Pheochromocytoma: Diagnosis and Anesthetic and Surgical Management

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KNOWLEDGE of the physiology, pharmacology and biochemistry of the sympathetic nervous system and the adrenal medulla has been accumulating rapidly during the past fifteen years. Investigations of the metabolism of the adrenergic mediators, epinephrine and norepinephrine, development of techniques for the measurement of these catecholamines and their major products of metabolism in body fluids and tissues, along with studies of their physiologic effects and the synthesis of pharmacologic antagonists, have resulted in a better understanding of autonomic disturbances. Some of the information and techniques useful to the diagnosis and management of patients with suspected or proven pheochromocytomas will be reviewed.

Physiologic Considerations

Pheochromocytomas are functioning tumors which arise in chromaffin tissue. In contrast to tumors developing from other cell types in the sympathetic nervous system, such as the sympathogonioma or neuroblastoma, the clinical significance of the pheochromocytoma lies chiefly in a "physiologic malignancy" rather than in the tendency to metastasize. The signs and symptoms of pheochromocytomas result from the release of the highly potent amines, epinephrine and norepinephrine by the tumor.

These neurohumors are normally present and are synthesized from the amino-acid precursors, phenylalanine and tyrosine, by adrenergic nerves and in the adrenal medulla (fig. 1). The adrenal medulla in response to a variety of serious disturbances perceived by the nervous system releases both epinephrine and norepinephrine into the blood stream for distribution to distant sites of action. Norepinephrine, the chemical mediator responsible for the excitation of adrenergic receptors, is released by post-ganglionic fibers of the sympathetic nervous system, and exhibits its major effects locally. The turnover of epinephrine and norepinephrine in the circulation is very rapid. The half-life of these compounds is less than one minute. This rapid removal is due partially to their metabolism by monamine oxidase and catechol-*o*-methyl transferase.[1] The major metabolic products found in the urine and estimates of their concentrations are shown in figure 1.

Circulating norepinephrine produces widespread vasoconstriction, causing increased peripheral resistance and resulting in increased systolic, diastolic and mean blood pressures. The direct effect on the heart is to increase the rate and force of contraction. In the intact individual, increased blood pressure stimulates reflex mechanisms which in turn result in bradycardia and decreased cardiac output which mask the direct cardiac effects. An important but frequently overlooked effect is the reduction of plasma volume caused by prolonged increases in circulating norepinephrine [2] and epinephrine.[3]

Epinephrine differs from norepinephrine in that it produces a dilatation of muscular and splanchnic blood vessels. The changes in arterial pressure produced by epinephrine depend to some extent upon the amount present and the state of relaxation or constriction of the splanchnic and skeletal muscular vessels. Small amounts of epinephrine, when administered to an individual with vasoconstriction, may produce an initial fall in blood pressure in spite of an increase in cardiac output. Usually, however, there is tachycardia, a rise in the systolic, fall in the diastolic and little

