

Bilateral removal of carotid bodies for asthma

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The removal of carotid bodies (glomectomy) for relief of asthma has been widely practised since Nakayama (1961) reported an improvement in 2,535 of 3,914 Japanese patients. Very variable results have been found. Improvement, for example, has been reported by Overholt (1963b) in 82% of cases with asthma treated by unilateral removal, by Sedwitz (1963) in 82%, by Fletcher, Gaikwad, and Bond (1963) in 75%, by Keim (1964) in 78%, by Kline, Ponce, Philippakis, and Amirata (1964) in 88%, and by Phillips (1964) in 91%. In contrast, in the only controlled studies, O'Rourke and O'Rourke (1964) and Marschke, Beall, Stern, and Murray (1965) found that unilateral glomectomy was no better than a sham operation. Segal and Dulfano (1965) emphasized the difficulty of assessing results by describing the clinical details of 15 patients treated elsewhere. None was considered to have benefited, although seven had been reported to be improved in accounts published elsewhere.

The value of glomectomy is not therefore established despite the large number of treated patients. Details of selection and assessment are so sparse that comparisons between reports cannot be made. Only 23 case histories are given by the above authors, 20 of which are recorded by authors (O'Rourke and O'Rourke 1963, 1964; Segal and Dulfano, 1965) who found poor results. Two of the other three histories report benefit after bilateral glomectomy (Keim, 1964).

We consider that assessment is impossible without adequate documentation of individual cases, and we describe the effects of bilateral removal of carotid bodies in three patients. The results have led us to abandon the operation. Physiological studies in two of these patients will be mentioned. They have been reported in detail by Holton and Wood (1965).

OPERATIVE TECHNIQUE

Under general anaesthesia the carotid bifurcation was exposed through a semi-oblique incision 5 cm. in length centred over it, the common facial vein being divided. The superior thyroid artery usually led the

dissection back on to the carotid bifurcation region, and, before proceeding further, local infiltration with 1 to 2 ml. 2% lignocaine (without adrenaline) was carried out with special attention to the tissues between the bifurcation, so as to minimize the risk of vaso-depressor reflexes during further dissection. Usually the superior thyroid artery was divided in order to rotate the carotid bifurcation and to expose its deep surface where the carotid body lies. The adventitia of the bifurcation and that of the adjoining 1 cm. of each of the three main vessels was dissected away, and in all cases this dissection led to the clear display of the carotid body. Histological confirmation was obtained in all six specimens. It is probable that the sinus nerve was damaged in all cases. The wound was closed routinely with a sealed vacuum drain, which was removed on the first or second post-operative day.

METHODS

LUNG FUNCTION TESTS The forced vital capacity (F.V.C.) and the timed forced expiration (F.E.V._{1.0} = forced expiratory volume in the first second) were measured with a spirometer as described by Horton and Phillips (1959). Isoprenaline inhalations were used to try to relieve airway obstruction. Inhalations were continued until no further improvement of F.E.V._{1.0} or F.V.C. occurred or until palpitations were induced.

MEASUREMENTS OF ARTERIAL BLOOD Arterial blood was sampled anaerobically. Arterial pH, partial pressure of carbon dioxide (Pco₂), and total bicarbonate were measured by the method of Siggaard Andersen, Engel, Jørgensen, and Astrup (1960). Arterial oxygen saturation was measured by a spectrophotometric method at wavelengths of 650 and 805 mμ, using a 0.5 mm. pathway perspex cuvette and Triton X-100 as a haemolysing agent (Deibler, Holmes, Campbell, and Gans, 1959). Rapid changes of arterial oxygenation were detected by an Atlas Universal ear oximeter.

