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Upper Airflow Obstruction and Pulmonary Function in Acromegaly: Relationship to Disease Activity

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SUMMARY

Pulmonary function and disease activity were assessed in a large series of patients with acromegaly (19 men and 16 women). Large lungs, defined as a vital capacity > 120 per cent of predicted normal occurred in six of 19 males and six of 16 females. Ten of the 12 patients with elevated vital capacity had active disease (growth hormone > 5 mU/l during a glucose tolerance test). There was no association with duration of disease. Diffusing capacity was normal overall but D_LCO > 120 per cent occurred in six of 14 females and one of 18 males. Significant intrathoracic airflow obstruction occurred in eight of 35 patients, six of whom were non-smokers. Upper (extrathoracic) airflow obstruction was the most common pulmonary function abnormality. A maximal expiratory/inspiratory flow ratio > 1.0 at 50 per cent vital capacity occurred in 13 of 18 males and four of 16 female patients, and there was an association with disease activity (17 of 25 subjects with active disease had upper airflow obstruction compared to one of nine in remission; $p = 0.01$). Nocturnal hypoxaemia occurred in three of 13 patients studied: six of this group had upper airways obstruction. They were all male with elevated growth hormone levels and upper airflow obstruction. In summary, in 35 acromegalics (26 with active disease), large lungs occurred in 12 patients (34 per cent) and upper airflow obstruction in 17 patients (50 per cent). The latter may develop nocturnal hypoxaemia—this was seen in three of six patients with upper airflow obstruction. Upper airways obstruction was more common in males (13 of 18 compared to four of 16 females: $p = 0.04$) and its presence in males should arouse suspicion of nocturnal hypoxaemia.

INTRODUCTION

Respiratory disorders are an important cause of morbidity and mortality in patients with acromegaly: Wright *et al.* reported that death due to respiratory disease was three times more likely in acromegaly [1].

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Pneumomegaly was first described by Harvey Cushing in 1927 [2]. The earliest reports suggested that this phenomenon was restricted to males [3, 4] but it has subsequently been described in female patients [5]. Diffusing capacity and transfer coefficient are usually normal suggesting that lung growth is due to an increase in alveolar size rather than alveolar number [3–5].

Hyperplasia of the soft tissues, including those of the larynx and upper airway, are a recognized feature of growth hormone excess: subsequent narrowing of the upper airway with the development of airflow obstruction has been documented [6–8]. Obstructive sleep apnoea, described by Guilleminault and others is a recognized but rare complication [9–11]. Peripheral airway obstruction has also been described and is attributed to the hyperplasia of the walls of the conducting airways [12].

Since data concerning the character, severity and frequency of respiratory abnormalities have been derived from studies based on relatively small groups of patients, it is not surprising that conflicting conclusions have arisen. The relationship of pulmonary function abnormalities to disease activity and duration is unclear: it has been suggested that significant abnormalities in pulmonary function are more likely to be associated with duration of the disease rather than growth hormone level.

The aim of our study was to perform a detailed assessment of pulmonary function and endocrine status on a large population of acromegalic patients in order to resolve some conflicting aspects.

METHOD

We performed detailed pulmonary function tests on 35 patients (19 males and 16 females) aged between 21 and 68 years. Twenty-six patients had active disease, defined by growth hormone levels during a glucose tolerance test of >5 mU/l, and nine patients were in remission. The duration of biochemically proven acromegaly was obtained from the clinical records. Twenty patients were non-smokers and 15 ex-smokers and smokers. One patient had asthma and two had had pulmonary tuberculosis in the past but had no chest symptoms at the time of study. Thirteen patients were being treated for systemic hypertension (four had angina pectoris). Three female patients had a palpable thyroid nodule. None had kyphoscoliosis or heart failure. Two patients were obese.

Pulmonary function measurements included the forced expired volume in one second (FEV_1) and the slow vital capacity (VC) using a bellows spirometer (Vitalograph, UK). Total lung capacity (TLC) was measured in a whole body plethysmograph and residual volume (RV) was calculated from TLC and VC. The diffusing capacity for carbon monoxide (D_LCO) was estimated by the single breath method (Ogilvie *et al.* 1957), as modified by Cotes and corrected for the current blood haemoglobin concentration [14]. The normal values for spirometry and lung volumes were taken from Quanjer *et al.* [15] and for the D_LCO from Bradley *et al.* [16].