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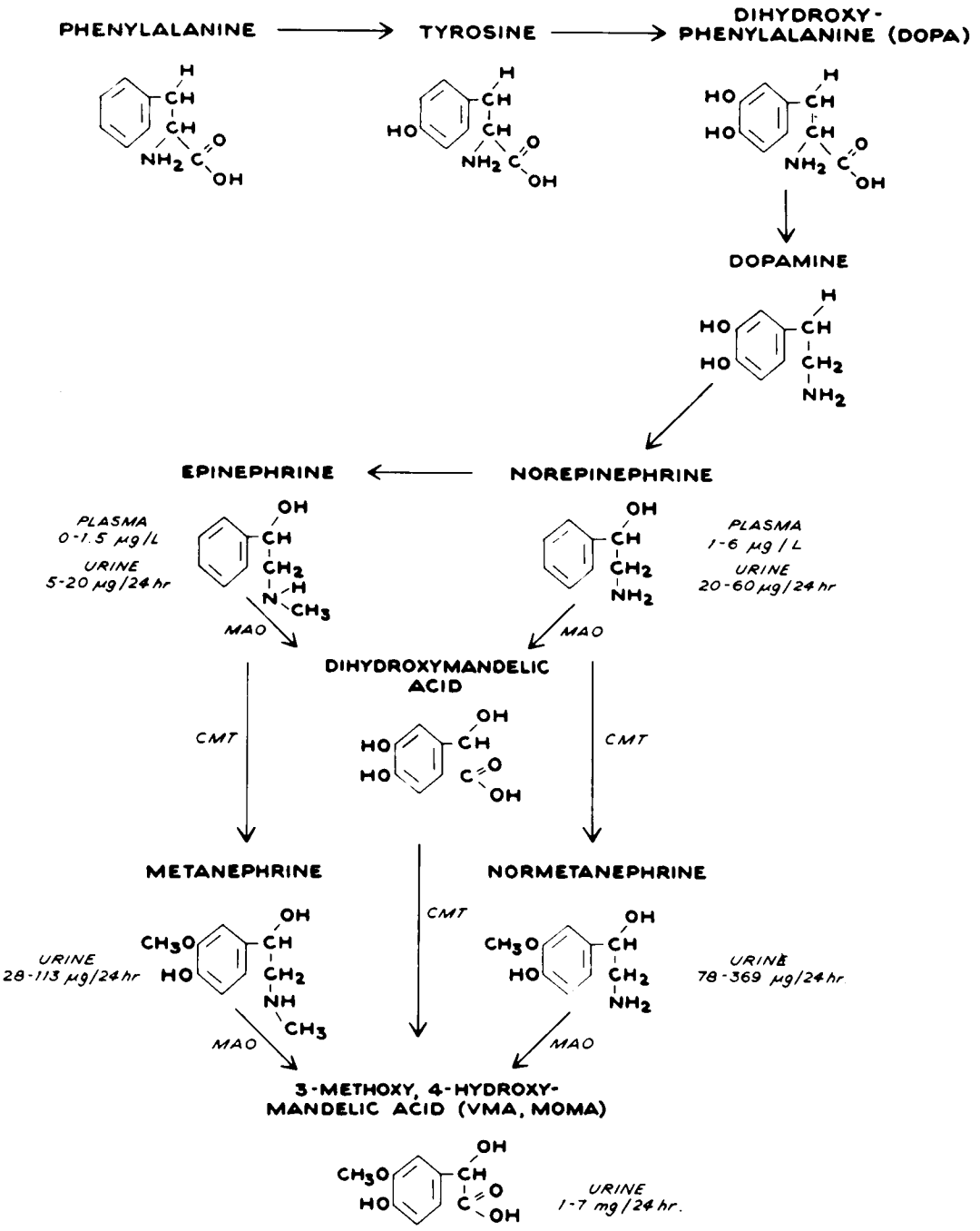

FIG. 1. The biosynthesis of epinephrine and norepinephrine and their metabolism by catechol-*o*-methyl transferase (CMT) and monamine oxidase (MAO). The sources of the above values for the amines and their metabolites are noted in the text, and the values vary according to the analytical procedure employed.

change or a slight fall in mean arterial pressures.

The adrenergic amines have prominent metabolic as well as hemodynamic effects. The increased oxygen consumption and elevation of blood glucose and lactic acid levels caused by epinephrine are much more marked than the increases produced by comparable amounts of norepinephrine. The glycogenolysis produced by these amines is due to activation of the enzyme phosphorylase.[4] In man, both amines, to a comparable degree, stimulate the mobilization of fat in the form of free fatty acids from adipose tissue.[5]

Diagnosis

Approximately 70 per cent of all pheochromocytomas reported as recently as ten years ago were diagnosed only at autopsy. Although this percentage should be considerably reduced now, autopsies still reveal undiagnosed pheochromocytoma. Apgar and Papper in 1951[6] estimated that the operative mortality rate was 24 per cent in patients in whom the presence of a pheochromocytoma had been established or suspected preoperatively. In contrast, they reported a mortality rate of more than 50 per cent in patients with unsuspected tumors undergoing unrelated surgical procedures. While there has been a further reduction in the mortality due to the surgical removal of these tumors in the former group of patients, the prognosis has not improved for the latter group. These observations clearly indicate that detection of these tumors and operative removal of them is of paramount importance even when symptoms are mild.