CASE HISTORIES

CASE 1 A 57-year-old housewife first developed episodic non-seasonal rhinorrhoea and breathlessness at the age of 24 years. Aged 44, following pneumonia, she became continuously wheezy, and in the next 13

TABLE I
SPIROMETRIC MEASUREMENTS BEFORE AND AFTER REMOVAL OF CAROTID BODIES

Case	Time in Relation to Operation	Before Isoprenaline Inhalation			After Isoprenaline Inhalation			Predicted Value F.V.C. (ml.)
		F.V.C. (ml.)	F.E.V. _{1.0} (ml.)	F.E.V. _{1.0} /F.V.C.	F.V.C. (ml.)	F.E.V. _{1.0} (ml.)	F.E.V. _{1.0} /F.V.C.	
1	Before	1,500	650	0.43	1,800	900	0.50	2,400
	10 weeks after	1,950	1,300	0.67	—	—	—	
	16 months after	1,900	1,300	0.68	2,000	1,400	0.70	
2	Before	2,100	1,450	0.69	2,700	1,900	0.70	2,450
	3 weeks after	2,250	1,600	0.71	—	—	—	
	11 months after	2,200	1,600	0.73	2,200	1,600	0.73	
3	Before	1,300	800	0.61	1,900	1,100	0.55	4,200
	2 weeks after	1,700	600	0.37	2,200	1,000	0.46	
	8 months after	1,000	600	0.60	1,800	800	0.44	

F.V.C. = forced vital capacity.

F.E.V._{1.0} = forced expiratory volume in 1 second.

Predicted values are derived from the formulae of Needham, Rogan, and McDonald (1954).

TABLE II

ARTERIAL BLOOD pH, OXYGEN SATURATION, PARTIAL PRESSURE OF CARBON DIOXIDE AND TOTAL BICARBONATE BEFORE AND AFTER REMOVAL OF CAROTID BODIES

Case	Time in Relation to Removal of Carotid Bodies	pH	Oxygen Saturation (%)	Partial Pressure CO ₂ (mm.Hg)	Total Bicarbonate (mMol l.)
1	Before	7.435	95.6	44.0	25.2
	1 week after	7.41	92.0	55.5	32.0
	16 months after	7.39	94.6	58.5	36.0
2	Before	7.42	98.0	40.0	27.3
	9 weeks after	7.41	96.0	45.5	29.3
	11 months after	7.36	93.6	45.0	26.0
3	Before	7.46	99.5	41.0	29.5
	3 days after	7.40	91.0	52.5	33.1
	8 months after	7.37	93.4	58.5	32.8
	10 months after	7.39	94.0	55.4	34.2

years she was admitted to hospital acutely breathless 32 times.

No clear cause was ever found for her asthma. A moderate blood eosinophilia (up to 700/c.mm.) was found on several occasions. She had domestic problems, and the suspicion was entertained that at times she failed to take her treatment.

Treatment with standard sympathomimetic and theophylline drugs was supplemented with cortisone (50 mg. daily) from the age of 48 years. Attempts to reduce the dose of cortisone led to severe episodes of asthma. She developed a red, round face, moderate oedema of both ankles, and thin, widely-bruised skin. Aged 53, her blood pressure became raised and out-patient measurements varied about a mean of 190/120 mm. Hg.

Aged 57, she was admitted for removal of carotid bodies. Arterial blood estimations and lung function tests are recorded in Tables I and II. An electrocardiogram showed left and right ventricular strain. The right carotid body was removed. Treatment with glucocorticoids was increased shortly before the operation. Her clinical condition was unchanged, and a week later the left carotid body was removed. Recovery was uneventful and treatment with cortisone

was reduced to the pre-operative level of 50 mg. daily.

Two months later she became extremely breathless and was readmitted. An eosinophilia was found in her blood (700/c.mm.) and sputum. Prednisone was substituted for cortisone and she was discharged taking 10 mg. daily. She remained mildly wheezy but did not require hospital admission in the succeeding 18 months. A year after starting treatment with prednisone she was able to reduce her daily dose to 7.5 mg. Attempts to reduce the dose further led to severe wheezing. Her blood pressure as an out-patient has been higher than before, with a mean level of 200/130 mm. Hg. She experiences frequent severe headaches. She is very pleased with the result of her operation.