Flow volume loops were created using a turbine flowmeter (Micromedical) to measure airflow rates at the mouth and lung volumes by integration of flow. The curves were displayed graphically (Fig. 1a). The shape of the curve was inspected for a flow 'plateau' (cut-off). The ratio of the mid VC expiratory flow to mid VC inspiratory flow (MEF_{50}/MIF_{50}) was calculated [17]. The FEV_1 and peak expiratory flow rate (PEFR) was recorded together with the loop. The FEV_1/PEFR ratio (FEV in ml divided by PEF in l/min) was calculated from the maximal values obtained [18]. The presence of lower (intrathoracic) airflow obstruction was assessed by low values of expiratory flow at 50 per cent and 25 per

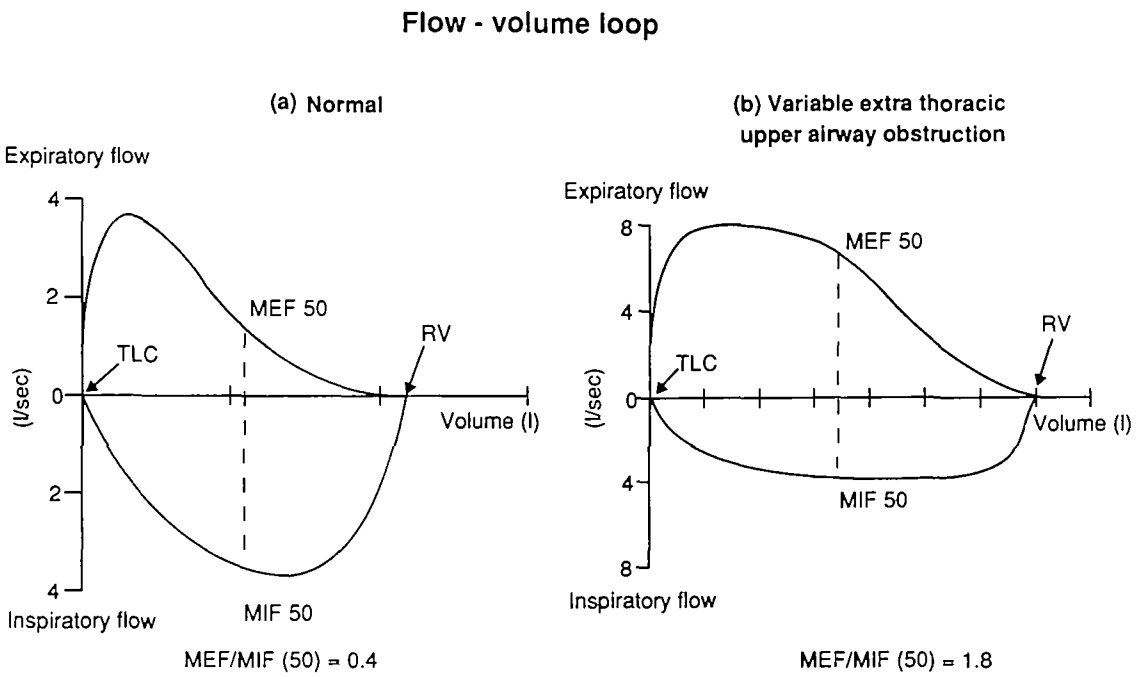

FIG. 1. Maximum flow-volume curves for two patients with acromegaly a) a small female patient with a normal curve, b) a large male patient with flow plateaux throughout inspiration and early in expiration. The ratio of expiratory and inspiratory flows at 50% vital capacity (MEF/MIF (50)) is < 1 in (a) and > 1 in (b).

cent of vital capacity (MEF_{50} and MEE_{25}), a low FEV_1/VC ratio (< 70 per cent) and a raised RV/TLC ratio (≥ 40 per cent). There was good concordance between these three indices.

Sleep oximetry was performed on 13 patients selected at random from the study group (six males and seven females), using a portable Ohmeda oximeter (Biox 3700) and a finger probe: the oximetry was performed in hospital in a quiet side room, beginning at the time of going to bed and ending on waking. The initial measurements represented wakefulness. The subjects were questioned about quality of sleep during the study, and all subjects reported an undisturbed night. No subject received hypnotic or sedative drugs.