The diagnosis of pheochromocytoma is comparatively simple in the patient who complains of episodic pounding headache, palpitations, vasomotor changes, sweating, anxiety and other symptoms associated with marked increases in arterial blood pressure. However, even in these patients careful questioning may be necessary to determine the true severity of the syndrome. Several of our patients had been treated for anxiety states and menopausal syndromes for as long as two years. In one patient, under treatment for menopausal symptoms, the true diagnosis was suspected by the physician only after his personal observation of a paroxysm during an office visit. Unusual symptoms such as paroxysmal hypotension occur in some patients.[7] In others the only manifestation reported was the presence of hypertension. Gitlow *et al.*[8] have extensively reviewed the clinical manifestations of pheochromocytomas and the frequency with which they occur.

The diagnosis of pheochromocytoma has been established in 16 patients during the past ten years at the University of California Medical Center in San Francisco. Patient 2 (table 1) died eight days after birth. Autopsy revealed severe cerebral damage thought to be the result of a breech extraction and prolapsed umbilical cord. Patient 13 was a 35 year old man with Lindau's disease who had had a cerebellar hemangioblastoma operated upon 15 years earlier. Pyelography was done because of the known frequency of hypernephroma in these patients. When this study was normal, retrograde aortography was performed and a small mass was found overlying the superior pole of the left kidney, near but not in the adrenal. Urinary excretion rates of epinephrine and norepinephrine were 11 and 145 μg./24 hours, respectively. He was normotensive and free of symptoms. His blood pressure did not increase during the induction of anesthesia and remained at 120/80 mm. of mercury until the mass was manipulated, at which time the blood pressure rose to 180/110 mm. of mercury. A blood transfusion was given when the tumor was removed, and the blood pressure stabilized at 110/60 mm. of mercury and remained at that level until the patient was discharged. This patient and patient 16 with neurofibromatosis like those with neurocutaneous syndromes reported by Glushien *et al.*[9] had tumors in the left adrenal region. Patients 1, 11 and 14 all noted the onset of symptoms during pregnancy. Patient 3 was the sister of patient 8. Patient 4 had been subjected two years earlier to a bilateral subtotal adrenalectomy for Cushing's syndrome. Her tumor was located in the remnant of the right adrenal. Fourteen patients were found to have symptoms which occurred or increased paroxysmally, although nine of these were never free of symptoms (table 1).

Since the manifestations of these tumors vary and the symptoms may be minimal, many patients who do not have the disease must be

TABLE 1. The Anesthetic Management of All Patients with Pheochromocytomas Operated Upon at the University of California Hospitals in the Past Ten Years

