

Magill forceps. After the pharynx was cleared of foreign bodies, the lungs were inflated with oxygen and the anesthetic continued. The patient awoke at the end of the operation and loudly bewailed the loss of her most treasured possessions (as was translated to us by the theater staff). The beads were returned to the patient who promptly replaced them in her mouth.

We should like to point out that prior to operation no attempt was made to engage the

patient in conversation, there being no common language. Further, as dentures are virtually unknown to the African population, the mouth was not inspected for foreign bodies. This proved to be a serious oversight of a routine precaution. Retaining valuables in the mouth is quite common among the Africans. It is hoped that this case report may prevent further incidents of this sort by alerting physicians going to African countries for the first time.

Halothane Anesthesia and Catecholamine Levels in a Patient with Pheochromocytoma

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The surgical excision of pheochromocytoma is a challenging problem for the anesthetist. Periods of acute hypertension due to increased liberation of the catecholamines can occur during induction of anesthesia, intubation of the trachea and surgical manipulation of the tumor. Various drugs, such as phentolamine (Regitine), piperoxan (Benodaine), or trimetaphan (Arfonad) have been used during anesthesia and operation to prevent these abrupt elevations of arterial blood pressure.¹

Recent findings in our laboratory indicate that halothane suppresses the sympatho-adrenal activity causing a depletion of epinephrine with no increase of norepinephrine in the cardiovascular tissues.² The rationale for the administration of halothane anesthesia for excision of adrenal pheochromocytoma is based on these findings. The following case report illustrates the advantages of halothane anesthesia in maintaining blood pressure within physiologic levels by suppression of circulating

catecholamine concentrations during operation in a patient with pheochromocytoma.

CASE REPORT

A 59 year old white married woman was admitted with a five-year history of fatigue, profuse sweating, itching and flushing. Her symptoms had become more severe and episodes of throbbing headache had developed approximately one year before admission.

Physical examination revealed a well-developed, slightly hyperpigmented woman, weighing 110 pounds without any acute distress. Blood pressure was 160/110 mm. of mercury in the supine position and 140/80 mm. of mercury in the upright position. Routine laboratory tests were normal. Urinary catecholamine excretion was 1075 μ g. per day (normal: 100 μ g. per day), and 3-methoxy, 4-hydroxymandelic acid (VMA) was 27.2 mg. per day (normal: 5 mg. per day). The day prior to operation, plasma catecholamine levels were still elevated (10 μ g./liter for norepinephrine and 1.2 μ g./liter for epinephrine). Electrocardiogram showed left ventricular hypertrophy and strain. The intravenous administration of phentolamine (5 mg.) resulted in a drop of arterial blood pressure from 160/70 to 80/60 mm. of mercury. The diagnosis of pheochromocytoma was made and the patient was scheduled for an exploratory laparotomy. The patient was given 500 ml. of plasma the day before operation.

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TABLE 1. Plasma Catecholamine Levels and Arterial Blood Pressure Before, During and After the Excision of Pheochromocytoma

Date and Time	Plasma Concentrations ($\mu\text{g./liter}$)		Arterial Blood Pressure (mm. Hg)	Remarks
	N.E.	E.		
July 10, 1962				
7:30 a.m.	1,660	2,540	220/120	Preanesthesia
8:11 a.m.	358	326	200/125	9 min. after 0.5% halothane
8:32 a.m.	69	35	160/105	Surgical manipulation of the tumor; 17 min. after 1% halothane
8:52 a.m.	214	57	215/105	Squeezing of the tumor during light anesthesia (0.5% halothane)
9:30 a.m.	59	29	190/100	Squeezing of the tumor during deep anesthesia (1% halothane)
11:10 a.m.	10	2	140/80	63 min. after the excision of the tumor; spontaneous respiration.
July 11, 1962	12.5	0.7	130/80	First postoperative day
July 13, 1962	0.44	0.02	105/75	Third postoperative day

ANESTHETIC AND OPERATIVE COURSE

The patient was premedicated with 100 mg. pentobarbital and 0.4 mg. scopolamine intramuscularly and a no. 18 Courmand needle was placed in the left brachial artery for recording systemic arterial blood pressure and for collection of arterial blood samples. Continuous and simultaneous recordings of arterial blood pressure and electrocardiogram were made on a Sanborn recorder. Arterial blood pH, P_{CO_2} and plasma and tissue catecholamine concentrations were determined by a previously described method.² Normal values of plasma catecholamine concentrations for this method, as obtained in our laboratory in twelve healthy individuals, were $1.0 \pm 0.12 \mu\text{g./liter}$ for norepinephrine and $0.4 \pm 0.06 \mu\text{g./liter}$ for epinephrine. Average percentage recoveries of catecholamines added to human plasma were 80 per cent for norepinephrine and 90 per cent for epinephrine.

