LUNG VOLUME AND RESPIRATORY MUSCLE POWER IN HYPERTHYROIDISM

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During the earlier part of this century a decrease in the vital capacity of patients with hyperthyroidism was noted.[1-3] Although Rabinowitch,[2] in his series of nearly 200 cases, found a relationship between the increase in basal metabolic rate (BMR) and the decrease in vital capacity, this was not confirmed by Lemon and Moersch.[3] These authors,[3] as well as Peabody and Wentworth[1] found a decrease in vital capacity while the patient was toxic; this returned to normal when toxic symptoms disappeared.

Two studies on lung-volume changes in hyperthyroidism appeared recently. In the study of Richards, Whitfield, Arnott and Waterhouse[4] a decrease in vital capacity was found in hyperthyroidism, but no significant change was observed in total lung capacity (10 patients). Stein, Kimbel and Johnson,[5] however, found no significant change in residual volume before and after therapy in 7 patients with hyperthyroidism, but they found a significant increase in respiratory muscle power as the condition was brought under control.

Following the suggestion of Mellville[6] that most patients with hyperthyroidism would be found to have a myopathy if sufficiently detailed tests of muscle power were undertaken, we decided to study patients before and after control of the hyperthyroidism, to ascertain whether changes in lung volume and respiratory muscular power would be a guide to a myopathy which might be present but not demonstrable by routine clinical examination.

MATERIALS AND METHODS

Only patients with clear-cut evidence of hyperthyroidism were used in this study. Treatment of these patients consisted of the administration of antithyroid drugs (propylthiouracil, tapazole or neo-mercazole) with appropriate bed rest and diet until symptoms were brought under control and the BMR had fallen to below +30. At this stage Lugol's iodine was added and surgical treatment undertaken, when the patient was considered suitable for operation. The pulmonary function tests were performed shortly after admission and again when the patient was under clinical control, but before surgical treatment was carried out.

Fourteen patients, of whom 12 were females and 2 males, were studied before and after treatment. Ten of these patients were White and 4 were of Cape Coloured stock. The initial BMR estimations ranged from +30 to +102, while the final BMR ranged from +1 to +26 (Table I). In 2 patients pulmonary function studies were repeated at intervals during the course of the illness.

Two patients (W.H. and H.G.) were in cardiac failure at the time of admission to hospital; they were not included in the study, until the condition of failure had been brought under control.

A normal chest roentgenogram was obtained in all but the 2 patients who had cardiac failure. In the 2 patients with cardiac failure all clinical evidence and radiological signs of pulmonary congestion had, however, disappeared before the pulmonary function studies were commenced.

The lung volumes were measured in duplicate on a Pulmotest (Godart) double spirometer calibrated as to volume and kymograph speed. A thermometer was inserted on the inspiratory side of the circuit near the bell and all volumes are related to BTPS.

The functional residual capacity was determined by the closed circuit, constant volume method, using helium as a tracer gas, as described by McMichael,[7] and modified by Gilson and Hugh Jones.[8] Residual volume was obtained by subtracting the expiratory reserve volume from the functional residual capacity.

The maximal mid-expiratory flow was calculated from a timed vital capacity tracing performed at a drum speed

TABLE I. ANTHROPOMETRIC DATA AND BASAL METABOLIC RATES AT DATE OF PULMONARY FUNCTION STUDY IN 14 PATIENTS WITH HYPERTHYROIDISM