Patient	Age	Sex	Tumor Site	Wt. Grams	Symptoms	Drugs Used for Induction	Relaxant	Anesthetic Agents	Regitine	Blood Transfused in Excess of Estimated Loss (ml.)	No. Hours Pressor Drugs Used†
1	30	F	Lt	67	C+I	Thiopental	—	N_2O+ether	I.V.	500	17
2	8 days	M	Rt	0.6	—	—	—	—	—	—	—
3	17	F	Lt	250	C+I	Thiopental	Curare	N_2O+Meperidine	I.V.+O	0	3
4	56	F	Rt	26	C+I	Thiopental	Succinylcholine	N_2O	I.V.	400	9
5	59	M	Rt	19	I	Thiopental	Succinylcholine	N_2O	I.V.	300	24
6	35	F	Lt	151	I	Thiopental	Curare	N_2O+Meperidine	I.V.	0	48
7	53	F	Lt	355	C+I	Thiopental	Curare	N_2O+Meperidine	I.V.+O	0	1.5
8	22	M	Rt	15	C+I	Thiopental	Succinylcholine	N_2O	I.V.+O	0	0
9	17	F	Rt	30	C+I	Thiopental	Succinylcholine	N_2O	I.V.+O	0	0.5
10	49	F	Rt	29	I	Thiopental	Succinylcholine	N_2O+ether	I.V.+O	200	0
11	17	F	Lt	90	I	Thiopental	Tubocurarine	N_2O	I.V.	0	5‡
12	61	F	Rt	64.5	I	Thiopental	Tubocurarine	Halothane	I.V.+O	750	0
13	35	M	Lt	19.5	None	Thiopental	Succinylcholine	N_2O	None	500	0
14	20	F	Lt	62.5	C+I	Thiopental	Succinylcholine	N_2O+Halothane	O*	750	0
15	49	F	Rt	16	C+I	Thiopental	Succinylcholine	N_2O+Halothane	O*	500	0
16	18	M	Lt	8.5	C+I	Thiopental	Succinylcholine	N_2O+Halothane (continuous epidural)	O*	700	0

C = Continuous.
I = Paroxysmal or intermittent.
I.V. = Intravenous (during surgical procedures).
O = Given orally for preoperative control of systems.
O* = Administered immediately preoperatively for blood pressure control during surgical procedure.
† = Given as continuous infusion.
‡ = Norepinephrine infusion terminated after blood transfusion in recovery room.
Except in patient 13, all tumors were adrenal in origin.

studied. It is not practical to study every patient with hypertension and certainly not all those scheduled for operation. However, the diagnosis must be considered in patients with hypertension under the age of 30; in patients with hypertension and evidence of hypermetabolism such as heat intolerance, sweating or weight loss; in hypertensive patients with paroxysmal episodes of any description; in cases of hypermetabolism in the absence of hyperthyroidism and in patients with diabetes mellitus and hypertension. The presence of a pheochromocytoma must also be excluded in patients with von Recklinghausen's syndrome or von Hippel-Lindau disease. A history of sweating, heat intolerance and weight loss and postural fall in blood pressure in patients with hypertension have been most valuable to us in suggesting the diagnosis.

Many procedures, measurements and tests are useful in screening patients for pheochromocytomas. However, none are sufficiently reliable to enable the physician to detect every case in a routine manner. Pharmacologic agents, particularly phentolamine (Regitine), to lower blood pressure, and histamine, to elevate blood pressure, had been widely used. Phentolamine is used to screen patients with persistent hypertension. A fall in blood pressure of 35/25 mm. of mercury within two minutes following the intravenous injection of 5 mg. of phentolamine is considered a positive test. False negative tests occur and false positive tests are frequent, particularly when the patient is azotemic or has been treated with sedative and narcotic drugs. Histamine, in doses of 0.025 to 0.05 mg. injected intravenously will provoke a paroxysm in patients with intermittent symptoms. A blood pressure increase of at least 60/30 mm. of mercury within four minutes of injection is considered positive when it exceeds the response provoked by the cold pressor test. False positive and negative results occasionally occur. The small but definite risk and the error involved in the use of these agents has stimulated the development and use of assays for the catecholamines and their metabolites. Most pheochromocytomas release sufficient amounts of catecholamines to produce significant increases in plasma levels of epinephrine and/or norepinephrine and in the urinary excretion of these amines and their metabolites. The data obtained from such assays must be used in conjunction with all other information available, including the circumstances under which the

study was conducted. A single measurement of these substances will not always be adequate nor is there agreement as to which assay will least often fail to detect pheochromocytomas.[10, 11] Care must be exercised to avoid spurious elevations in values obtained in the procedure employed, produced by foods and drugs.

