal, a finding not previously reported. Unfortunately no normal epididymis was available for comparison with the sample from a patient, but 12% of microtubular abnormalities is unlikely to represent an important ciliary defect. Non-quantitative assessments also suggest normal epididymal cilia.[2 5]

This study has shown that mucociliary clearance is abnormal in Young's syndrome but found in vitro ciliary function and ultrastructure to be normal. The primary defect in Young's syndrome remains obscure but the impaired clearance in nose and bronchi[12] and impaction of sperm in the head of the epididymis may represent a generalised abnormality of epithelial secretions. Further studies are in progress to assess whether pharmacological modification of these secretions could effect clinical improvement.

References

1 Young D. Surgical treatment of male infertility. *J Reprod Fertil* 1970;**23**:541–2.

2 Hendry WF, Knight RK, Whitfield HN, *et al.* Obstructive azoospermia: respiratory function tests, electron microscopy and the results of surgery. *Br J Urol* 1978;**50**:598–604.

3 Afzelius BA. The immotile cilia syndrome and other ciliary diseases. *Int Rev Exp Pathol* 1979;**19**:1–43.

4 Neville E, Brewis RAL, Yeates WK, Burridge A. Respiratory tract disease and obstructive azoospermia. *Thorax* 1983;**38**:929–33.

5 Handelsman DJ, Conway AJ, Boylan LM, Turtle JR. Young's syndrome. Obstructive azoospermia and chronic sinopulmonary infections. *N Engl J Med* 1984;**310**:3–9.

6 Schanker HMJ, Rajfer J, Saxon A. Recurrent respiratory disease, azoospermia, and nasal polyposis. *Arch Intern Med* 1985;**145**:2201–3.

7 Greenstone MA, Dewar A, Cole PJ. Ciliary dyskinesia with normal ultrastructure. *Thorax* 1983;**38**:875–6.

8 Rutland J, Cole PJ. Nasal mucociliary clearance and ciliary beat frequency in cystic fibrosis compared with sinusitis and bronchiectasis. *Thorax* 1981;**36**:654–8.

9 Rutland J, Cole PJ. Non-invasive sampling of nasal cilia for measurement of beat frequency and study of ultrastructure. *Lancet* 1980;**ii**:564–5.

10 Rutland J, Dewar A, Cox T, Cole PJ. Nasal brushing for the study of ciliary ultrastructure. *J Clin Pathol* 1982;**35**:357–9.

11 Le Lannou D, Verger JP, Kernec J, Segalen J, Lescoat D, Lobel B. Structure de l'epithelium bronchique dans l'association infertile masculine et bronchiectasie. *INSERM*1981;**103**:117–22.

12 Pavia D, Agnew JE, Bateman JRM, *et al.* Lung mucociliary clearance in patients with Young's syndrome. *Chest* 1981;**80**(suppl):892–5.