	Initials	*Sex*	*Race*	*Age*	*Height in cm.*	*Initial pulmonary function test*		*Final pulmonary function test*	
						BMR	*Date of study*	*BMR*	*Date of study*
1	A.B.	F	E	55	157	+ 43	12 September 1959	+15	20 November 1959
2	M.M.S.	F	E	60	158	+ 76	10 December 1959	+22	31 March 1960
3	W.H.	M	C	60	172	+ 50	14 June 1960	+14	20 July 1960
4	R.dT.	F	E	61	170	+ 51	24 June 1960	+ 1	12 August 1960
5	M.A.	F	C	60	150	+ 33	1 July 1960	+12	21 July 1960
6	H.G.	F	E	60	158	+ 53	21 July 1960	+23	11 September 1960
7	P.J.F.	M	E	34	183	+ 60	22 August 1960	+26	16 September 1960
8	C.C.	F	E	23	163	+ 42	19 September 1960	+15	20 November 1960
9	H.D.	F	C	53	155	+102	8 February 1961	+26	24 April 1961
10	T.S.	F	C	20	169	+ 41	2 March 1961	+11	22 March 1961
11	M.E.W.	F	E	29	158	+ 49	13 March 1961	+15	9 May 1961
12	M.R.	F	E	38	168	+ 72	16 March 1961	+17	11 April 1961
13	M.D.C.	F	E	54	150	+ 86	7 April 1961	+19	1 May 1961
14	S.M.	F	E	19	170	+ 30	18 April 1961	+ 8	3 June 1961

F=Female M=Male E=White C=Coloured

of 1,200 mm. per minute, and is expressed as litres per second.[9]

The only fairly specific test for respiratory muscle power is the measurement of maximal inspiratory and expiratory pressures recorded at the mouth with little or no airflow. Maximum pressures vary with physical fitness and training.[10] For the past 3 years we have measured airway pressures at the mouthpiece at the volume-level of the total lung capacity and residual volume as observed on the tracing. This was done by switching the patient by means of a two-way valve to a small chamber connected to a Statham P23D pressure transducer which recorded on a Sanborn Polyviso recorder. Recent reports indicate that this procedure is also being followed at other laboratories in preference to the mercury manometer.[5,11]

The prediction formulae used are those of Goldman and Becklake[12] for the vital capacity, residual volume and total lung capacity using sex, age and height, but not body weight or body surface area. The maximal breathing capacity was predicted from the data of Needham, Rogan and McDonald[13] using sex and age, but not body weight or surface area. As their values are at ATPS, and our values are expressed as BTPS, 9% was added to their values.

All patients were studied in a comfortable sitting position.

In a series of more than 60 normal subjects studied in this laboratory, the lung volumes corresponded to the normal predicted values obtained from these formulae. (Unpublished data.)

The statistical analysis of the data was done using the test of significant difference in paired data[14].

The correlation coefficient was calculated for the various lung volume subdivisions with the respiratory muscle power and with the BMR, using the formula for small values of N.[15]

TABLE II. LUNG VOLUME, MAXIMUM MID-EXPIRATORY FLOW RATE, MAXIMAL BREATHING CAPACITY AND RESPIRATORY MUSCLE POWER BEFORE AND AFTER CONTROL OF HYPERTHYROIDISM