Normal values for epinephrine, norepinephrine and their metabolites appear in figure 1. The plasma levels in the figure were obtained using a modification of the ethylenediamine technique.[12] These concentrations are higher than those reported by Wallace *et al.*[13] and by most investigators using a trihydroxyindole procedure. Although the lower values are more accurate estimations of the concentrations of these amines, most investigations of patients with pheochromocytomas have been done using methods with normal ranges comparable to those illustrated. Values for the urinary excretion of the metanephrines are tentative and those of Smith and Weil-Malherbe[14] are shown. Although the rate of excretion in normal subjects reported by different laboratories have not been in agreement, the order of magnitude appears to be correct.[14-16] They are all lower than values anticipated on the basis of the metabolism of radioactive catecholamines injected intravenously.[17]

In general, the patients with persistent hypertension and other symptoms or frequent paroxysms can be expected to show elevations in plasma and urinary amine levels and 3-methoxy-4-hydroxy mandelic acid excretion. Care, however, must be exercised in evaluating patients whose attacks are intermittent and infrequent and of short duration. In these patients, plasma should be obtained during a spontaneous attack or one induced by histamine. Urine specimens should also be collected during periods in which the patient has clinical attacks. Since epinephrine and norepinephrine appear in the urine earlier than their products of metabolism[17] the exact timing of the collection will depend upon which substance is to be measured. The small amount of these potent amines required to produce brief attacks may not cause much alteration in the 24 hour excretion of the hormones or their metabolites.[12, 18] To minimize difficulty in confirming the diagnosis in such patients, activity should be controlled during collections. Normal individuals when emotionally and physically stimulated may release even greater amounts of catecholamines than some patients with pheochromocytoma, and many laboratories will report, as normal, values as high as 200 μg. of catecholamines per day.

Localization

When the diagnosis of pheochromocytoma has been made, every effort must be directed toward the location of the tumor in order to properly plan the surgical procedure. According to Gitlow *et al.*,[8] 98 per cent of the tumors reported were found in the abdominal cavity. Approximately 90 per cent of these were found in or near the adrenal gland, more commonly on the right side. The next most frequent site was the thorax and only two of the extra-abdominal tumors, a cervical and an intracranial lesion, were not visualized by roentgenographic examination of the chest. Although multiple tumors occur in approximately 15 to 20 per cent of all patients reported, their occurrence in children may be as high as 50 per cent. Reported tumors vary in size from less than one gram to several kilograms; the majority, however, weigh less than 100 grams. Approximately 20 to 25 per cent of pheochromocytomas can be localized by palpation or inducing a paroxysm by massage over some portion of the abdomen. Tumors occurring outside the region of the adrenals have been most commonly found in the paraganglia, the organ of Zuckerkandl and in the urinary bladder. The localization of tumors in the bladder is facilitated by the association of symptoms with the act of micturition.

Finding a significant amount of epinephrine in the urine or plasma strongly suggests an adrenal medullary origin. However, the absence of epinephrine does not exclude the adrenal as the site, since the majority of norepinephrine-producing tumors are also found there. Epinephrine-producing tumors may also be found in the organ of Zuckerkandl,[19] and we have studied one patient, not treated at this hospital,[20] who had an epinephrine-producing pheochromocytoma of the bladder. Her plasma levels were 7.4 μg. of norepinephrine and 2.5 μg. of epinephrine per liter, and the tumor contained 0.6 and 0.3 mg. per gram

of tumor of norepinephrine and epinephrine, respectively. The latter values were obtained after chromatographic separation of the amines.

Additional procedures are frequently required to localize the tumor, including intravenous pyelograms, presacral oxygen or carbon dioxide contrast studies, tomograms of the kidney and various combinations of these techniques. Aortography is useful, and the risk has been reduced by injection of the dye into a catheter inserted through the femoral artery.

The analysis of catecholamines in several plasma samples obtained through a radiopaque catheter, introduced into the vena cava under radiographic control, has also been useful in localizing the level of these tumors.