Continuous recording of percentage arterial oxygen saturation (SaO_2) by the oximeter were displayed and the average SaO_2, lowest SaO_2 and the time (minutes) $SaO_2 < 90$ per cent during sleep were recorded. The duration of the study (hours) was recorded. Three patients with abnormal oximetry had repeat studies to confirm the reliability of the oximetry. No video recordings of EEG or EMG monitoring of sleep or sleep staging were made.

Statistical Analysis

Data were analysed using multiple linear regression with a Backward-Stepwise technique. This method involved regressing a number of dependent variables against an independent variable. The p values obtained indicated the significance of the relationship between each dependent variable to the independent variable. The dependent variable with the least statistically significant p value was excluded from further regression analysis. A stepwise technique of exclusion of the least significant dependent variable proceeded until regression

TABLE 1. *Pulmonary function and endocrine status in 16 women with acromegaly*

	Age (years)	Smoking[a]	Duration (years)	GH level mu/l		Status[c]	FEV/VC%	VC%	TLC%	RV%	DLCO%	KCO%	MEF_{50}/MIF_{50}	FEV/PEFR
				Fasting	Post GTT[b]									
1	50	×	1	9.3	9.1	+	79	148	128	105	132	101	1.1	8.9
2*	57	×	17	3.2	4.0	−	78	117	104	97	77	79	0.7	6.6
3*	42	×	3	74.2	52.2	+	76	146	148	159	124	99	0.6	8.5
4	60	−	3	16.1	9.5	+	84	123	106	97	114	103	0.6	11.5
5	58	+	10	5.0	4.1	−	63	88	—	—	85	102	1.0	12.5
6	50	+	9	19.5	15.9	+	79	115	108	110	122	107	2.0	7.8
7	57	−	8	16.6	8.1	+	71	106	—	—	—	—	0.5	6.3
8	53	−	1	8.3	8.3	+	82	126	98	64	144	131	0.7	6.4
9*	54	−	6	13.9	12.7	+	79	104	77	54	109	126	1.5	10.1
10	28	−	1	—	—	+	88	98	85	47	77	88	0.9	6.9
11	40	−	1	2.6	1.0	−	82	145	115	59	128	110	0.9	10.4
12	51	−	1	9.3	8.3	+	75	143	117	88	127	108	1.6	12.3
13*	65	+	6	6.5	8.3	+	76	99	—	—	78	111	1.9	8.9
14	64	−	15	1.7	2.6	−	50	91	115	166	110	117	0.6	12.0
15*	68	−	8	2.2	1.7	−	71	100	—	—	—	—	0.5	6.8
16*	36	+	1	16.6	12	+	75	93	96	114	90	99	1.0	8.4
Mean	52		5.7	13.67	10.5		75.5	113	108	96.6	108	105	1.0	9.0
1 SD	±10		±5.17	±17.7	±15		±8.9	±23	±18.9	±38	±22.8	±13.5	±0.5	±2.3

[a] × ex-smoker; + smoker.
[b] Minimum value within 120 min after glucose.
[c] Status: + active − remission.
* Sleep study subjects.

TABLE 2. *Pulmonary function and endocrine status in 19 men with acromegaly*

Men	Age (years)	Smoking	Duration	GH level mu/l		Status	FEV/VC%	VC%	TLC%	RV%	DLCO%	KCO%	MEF_{50}/MIF_{50}	FEV/PEFR
				Fasting	Post GTT									
1	45	–	1	9.4	6.7	+	68	116	113	124	106	102	1.0	10
2	46	×	7	115	193	+	78	135	—	—	120	110	1.8	10
3	63	–	8	14.5	17.5	+	74	126	95	76	98	108	1.3	9.5
4	54	+	2	13.1	15.1	+	71	128	131	148	115	106	1.4	9.3
5	44	×	17	5.2	3.3	–	76	130	—	—	92	76	0.9	8.7
6	39	×	2	8.7	7.1	+	82	119	114	113	72	66	1.8	11
7	28	+	1	12.6	11.3	+	85	96	87	68	74	88	1.5	8.0
8	30	–	1	10.9	13.4	+	68	112	—	—	72	78	—	—
9	51	–	4	31.7	40.5	+	82	114	128	164	140	129	1.3	9.5
10	51	–	1	23.4	20.5	+	76	110	93	71	86	108	1.3	7.3
11	21	–	3	106	132	+	83	120	106	94	64	73	1.8	9.6
12	44	+	9	4.3	3.8	–	73	98	78	42	87	108	0.6	8.8
13	46	×	15	6.4	5.7	+	78	118	112	120	99	90	1.2	9.5
14	59	×	3	1.7	2.6	–	74	93	99	124	93	133	1.1	7.5
15	61	–	3	15.3	4.1	+	58	128	94	52	—	—	1.5	8.2
16	64	–	1	>100	>100	+	74	79	69	65	71	109	1.5	7.3
17	46	–	4	11.5	10.9	+	79	108	100	98	67	77	1.5	7.5
18	29	–	4	45	—	+	85	144	113	42	94	85	0.6	10.4
19	50	–	14	6.2	4.8	–	76	97	91	88	89	128	0.3	6.3
Mean	45.8		5.2	28.4	34.7		76.8	114	101.4	94.3	91.0	96.8	1.3	8.8
1 SD	±12.2		±5.0	±36.4	±2.8		±6.65	±16.3	±16.8	±36	±20	±19	±0.5	±1.28