Arterial blood pressure prior to the induction of anesthesia was 220/120 mm. of mercury. The preanesthetic electrocardiogram revealed left ventricular hypertrophy and regular rhythm with a rate of 130/minute. *Preanesthetic plasma catecholamine concentrations were 1,600 $\mu\text{g./liter}$ for norepinephrine and 2,540 $\mu\text{g./liter}$ for epinephrine (table 1).* Anesthesia was induced with 50 mg. of thiopental

intravenously, following 100 per cent oxygen breathing. The trachea was intubated with a no. 9 McGill cuffed-endotracheal tube after 40 mg. intravenous succinylcholine. Halothane in oxygen was administered from a Fluotec vaporizer † using a nonbreathing system. Ventilation was controlled by means of a volume-limited pressure-variable ventilator. The minute volume was set to maintain arterial P_{CO_2} levels within 25 to 28 mm. of mercury to minimize the effects of carbon dioxide tension upon the cardiac rhythm. The administration of varying inspired concentrations of halothane was adjusted to attempt to avoid any precipitous hypertensive episodes and to maintain the blood pressure within normotensive levels. There was a slight blood pressure overshoot during the induction of anesthesia with thiopental and succinylcholine and the intubation of the trachea (250/135 to 270/135 mm. of mercury). There were two episodes of transient cardiac arrhythmias which consisted of bigeminy and premature ventricular contractions between 7 to 9 minutes after the induction of anesthesia. The administration of 0.5 per cent halothane resulted in a decrease in

† Calibration of the Fluotec vaporizer by means of gas chromatography revealed that it delivers halothane 0.5, 0.9, 1.3 and 1.8 in volume per cent with the dial settings of 0.5, 1.0, 1.5 and 2.0, respectively.

blood pressure to 200/125 mm. of mercury and a reduction of plasma norepinephrine concentration to 358 $\mu\text{g./liter}$ and epinephrine concentration to 326 $\mu\text{g./liter}$ (table 1).

There were no demonstrable changes in blood pressure which had stabilized at 155/100 mm. of mercury when the surgical incision was made. Exploration of the left kidney and suprarenal area revealed no abnormalities, and blood pressure remained unchanged. On palpation of the upper pole of the right kidney, a solid mass was identified as a tumor of the right adrenal gland. Manipulation of this adrenal tumor produced no significant changes in the arterial blood pressure (160, 105 mm. of mercury). Within 30 minutes after the start of halothane anesthesia, the plasma catecholamine level was further decreased and not influenced by the surgical manipulation of the tumor (norepinephrine 69 $\mu\text{g./liter}$ and epinephrine 35 $\mu\text{g./liter}$). At one point the level of anesthesia was intentionally lightened by decreasing the inspired halothane concentration from 1.0 to 0.5 per cent and the surgeon was asked to squeeze the tumor vigorously. There was at this time an increase of arterial blood pressure (215/105 mm. of mercury) associated with an increased plasma catecholamine concentration (norepinephrine 214 $\mu\text{g./liter}$ and epinephrine 57 $\mu\text{g./liter}$) and occurrences of bigeminal rhythm for 24 seconds (50 beats). When anesthesia was intentionally deepened by increasing inspired halothane concentration to 1.0 per cent, the vigorous squeezing of the tumor caused elevation of arterial blood pressure to only 190/100 mm. of mercury. The plasma catecholamine levels at this time were 59 $\mu\text{g./liter}$ for norepinephrine and 29 $\mu\text{g./liter}$ for epinephrine. The plasma catecholamine level was markedly reduced after the excision of the tumor (norepinephrine 10 $\mu\text{g./liter}$ and epinephrine 2 $\mu\text{g./liter}$), and the blood pressure fell to 150/90 mm. of mercury.

Within four minutes after the surgical excision of the tumor, the arterial blood pressure became 120/80 and intravenous phenylephrine (0.05 per cent) was administered intermittently until 11:12 a.m. (total dose 21 mg.). Neosynephrine was then replaced by the intermittent administration of norepinephrine (0.016 mg./ml. in Hartman solution). Nor-

epinephrine was only administered when systolic pressure fell below 100 mm. of mercury during the immediate postoperative period and the first postoperative day during which period the arterial blood pressure was maintained around 138/80 mm. of mercury.