The reported frequency of fruitless explorations for pheochromocytomas varies but has been as high as 25 per cent. At present, using the procedures outlined above, it should not be necessary, with rare exceptions, to resort to surgical exploration to establish the diagnosis, nor can exploration be depended upon to exclude the presence of a pheochromocytoma. However, such a procedure may be required to locate the source of the amines even after the diagnosis has been firmly established, particularly since a similar clinical picture has been reported with adrenal medullary hyperplasia.[21, 22]

Preoperative Preparation

Iseri *et al.*[23] first reported the value of oral phentolamine in the preoperative and surgical management of these patients. Others have used agents such as dibenamine with a more prolonged action and found them helpful. Most of the patients treated at this hospital in the last 10 years have received oral phentolamine preoperatively to alleviate their symptoms. In the past three years an effort has been made to establish adequate control of symptoms both before and during the surgical procedure by using oral phentolamine. Since a patient will occasionally show a striking fall in blood pressure or marked tachycardia with the initial dose of phentolamine, a test dose of 12.5 to 25 mg. is administered under careful observation. Frequent measurements of blood pressure are made to ascertain the length of action of this dose, and thereafter the dose and the frequency of administration are increased until satisfactory control of symptoms is evident. It is frequently difficult, impossible or unnecessary to restore the blood pressure to completely normal levels, particularly in patients with persistent hypertension. Although doses as high as 200 mg. every two hours have been used, most of our patients have become asymptomatic on doses of 50 to 100 mg. every four hours. Administration of the drug is then continued and the last dose given just before operation. After treatment with the blocking agent has been instituted, localization studies may be carried out without inducing serious symptoms. When the hematocrit determination is repeated after several days of treatment, a reduction is usually noted. Brunjes *et al.*[24] have reported that patients with pheochromocytomas may have a chronic hypovolemic state and a decreased red cell mass preoperatively. In their patients the total body hematocrit was considerably lower than the venous hematocrit. When restudied after surgical removal of a pheochromocytoma, the plasma volume became normal and the discrepancy between venous and total body hematocrit decreased. Since blood transfusions are not without hazard, restoration of the blood volume by treatment with oral phentolamine is valuable.

During exploration if the tumor has not been localized preoperatively, or if multiple tumors are suspected, complete adrenergic blockade should be avoided so that manipulation of masses containing catecholamines will produce a rise in blood pressure, thereby facilitating identification.

Anesthetic Management

Since hypoxia as well as catecholamines appears to increase myocardial irritability, adequate ventilation during the procedure and pretreatment with phentolamine should minimize the incidence of arrhythmias and prevent serious alterations in blood pressure. Rapid induction with thiopental has been used with excellent results in our patients and in those reported by others. Tracheal intubation is accomplished only after proper relaxation has been obtained with curare or succinylcholine. Although nitrous oxide and oxygen have been used more extensively, ether and halothane have been found satisfactory. Reservations