analysis of the last remaining dependent variable had been completed. Further statistical tests were then performed as appropriate.

RESULTS

The pulmonary function and endocrine status of 19 males and 16 females with acromegaly is presented in Tables 1, 2 and 3. The average age of the group was 48.7 years ± 12. The mean duration of the disease was 5.6 years ± 5, with a range of 1–17 years. Twenty-six patients, 15 men and 11 women, had active disease. The highest levels of growth hormone were found in men; the fasting level for men was 28.4 mu/l ± 36.4 compared to 13.6 mu/l ± 17.7 in women. There was no significant difference in smoking history between the sexes.

Lung Volumes

Both men and women with acromegaly had larger vital capacities than would be predicted for their age, height and sex. For both sexes together the mean vital capacity as per cent predicted normal (VC%) was 114.6 ± 18. There was no significant difference between the sexes, but in both groups there was a wide range of values. The vital capacities were as high in non-smokers (VC% 115 ± 18) as in smokers and ex-smokers (VC% 114 ± 18). TLC was greater in smokers and ex-smokers (TLC% 114 ± 17) compared to non-smokers (TLC% 100 ± 18). The TLC for both sexes together was 104 ± 18. The vital capacity was > 120 per cent in 12 patients (34 per cent), six males and six females. Ten (83 per cent) of these patients had active disease. Patients with active disease had a mean VC% 117 ± 17 compared to those in remission with a VC% 103 ± 23. However there was no significant statistical association between lung size and disease activity (unpaired t test $p = 0.12$).

There was no association between a large vital capacity and disease duration: subjects with acromegaly for more than 8 years did not have larger lungs than those with acromegaly for less than 8 years. Six patients (50 per cent) with a VC% > 120 had upper airway obstruction

TABLE 3. *Disease duration, lung size, (as vital capacity % predicted) and extent of upper airflow obstruction (MEF_{50}/MIF_{50}) in male and female subjects*

	N	Mean	SD	Min	Max
Duration (years)					
Women	16	5.7	5.2	1	17
Men	19	5.2	5.0	1	17
Group	35	5.5	5.0	1	17
VC%					
Women	16	113	23.6	71	148
Men	19	114	16.3	79	144
Group	35	114	19.7	71	148
MEF_{50}/MIF_{50}					
Women	16	1.0	0.5	0.5	2.0
Men	18	1.3	0.5	0.3	2.2
Group	34	1.2	0.5	0.3	2.2

with a $MEF_{50}/MIF_{50} > 1$. Twelve patients (54 per cent) with a VC% < 120 had a $MEF_{50}/MIF_{50} > 1$. Two of six women had a VC% > 120 and a $MEF_{50}/MIF_{50} > 1$ compared to four of six men. Nevertheless, there was no significant statistical association between large volume lungs and the development of upper airway obstruction for either sex (men $p = 49$, women $p = 0.58$).

Multiple regression analysis for correlation between lung size (VC%) and sex ($p = 0.99$; $r = -0.04$), duration ($p = 0.98$; $r - 0.015$) and MEF_{50}/MIF_{50} ($p = 0.986$; $r = -0.7$) disease status ($p = 0.18$; $r = 14.9$) showed no significant association between lung size and these variables.