Name	Vital capacity				Residual volume				Total lung capacity			
	Before		*After*		*Before*		*After*		*Before*		*After*	
	Litre	*%*	*Litre*	*%*	*Litre*	*%*	*Litre*	*%*	*Litre*	*%*	*Litre*	*%*
A.B.	3·210	114	3·439	122·8	3·418	212·4	2·776	172·0	6·628	153	6·215	143·5
M.M.S.	2·029	66·7	2·710	87·4	—	—	—	—	—	—	—	—
W.H.	3·336	86·2	3·661	94·6	5·117	230·4	1·005	45·3	8·435	123·4	4·666	68·11
R.dT.	3·592	106·3	3·703	109·5	5·741	274·6	3·208	153·4	9·333	176·0	6·910	130·30
M.A.	2·297	97·7	2·230	94·8	2·548	176·9	1·028	71·4	4·845	129·8	3·258	87·3
H.G.	2·949	106·5	3·396	122·6	2·257	133·6	1·439	85·2	5·206	119·4	4·835	110·9
P.J.F.	4·059	75·8	4·607	89·2	6·780	340·7	3·201	160·8	10·839	149·7	7·808	107·8
C.C.	3·193	86·3	3·353	90·6	3·525	238·1	1·868	126·1	6·718	130·9	5·221	101·8
H.D.	1·903	68·4	2·126	77·8	2·223	142·5	2·056	134·4	4·126	96·6	4·182	96·4
T.S.	3·610	89·6	3·823	98·7	2·671	162·8	1·652	100·7	5·078	91·4	5·475	97·2
M.E.W.	3·240	99·0	3·408	102·2	2·253	166·0	2·350	170·6	5·443	119·0	5·763	123·4
M.R.	2·264	72·0	3·142	85·0	3·825	217·0	2·178	121·6	6·449	121·0	5·320	99·1
M.D.C.	2·718	110·4	2·707	110·0	4·630	335·5	2·292	166·1	7·919	193·0	4·999	132·2
S.M.	2·444	59·0	2·627	63·4	4·974	297·8	1·149	68·8	7·418	129·7	3·776	66·0
Mean	2·9431	88·42	3·2094	95·97	3·843	225·25	2·015	121·26	6·808	133·3	5·264	104·9
S.D.	± 0·6110	± 17·23	± 0·6496	± 15·84	± 1·382	± 67·14	± 0·7259	± 41·64	± 1·87	± 27·49	± 1·19	± 22·56
	t = 4·34 P<0·001				t = 5·056 P<0·001				t = 4·08 0·01<P>0·001			

Name	Maximal breathing capacity				MMEF		RV/TLC%		Maximal pressures: Expiratory		Maximal pressures: Inspiratory	
	Before		*After*		*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*
	Litre	*%*	*Litre*	*%*	*L./sec.*	*L./sec.*			*mm. Hg*		*mm. Hg*	
A.B.	82·3	100·6	56·3	68·8	2·8	3·8	51·6	44·6	—	—	—	—
M.M.S.	59·9	78·9	31·8	41·8	2·7	1·3	—	—	36	45	22	42
W.H.	56·6	53·2	68·7	64·5	4·6	3·1	60·5	21·5	84	110	45	78
R.dT.	97·1	127·7	100·9	132·8	2·8	3·2	61·5	46·4	32	106	20	76
M.A.	38·3	50·4	45·2	59·4	1·4	1·1	52·6	31·6	62	78	16	38
H.G.	51·3	67·2	56·7	74·3	4·9	1·2	43·4	29·8	26	55	18	25
P.J.F.	102·1	71·8	146·3	102·8	4·2	2·9	62·5	40·9	52	92	28	62
C.C.	67·6	63·2	90·1	84·2	3·8	4·7	52·5	35·7	—	—	—	—
H.D.	55·9	68·0	82·8	100·9	1·2	2·0	53·9	49·1	12	48	26	40
T.S.	98·4	90·3	69·8	64·0	2·7	3·1	52·6	30·2	40	35	36	19
M.E.W.	100·6	96·7	47·5	45·7	3·1	3·4	41·0	40·8	36	40	25	78
M.R.	63·4	68·2	66·3	71·3	1·4	0·9	59·3	40·9	32	44	4	42
M.D.C.	41·4	50·5	49·0	59·8	2·4	3·0	58·5	45·8	34	44	15	26
S.M.	62·7	57·5	65·6	60·2	2·5	3·0	67·0	30·4	30	48	18	43
Mean	69·83	74·6	69·79	73·7	2·89	2·62	55·14	37·5	39·7	62·1	22·7	47·4
S.D.	± 21·40	± 21·45	± 27·73	± 23·57	± 1·11	± 1·09	± 7·26	± 7·96	± 17·88	± 25·8	± 10·1	± 20·18
	t=0·135 P>0·80				t=0·771 P<0·5>0·4		t=3·988 P<0.01>0·001		t=3·702 P<0·01>0·001		t=3·406 P<0·1>0·001	

RESULTS

The results expressed in litres BTPS and their percentage of the predicted normal are set out in Table II. The respiratory muscle power is recorded in millimetres of mercury.