On the first postoperative day, the concentrations of plasma norepinephrine and epinephrine were 12.5 $\mu\text{g./liter}$ and 0.7 $\mu\text{g./liter}$, respectively. On the second postoperative day, the arterial blood pressure remained at 130/80 mm. of mercury and on the third postoperative day, the arterial blood pressure was 105/75 mm. of mercury, and the plasma norepinephrine and epinephrine concentrations were 0.44 $\mu\text{g./liter}$ and 0.02 $\mu\text{g./liter}$, respectively.

Biopsy of the tumor tissue showed an almost completely encapsulated mass of pheochromocytoma with scattered areas of cystic degeneration. It contained 2,360 $\mu\text{g.}$ epinephrine per gram excised tumor tissue and 3,840 $\mu\text{g.}$ norepinephrine per gram of tissue. The patient was discharged without any significant complications on the twentieth postoperative day. The followup evaluation on September 6, 1962, and January 17, 1963, revealed essentially negative findings.

DISCUSSION

This case illustrates the influence of halothane anesthesia upon the circulating catecholamine levels in a patient with pheochromocytoma. Plasma concentrations of epinephrine and norepinephrine decreased during the administration of halothane and remained lowered at the time of the start of operation, before, during and after the surgical manipulation and following the excision of the tumor. Responses of blood pressure to the intentional manipulation of the tumor differed at two different anesthetic levels due to changed inspiratory concentrations of halothane. The changes in plasma catecholamines during this intentional squeezing of the tumor paralleled changes in blood pressure. These findings were in accord with the other studies showing that the sympatho-adrenal response to hypercarbia was reduced³ and that the plasma catecholamine concentration was unchanged during halothane anesthesia,⁴ suggesting that this agent suppressed the sympatho-adrenal system response

during anesthesia. Therefore, it is reasonable to assume that halothane caused a decrease in the liberation of catecholamines from the tumor site because of the inhibition of sympathoadrenal activity. Evidently, any sympathetic stimulation can trigger the liberation of catecholamines from the chromaffin tissue elsewhere in the body. The decreased plasma catecholamine concentrations observed during halothane anesthesia in a patient with pheochromocytoma may be related to the action of halothane in blocking the liberation of catecholamines rather than the effects of this anesthetic agent upon catecholamine metabolism. Therefore, halothane can be regarded as a retrievable adrenergic blocking agent causing inhibition of liberation of circulating catecholamines in patients with pheochromocytoma.

It has been stated that halothane should be avoided in patients with pheochromocytoma because of the hazard of cardiac arrhythmias.¹ This was based upon the findings that the administration of exogenous epinephrine during halothane anesthesia in animals caused cardiac arrhythmias.^{5,6} In the present case the use of halothane anesthesia in the presence of high levels of circulating endogenous catecholamines due to pheochromocytoma resulted in occasional, transient arrhythmias. These findings are in agreement with others⁷ showing that halothane did not produce serious changes in cardiac rhythm in a patient for excision of pheochromocytoma. The high oxygen concentration in the inspired gas and the lowered levels of P_{CO_2} maintained throughout the entire anesthetic course can rule out hypoxia and hypercarbia as causes of arrhythmias. It has also been demonstrated that cardiac arrhythmias occur during halothane anesthesia in patients without hormonal and cardiac pathology.⁸ Therefore, halothane anesthesia does not seem to sensitize the myocardium to cause any additional changes in cardiac rhythm in the presence of increased levels of circulating endogenous catecholamine concentrations.

The use of blood transfusion to control the blood pressure without the use of vasopressors following the excision of the pheochromocytoma under halothane anesthesia in the post-

operative period was recently reported.⁷ The reason for the need of vasopressor agents following the surgical removal of the tumor in the present case may be related to a decrease of functioning blood volume. Recently, it has been reported that the circulating blood volume in patients with pheochromocytoma is reduced and that adequate restoration of the plasma volume prior to operation and anesthesia can reduce the incidence of hypotension following excision of the tumor.^{9,10} Although the restoration of the circulating blood volume may be of value in preventing postoperative hypotension in these patients, the use of adrenergic blocking agents administered prior to anesthesia and during operation to prevent hypertension during manipulation and excision of the tumor may, in fact, result in a precipitous fall of arterial blood pressure.

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