Lower Airway Obstruction

Four male and four female patients had FEV/VC ratios < 73 per cent; four male patients had FEV/VC ratios of 73–74 per cent but all had RV/TLC ratios in the normal range. MEF_{50} and MEF_{25} flow rates did not identify additional patients with lower airflow obsruction who were not already revealed by an abnormal FEV/VC ratio. Clearly, a low MEF_{50} would reduce the MEF_{50}/MIF_{50} ratio and mask the presence of upper airflow obstruction. Six of the eight patients with lower airflow obstruction had MEF_{50}/MIF_{50} ratios $\leqslant 1.0$ and cannot exclude the presence of upper airflow obstruction as well in these patients.

Upper Airway Obstruction

Flow-volume loops were obtained in 34 patients (see Fig. 1): the characteristic appearance of upper airway obstruction, namely a greater reduction in inspiratory flow compared to expiratory flow, was identified in 15 of these (Fig. 1b).

TABLE 4. *Criteria for diagnosis of upper airway obstruction (UAO)*

N = 34	No. with UAO
Inspection of loop	15
$MEF_{50}/MIF_{50} > 1.0$	18
$MEF_{50}/MIF_{50} > 1.2$	16
FEV/PEFR > 8	20
FEV/PEFR > 10	9
2/3 Criteria positive	
1. $MEF_{50}/MIF_{50} > 1$ FEV/PEFR > 8 Inspection	17
2. $MEF_{50}/MIF_{50} > 1.2$ FEV/PEFR > 8 Inspection	16
3. $MEF_{50}/MIF_{50} > 1$ FEV/PEFR > 10 Inspection	3
4. $MEF_{50}/MIF_{50} > 1.2$ FEV/PEFR > 10 Inspection	3

A $MEF_{50}/MIF_{50} > 1$, the standard criterion for upper airway obstruction, was noted in 18 patients (Table 4). A $MEF_{50}/MIF_{50} > 1.2$, a less sensitive but more specific criterion, identified 16 of these. A FEV/PEV ratio > 10, which is a recognized criterion for diagnosing upper airways obstruction, was demonstrated in nine patients. A FEV/PEF ratio > 8 identified 20 patients as having upper airways obstruction. Combining inspection of the flow-volume curve for flow plateaux or 'cut off' and abnormal values of MEF_{50}/MIF_{50} and FEV/PEF, we made a definite diagnosis of upper airways obstruction if two out of three criteria were positive. In fact the MEF_{50}/MIF_{50} ratio > 1 alone identified an equal number of patients as any combination of two of the three criteria, and in subsequent analysis of our data, we used the generally accepted definition of a $MEF_{50}/MIF_{50} > 1$.

Eighteen patients (52 per cent) had upper airflow obstruction: 72 per cent ($n = 13$) of males compared to 31 per cent ($n = 5$) of females. This difference was statistically significant with ($p = 0.04$ χ^2 test).

Twenty-five patients (68 per cent) with active disease (mean $MEF_{50}/MIF_{50} = 1.28 \pm 0.5$) had a $MEF_{50}/MIF_{50} > 1$, compared to nine (11 per cent) of those in remission (mean MEF/MIF 0.69 ± 0.25). This was statistically significant ($p = 0.01$, unpaired t test). Twelve of 14 men (85 per cent) and five of 11 women (45 per cent) with active disease had upper airways obstruction. The mean fasting growth hormone level was 38.9 ± 43.6 mu/l, for these men and significantly lower in the women, at 11.7 ± 5 mu/l. Logistic regression of the odds of having upper airways obstruction on sex and growth hormone level showed that men were 5.5 times more likely to be affected than women. There was no statistically significant relationship between growth hormone level and the development of upper airways obstruction ($p = 0.64$).

Upper airways obstruction was no more common in subjects with acromegaly for longer than 8 years than in those affected for a shorter period of time. Multiple regression analysis between MEF_{50}/MIF_{50} and disease duration ($p = 0.9$; $r = 0.007$), lung size ($p = 0.9$; $r = -004$), disease status ($p = 0.001$; $r = 0.57$) and sex ($p = 0.13$; $r = 0.57$) showed that disease status was strongly associated with the development of upper airways disease, while duration and lung size were not. Intrathoracic airway obstruction was uncommon, being found in only eight patients (23 per cent).