CASE 2 A 53-year-old nun developed non-seasonal rhinorrhoea and nasal polyposis at the age of 20 years. At the age of 43 she developed persistent asthma. Aspirin was the only factor which clearly made the asthma worse. When aged 46 she was treated with prednisone and continued to take 20 or 15 mg. a day; her asthma was moderately well controlled. She increased in weight and developed a round plethoric face and glycosuria. For 18 months before admission she experienced intermittent frontal headaches. There was a family history of hypertension and diabetes mellitus, but none of pulmonary disease.

On examination she had a red round face, small bilateral nasal polypi, and there were a few scattered crepitations. There were no other abnormal clinical findings. Her blood pressure was 140/90 mm. Hg. There was a mild blood eosinophilia (550/c.mm.) and a markedly diabetic oral glucose tolerance curve. The results of arterial blood and lung function tests are recorded in Tables I and II.

Both carotid bodies were removed on the same day. Treatment with glucocorticoids was temporarily increased. Slight hoarseness and marked glycosuria occurred for a few days; otherwise recovery was uneventful. Her scar was neatly covered by her wimple. The blood pressure did not rise for the first 10 days.

In the subsequent 11 months her breathlessness has continued unchanged. Attempts to reduce her treatment with prednisone have increased the severity of her asthma. She has continued to experience frequent and severe frontal headaches. Her blood pressure taken in the out-patient department has been higher than before (150/100 mm. Hg). She does not feel that the operation has helped her.

CASE 3 A 44-year-old insurance agent had experienced very severe chronic breathlessness since infancy. Aged 35 he began treatment with glucocorticoids; when aged 42 corticotrophin (A.C.T.H.), 20 i.u. every other day, was substituted with slight benefit.

Despite many admissions to hospital no clear cause for his asthma was found. He was often depressed, and sometimes this appeared to aggravate his breathlessness. He had been treated without benefit with electroconvulsive therapy when aged 40, and subsequently would not accept psychiatric advice.

On examination he was breathless, his chest was markedly barrel-shaped, and expansion was poor. Expiration was grossly prolonged with many wheezes. Otherwise there were no abnormal findings. His blood pressure was 140/90 mm. Hg. Results of arterial blood and lung function tests are recorded in Tables I and II.

Before operation treatment with A.C.T.H. was increased and he received premedication with pethidine, 100 mg., levallorphan tartrate, 0.6 mg., promethazine, 25 mg., and atropine, 0.6 mg. Cheyne-Stokes breathing occurred which was thought to be a temporary effect of the pethidine. Both carotid bodies were removed. Following infiltration of lignocaine on the second side, the pulse rose from 90 to 110/minute and the systolic pressure rose temporarily from 100 to 130 mm. Hg.

On recovery of consciousness respiration was irregular and prolonged periods of apnoea occurred during which he was tense and distressed. Treatment with nikethamide and aminophylline was without effect. In the 12 hours following operation the blood pressure rose to 195/135 mm. Hg.

During the next eight days episodes of irregular breathing continued and the respiration rate at times fell to 4/minute. He felt ill and complained of severe frontal headaches and dizziness on standing. His blood pressure fluctuated between 200/150 and 150/90 mm. Hg. There was no postural hypotension. He remained wheezy.

On the sixteenth day, after eight days of regular breathing at a normal rate, his respiratory response to breathing 10% oxygen in nitrogen was studied. Ventilation did not increase and arterial oxygen saturation fell sharply to 37%. Breathing became irregular again, slowly becoming normal in rate and rhythm in the next three weeks. Six weeks after operation 10% oxygen in nitrogen was administered again twice. On one occasion ventilation increased, but on the other ventilation decreased, marked arterial

desaturation occurred, and he appeared unable to breathe properly except on command.

He continued to be very breathless and wheezy and to experience intermittent malaise, dizziness, and headache. Treatment with A.C.T.H. had to be increased to 20 i.u. daily. His blood pressure remained labile, ranging from 180/100 to 100/70 mm. Hg.

He was unable to return to work because of his breathlessness and dizzy episodes. He was extremely disappointed and depressed with the result of the operation.