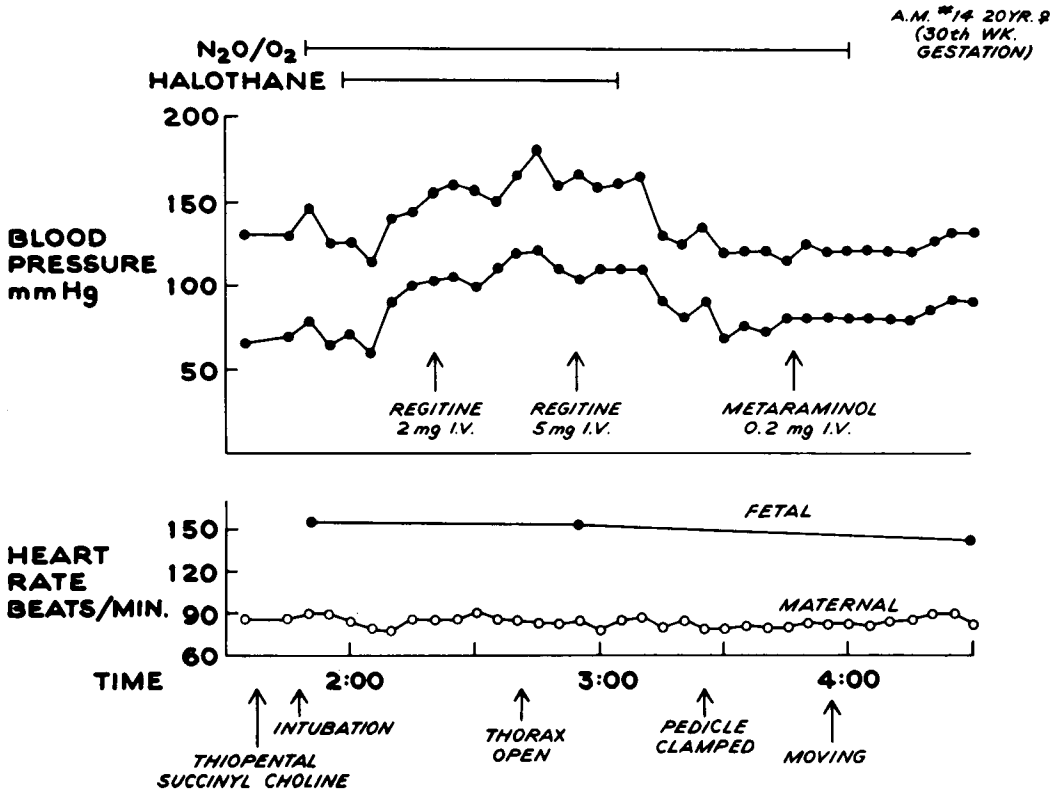

FIG. 2. The anesthesia record of a 20 year old woman who underwent surgical removal of a left adrenal pheochromocytoma during her 30th week of pregnancy. The patient was treated with phentolamine, 50 mg. every four hours, until the time of operation. Note the lack of effect of additional phentolamine given intravenously at operation and the stability of the blood pressure after the tumor had been removed.

against the use of curare, because of its "histamine-like action," and ether, because of its "sympathomimetic qualities," have not been supported by our clinical experience. Good relaxation must be provided since tumors may not be easily accessible, particularly through abdominal incisions. In a few clinics spinal anesthesia has been used with satisfaction.

The majority of deaths attributed to treatment of these tumors has been caused by irreversible hypotension following their removal. Cerebral vascular accidents and congestive heart failure following uncontrolled elevations in pressure during the procedure also occur. The control of hypertensive crises may be accomplished by the use of a constant intravenous infusion of diluted phentolamine, first suggested by Grimson *et al.*[25] However, the entire procedure has been simplified by the use of oral phentolamine or longer acting agents, supplemented if necessary by intravenous phentolamine.

The majority of reports on the control of hypotension following the removal of a pheochromocytoma emphasize the use of pressor agents. It is now very clear that the fall in blood pressure is not due primarily to a resetting of pressor receptors or an acquired resistance to the pressor effects of endogenously released norepinephrine as many have postulated. The major factor appears to be the reduction of blood volume. In these patients blood pressure can be sustained at a desirable level by the transfusion of blood beyond the amount of estimated loss in order to restore a normal blood volume. Expansion of the blood volume preoperatively by oral phentolamine administration as suggested by Johns