Diffusing Capacity

The single breath diffusing capacity for carbon monoxide (DLCO) was 91 ± 20 percent predicted in men and 108 ± 22 per cent predicted in women. The diffusion per unit volume (KCO) was 97 ± 19 and 105 ± 13 per cent predicted respectively. Six women (25 per cent) and two men (10 per cent) had a $D_LCO > 120$. In one woman and three men the KCO% was > 120.

Sleep Oximetry

The sleep oximetry studies are presented in Table 5. Sixteen studies were performed on 13 patients (seven men and six women). The mean age of the group was 48 ± 12 years. The mean duration of acromegaly was 7.9 ± 5 years and the mean fasting growth hormone level 28.8 mu/l. Nine patients had active disease (five men and four women) and six patients had upper airway obstruction (four men and two women).

The resting awake SaO_2 was normal in all patients (mean 96 per cent). A significant hypoxaemic episode, defined by a fall in $SaO_2 < 90$ per cent for more than 5 minutes, was identified in three male subjects. Repeat studies in these patients confirmed the findings. All three men had active disease, mean growth hormone 45.3 mu/l (range 14.5–115 mu/l) large

TABLE 5. *Sleep oximetry on 13 patients with acromegaly*

Pt no	Sex	Smoking	Age	GH Level (mu/l)		Duration (years)	Study (hours)	Mean SaO_2 (awake)	Mean SaO_2 (sleep)	Lowest SaO_2 (sleep)	SaO_2 <90% duration (min)	MEF_{50}/MIF_{50}	FEV/VC
				Fasting	Post GTT								
15	F	–	68	2.2	1.7	8	6.2	97	95	91	—	0.5	71
13	F	+	65	6.5	8.3	6	7.2	98	95	81	2.5	2.2	76
9	F	–	54	13.9	12.7	6	7.9	97	96	89	0.2	1.8	79
—	F	×	41	1.0	1.0	9	7.5	94	92	89	0.8	0.6	64
2	F	×	57	3.2	4.0	17	7.0	97	95	94	—	0.7	78
3	F	×	42	74.2	52.2	3	7.7	98	96	91	—	0.6	76
16	F	+	36	16.6	12	1	7.9	96	96	89	0.4	1.0	75
3	M	–	63	14.5	17.5	8	7.9	96	90	83	14.2	1.25	74
11	M	–	21	106	131	3	6.8	96	95	84	2.6	1.6	83
13	M	×	46	6.4	5.7	15	7.9	95	88	64	205	1.2	78
5	M	×	44	5.2	3.3	17	5.6	95	95	90	—	0.9	76
2	M	×	46	115	193	7	7.8	95	89	64	202	1.8	78
1	M	–	45	9.4	6.7	1	7.6	96	95	90	—	1.0	68
			48 ±11.7	28.78 ±40.9	35 ±59	7.9 ±5.6	7.3 ±0.7	96 ±1.2	93.8 ±2.5	85.5 ±6.1	76.9 ±109.4	1.1 ±0.5	75.6 ±54

lungs, (mean VC% 126 ± 85) and upper airflow obstruction (mean MEF_{50}/MIF_{50} 1.4 ± 0.2). No women showed significant arterial desaturation compared to half the men. Hypoxaemia was not found in patients without upper airflow obstruction, but three of the four men with upper airways obstruction had hypoxaemia during sleep. Four of five males with active disease had upper airflow obstruction compared to two of the four women. Active disease without upper airways obstruction was not associated with hypoxaemia during sleep.

DISCUSSION

Large lungs are a well recognized feature of acromegaly, especially in males [2–5]: it has been suggested that large lungs are found less frequently in women because of an inhibiting effect of oestrogens [22]. Our study confirms that large lungs develop in women and there was no significant difference between the sexes. The increase in lung size was associated with a proportional increase in single breath diffusing capacity for carbon monoxide (D_LCO), demonstrating that the diffusion per unit lung volume was normal.

There was no association between lung size and smoking history nor between lung size and disease activity, in agreement with previous studies [12]. A definite association between lung size and disease duration has not been well documented. Harrison and colleagues reported that pneumomegaly was found more frequently in acromegalic patients with a duration of disease longer than 8 years [12]. Although our study did not show any association between large lung size and duration of disease, the latter was obtained from clinical records and the disease may be present long before it is documented biochemically. This may explain our failure to demonstrate any relationship.