DISCUSSION

BILATERAL REMOVAL Bilateral removal of carotid bodies was reported by Nakayama (1962) to have improved 414 of 461 patients with asthma. The patients were assessed more than six months after operation, but the methods were not specified. Nakayama (1963) reported that bilateral glomectomy led to a loss of 'air hunger', so that patients could be unaware of anoxia. He recommended that bilateral glomectomy should not be performed. Overholt (1963b) and Fletcher *et al.* (1963) removed both carotid bodies from seven patients while performing a large series of unilateral operations but did not report the results separately. Keim (1964) briefly described improvement in two men.

One of the patients described here was able to reduce her annual number of admissions to hospital after bilateral glomectomy, but clinical improvement did not occur for several months until her drug treatment was changed, so that the improvement cannot easily be attributed to the operation. The other two patients have not improved. None was able significantly to reduce treatment with steroids. Simple lung function tests are notoriously poor indicators of the severity of chronic asthma, but they match the clinical findings by showing improved results in one patient and no improvement in the others. Random resting arterial blood estimations showed small decreases of pH and oxygen saturation and increased partial pressure of carbon dioxide in each patient, suggesting that a reduction of effective resting pulmonary function had occurred in all.

Physiological studies on patients 2 and 3 (Holton and Wood, 1965) showed that for several weeks after operation there was abolition of the normal ventilatory response to anoxia, and abolition of cardiovascular baroreceptor reflexes which help to maintain a constant blood pressure in the intact human. Both these temporary effects appear to be undesirable, as is the sustained increase of blood pressure which occurred.

The operation has not produced any definite

clinical benefit and has been followed by undesirable permanent and temporary effects. We do not intend to remove both carotid bodies again.

UNILATERAL REMOVAL Unilateral removal of carotid bodies for asthma has been performed frequently. It has been recommended for asthma, for emphysema (Sedwitz, 1963; Phillips, 1964; Shek, 1964), and also for Buerger's disease, 'post-prandial symptoms following gastro-intestinal surgery', and the pain of terminal carcinoma (Nakayama, 1961, 1962, 1963). Techniques of operation have varied. Nakayama (1961), for example, removed the carotid body alone and spared the sinus nerve, whereas Phillips (1964) removed the adventitia from the carotid arteries for 38 mm. each way to interrupt as many nerve fibres as possible. Both reported excellent results in large numbers of patients with asthma. There were no control observations. Comroe (1963) described glomectomy as unjustifiable without control procedures. Overholt (1963a) replied that he had a rough control by observing his patients for a long time, and drew attention to Nakayama's claim to have helped most of 50 patients who had not been relieved by previous unsuccessful attempts to remove a carotid body. Clearly neither of these are satisfactory control procedures. Only two controlled trials have been reported (O'Rourke and O'Rourke, 1964; Marschke *et al.*, 1965). These showed that unilateral glomectomy for asthma was no more effective than a sham operation, although improvement, as judged by patients and doctors, was common in both groups. The negative results suggest that attempts to find a physiological explanation for the reputedly beneficial effects of unilateral glomectomy (Overholt, 1962, 1963b; Sedwitz, 1963; Phillips, 1964) are unnecessary.

Unilateral glomectomy seems greatly to be preferred to bilateral removal, but since a sham operation is as effective as unilateral removal, the sham operation should presumably be the surgical treatment of choice so that the operative and physiological risks may be minimized.

SUMMARY

Three patients with severe asthma were treated by bilateral removal of carotid bodies. One has improved (probably for other reasons) and two have not. None has significantly reduced treatment with steroids. A sustained increase of blood pressure has occurred in two patients, and for

several weeks after operation there was failure to respond to anoxia and impairment of baroreceptor reflexes. Effective pulmonary function, as measured by arterial pH, oxygen saturation, and partial pressure of carbon dioxide, has deteriorated.

Bilateral removal of carotid bodies is considered to have harmed rather than helped these patients.

We wish to thank Dr. P. Holton for performing physiological studies, Dr. D. Redstone for performing arterial blood estimations, Miss R. A. Mace for invaluable secretarial help, and to pay tribute to the great fortitude of our patients who cheerfully underwent repeated studies.

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ADDENDUM

Case 1 died unexpectedly at home in status asthmaticus 25 months after operation.