The mean values and their standard deviations are presented with the t-value and the probability that the observed change is due to chance.

The maximal breathing capacity and maximal mid-expiratory flow-rate do not show significant changes from the values before treatment ($P > 0{\cdot}80$ and $P < 0{\cdot}5 > 0{\cdot}4$ respectively.)

A highly significant change was observed in the values for before and after estimations of vital capacity and residual volume ($P < 0{\cdot}001$) and a significant change in the total lung capacity, RV/TLC% ratio, and maximal expiratory and inspiratory pressures ($P < 0{\cdot}01 > 0{\cdot}001$).

In the patients H.G. and H.D., where serial pulmonary function studies were undertaken during the period of toxicity and again after the condition had been brought under control, it could be seen that respiratory muscle power increased steadily, but that there was at first an increase in residual volume before it returned to near normal values (Figs. 1 and 2).

These findings suggested that some of the changes in lung volume might be dependent on changes in respiratory muscle power, while others may be more directly influenced by changes in the degree of toxicity as reflected in the BMR estimations, and are not dependent to the same extent on changes in respiratory muscle power.

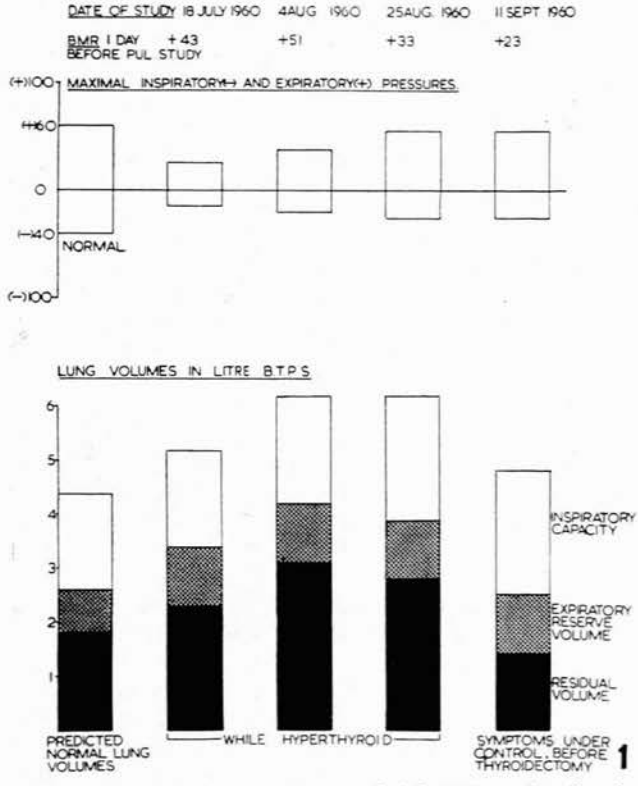

Fig. 1. Patient H.G., age 60 years, height 158 cm. Predicted normal lung volume and respiratory muscle power (on left), and changes observed on 4 occasions during the course of treatment.