Upper airway obstruction is frequently found in acromegaly and has a multifactorial pathophysiology. Hyperplasia of the soft tissues, enlargement of bone, and cartilage, and reduced pharyngeal muscle tone lead to narrowing of the upper airway. Respiratory muscle strength was not measured in this series (VC being normal or increased) but muscle weakness *per se* is not associated with upper airflow obstruction. Obesity and thyroid goitre are also found in acromegaly. Rees and Ayres speculated that upper airways obstruction may be associated with sleep apnoea [23].

Upper airway obstruction was shown to be a frequent complication of acromegaly, occurring in 52 per cent of patients, and its presence showed a statistically significant correlation with sex, being more common in men than in women. There was also a significant association between upper airways obstruction and disease activity, particularly in men. Although the mean growth hormone level was greater in men than in women, the growth hormone level *per se* was not directly associated with the development of upper airways obstruction, nor were upper airways obstruction or lung size.

Excessive daytime somnolence, habitual snoring and morning headaches are features of obstructive sleep apnoea syndrome [9, 24]. Although many acromegalics suffer from headaches and snoring, the obstructive sleep apnoea syndrome is a rare complication of acromegaly. It is, however an important cause of respiratory morbidity and premature mortality [9, 24], and it is therefore important to diagnose this disorder. Obstructive sleep apnoea syndrome occurs predominantly in men [25]; although androgens have been shown to play a role in the pathophysiology [26], and women with acromegaly may have increased levels of androgen, fewer women are affected [4, 27].

Endoscopic findings in acromegalics with sleep apnoea have provided conflicting theories about the sequence of events leading to upper airway obstruction. Cadieux *et al.* claimed that the primary and necessary factor underlying sleep apnoea was closure of the hypopharynx, leading to obliteration of the airway, and that involvement of the tongue was a secondary

event in the development of obstruction [8]. Mezon stated that prolapse of the enlarged tongue was the primary aetiological factor [10]. The prolapsing tongue narrows the upper airway, with subsequent generation of negative pressure in the pharynx during inspiration and collapse of the pharynx. On the other hand, the presence of upper airways obstruction, as demonstrated by the flow volume loop has not shown to be a sensitive predictor for obstructive sleep apnoea syndrome [27].

Other sleep disorders have also been recognized in acromegaly. Perks *et al.* reported patients with central sleep apnoea and mixed apnoea [27]: the former suggested the possibility of a defect in central ventilatory control. The hypercapnic ventilatory response was normal in a group of acromegalics with active and inactive disease and was not affected by disease status [11]. None of these subjects had central apnoea.

The exact relationship of sleep apnoea syndrome to growth hormone excess is unclear. Hart *et al.* demonstrated sleep apnoea syndrome only in patients with active disease [11]; others have found significantly higher growth hormone level in acromegalics with sleep apnoea syndrome compared to those without [26, 27], suggesting that this is a reversible condition. Nevertheless, the majority of investigators have reported that treatment of acromegaly does not cure sleep disturbance. Interestingly, while obesity and hypertension are risk factors for the development of obstructive sleep apnoea syndrome in the general population, Perks *et al.* [27] found that this is not the case in acromegaly.

Thirteen acromegalic patients were screened for nocturnal hypoxaemia: there were no significant abnormalities in women, although hypoxaemia occurred in 50 per cent of the men [4, 27], all of whom had upper airflow obstruction. Although women with upper airflow obstruction did not demonstrate sleep hypoxaemia, obstructive sleep apnoea is probably a rare event in women anyway, and a large population of females would need to be studied to assess the relationship between the two conditions. Seventy-five per cent of men with upper airflow obstruction developed hypoxaemia during sleep, and in males, therefore the latter appears to be a reliable predictor of sleep hypoxaemia, contrary to the report of Perks *et al.* [27]. Nocturnal hypoxaemia was associated with active disease: patients in remission did not have hypoxaemia. Successful treatment of acromegaly therefore may be adequate treatment for sleep apnoea syndrome.

Sleep oximetry is a simple method for screening patients for nocturnal hypoxaemia which was found to be reliable: we recommend that male acromegalics with upper airflow obstruction should be screened by this method. If significant hypoxaemia is demonstrated polygraphic sleep studies should be performed in a specialized laboratory.

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