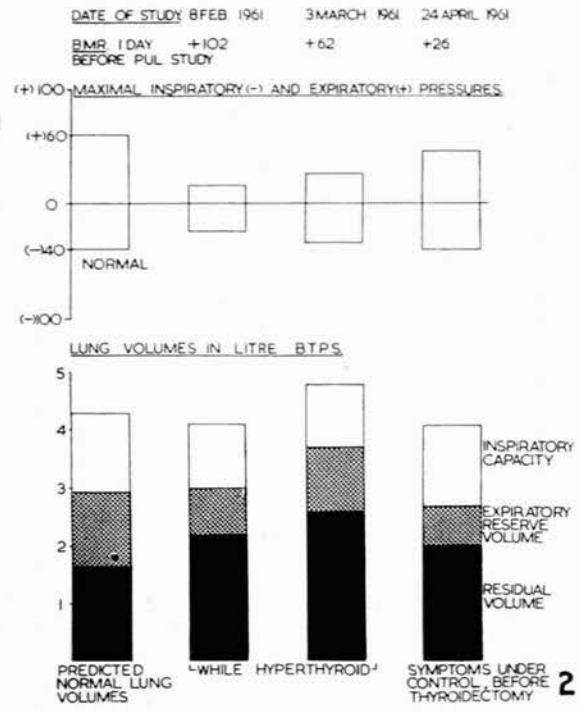

Fig. 2. Patient H.D., age 53 years, height 155 cm. Predicted normal lung volume and respiratory muscle power (on left), and changes observed on 3 occasions during the course of treatment.

We therefore calculated the correlation coefficients between respiratory muscle power and lung volume; and between lung volume and BMR (Table III).

At the 5% level of significance the vital capacity is the only lung volume that correlates significantly with respiratory muscle power, while the residual volume shows a highly significant correlation with the BMR (significant at 1% level).

TABLE III. CORRELATION COEFFICIENTS OF LUNG VOLUME WITH RESPIRATORY MUSCLE POWER AND BMR

A. CORRELATION COEFFICIENTS BETWEEN RESPIRATORY MUSCLE POWER AND LUNG VOLUME

	Expiratory	*Inspiratory*
Vital capacity	+0·4378	+0·4274
Residual volume	−0·0904	−0·2699
Total lung capacity	+0·0481	−0·3371

Significance levels r=0·4227, significant at 5% level.
r=0·5368, significant at 1% level.

B. CORRELATION COEFFICIENTS BETWEEN LUNG VOLUME AND BASAL METABOLIC RATE

Vital capacity	−0·3292
Residual volume	+0·5369
Total lung capacity	+0·3320

Significance levels: r=0·3809, significant at 5% level.
r=0·4869, significant at 1% level.

DISCUSSION

Our study confirms the finding of Stein *et al.*[5] of a significant increase in respiratory muscle power as the condition of hyperthyroidism is brought under control, and the increase in respiratory muscle power shows a positive correlation (significant at the 5% level) with the increase in vital capacity.

The decrease in residual volume, found by Richards *et al.*[4] to be significant ($P = 0.01$), could not be confirmed by Stein *et al.*[5], but was found to be highly significant ($P < 0.001$) in this study. As the change in residual volume correlates with the BMR, the discrepancy in the results could be explained by differences in the severity of the clinical condition in the different studies. All 3 reported series are rather small (Stein *et al.* 7 cases;[5] Richards *et al.* 10 cases;[4] this study 14 cases), and hyperthyroidism can vary widely in its range of toxicity. The average BMR, calculated from the data of Stein *et al.* for 7 patients, was +43·7 and in our series +56·3. Richards *et al.*[4] calculated correlation coefficients between lung volume and BMR in hyperthyroidism and, although none of their values reached statistically significant ratings at the level of 5%, the highest correlation coefficient was obtained between BMR and functional residual volume, total lung capacity and residual volume (+0·58, 0·47 and 0·36 respectively as against +0·03 for vital capacity).

It is evident from the figures of Stein *et al.*,[5] Richards *et al.*,[4] and the present study, that in hyperthyroidism the vital capacity is decreased, while the residual volume shows a decrease as the condition is brought under control. The significance of this finding varies statistically. Richards *et al.*[4] found the same changes in anaemic subjects, but contrary to the position in hyperthyroidism, there was a correlation between these changes and the severity of the anaemia. The fact that decreased respiratory muscle power accounts for part of the changes in vital capacity, and the severity of the condition for part of the changes in residual volume, might explain the findings of Richards *et al.*[4] in hyperthyroidism.

Serial studies on 2 patients during the phase of toxicity show that respiratory muscle power increases steadily after the commencement of therapy while the residual volume actually increases for a while after the start of therapy. The muscles mainly involved in expiration are the abdominal muscles,[16] and since expiratory muscle power is also diminished in hyperthyroidism, weakness of these muscles may be postulated. Brody *et al.*[17] demonstrated that in cats the abdominal muscles and viscera impose a steady force tending to reduce functional residual capacity and residual volume. Inactivity in bed might further reduce this force with a resultant increase in residual volume. Against this explanation is the fact that a better negative correlation was found with inspiratory muscle power and residual volume than with expiratory muscle power.

The maximal breathing capacity is influenced by endurance of respiratory muscle effort, as well as by respiratory muscle power.[10] The finding of a decrease in maximal breathing capacity and an increase in maximal pressures (MMS, MEW) probably signify a decrease in endurance of muscular effort. In one instance (T.S.) there was a decrease in both maximal breathing capacity and maximal pressures.

The total lung capacity is increased mainly owing to the increase in residual volume, and would thus be expected to be influenced to that extent by the severity of the clinical condition. The vital capacity might, however, be decreased to such an extent that changes in total lung capacity become minimal. An increase in respiratory muscle power, by increasing the vital capacity, could then lead to a disproportionate increase in total lung capacity if the residual volume has not yet decreased. (See data for H.D., Fig. 2.) This study confirms the finding of Stein *et al.*[5] that there is respiratory muscle weakness in hyperthyroidism, and we could show that this correlates with the decrease in vital capacity. The increase in residual volume cannot be explained satisfactorily, since this correlates best with inspiratory rather than expiratory muscle power, but does not attain statistical significance at the 5% level, the only significant correlation being that with changes in the BMR. The increase in total lung capacity, in those cases where it is marked, can only be explained on the assumption that certain anatomical changes occur, such as a downward movement of the diaphragm owing to loss of abdominal muscle tension. Loss of muscle tone owing to the fact that patients were treated in bed might possibly explain the increase in residual volume after treatment had begun in cases H.G. and H.D. If this applies to all cases, it would mean that larger changes in total lung capacity and residual volume would be observed if patients were first studied after treatment had been started and the patient had been in bed, than if a patient were initially studied on admission and again later.

The finding of a large decrease in total lung capacity as occurred in cases W.H., D.d.T., P.J.F., M.D.C. and S.M., after therapy, was however unexpected, although large changes in total lung volume have been reported. In a myxoedematous patient with no demonstrable pulmonary disease Wilson and Bedell found an increase in total lung volume from 78 to 110% of normal after thyroid therapy.[18] The mean total lung volume in 10 patients with hyperthyroidism decreased from 4·74 to 4·63 litres in the study by Richards *et al.* and, although not statistically significant, it is noteworthy that in 9 anaemic patients from the same study the mean total lung volume remained exactly the same (4·91) before and after therapy.

SUMMARY

1. In 14 patients with hyperthyroidism, studied before and after control of their symptoms, but before thyroidectomy, a decrease in respiratory muscle power, which returns to normal after control of the condition, was confirmed.

2. The residual volume was found to be increased during the toxic period, and it showed a significant reduction after therapy had been applied.

3. The changes in vital capacity were found to correlate with respiratory muscle power changes, while the residual volume changes correlated with changes in the BMR.

4. In 2 patients serial studies were carried out during the toxic state, and it was observed that respiratory muscle power increased towards normal while undergoing treatment. The residual volume did not return to normal before

control of the condition, and actually increased after initiation of therapy.

5. Although the underlying mechanism for these changes is not completely understood, our results show that the decrease in respiratory muscle power might be an important factor in the changes in lung volume in patients with hyperthyroidism, but also that the increase in residual volume is more closely related to the severity of the condition than to the changes in respiratory muscle power. The decrease in vital capacity seems to be a gross index of respiratory muscle weakness in hyperthyroidism.

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