and Brunjes [26] can reduce the need for transfusion of blood. Prolonged administration of pressor agents for maintenance of blood pressure is eliminated by restoration of blood volume. This is illustrated by the pulse and blood pressure changes during anesthesia and surgery in one of our patients (fig. 2). This patient, a 20 year old woman in the thirtieth week of gestation, was noted at the twenty-second week of pregnancy to have a trace of albumin and glucose in her urine. Sweating and hypertension were noted at the twenty-sixth week. Because she failed to respond to antihypertensive therapy, her physician suspected a pheochromocytoma and referred her to the hospital for further study. When the diagnosis was established she was treated with phentolamine and her symptoms were adequately controlled on 50 mg. every four hours. The injection of 0.025 mg. of histamine caused no elevation above her resting blood pressure level of 140/90 mm. of mercury two hours after taking the medication. That her lack of symptoms was due to the treatment was suggested by finding plasma levels of 10.4 and 2.4 μg./liter of norepinephrine and epinephrine while given phentolamine. During surgical removal of the tumor, femoral artery blood pressures were recorded and rapid fluctuations were not observed. Phentolamine was given twice intravenously in doses of 2 and 5 mg. during the procedure to test the extent of adrenergic blockade and little change in pressure was noted (fig. 2). Upon ligation of the vessels draining the tumor there was a fall in blood pressure but pressor drugs were not required. Her course was typical of patients prepared in this manner.

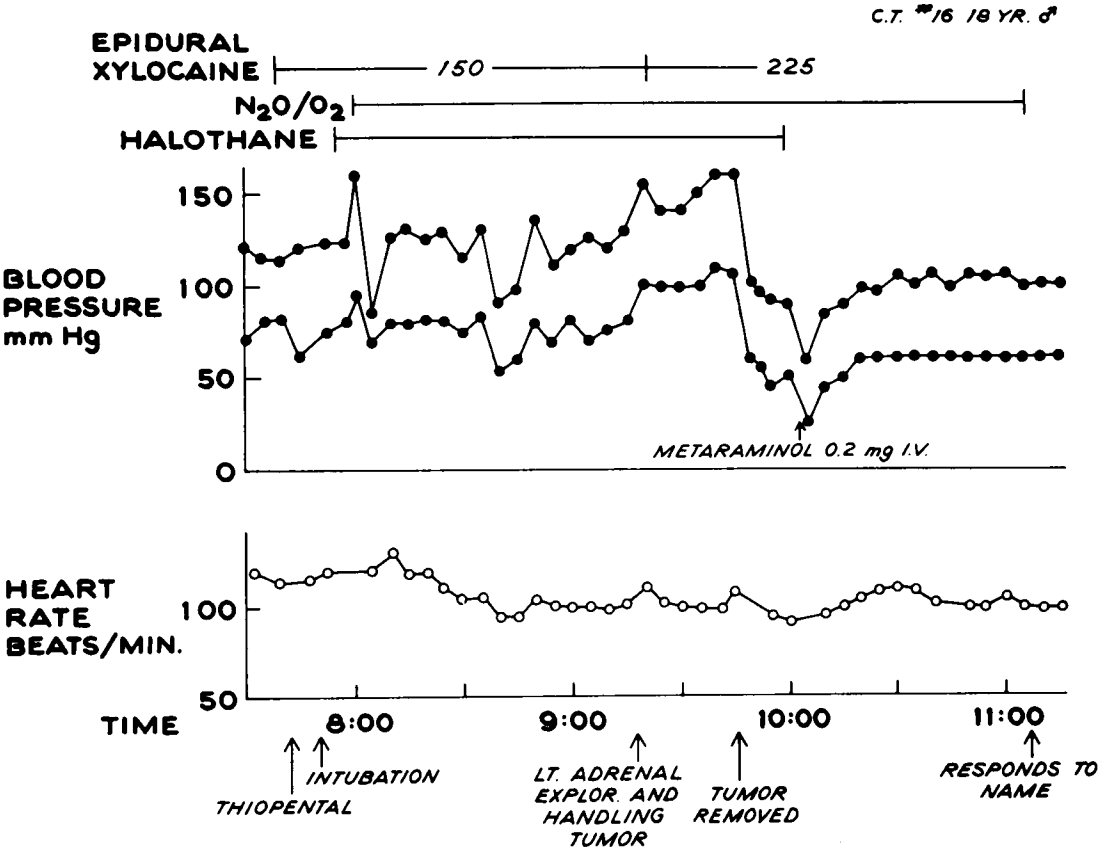

FIG. 3. The anesthesia record of an 18 year old male with von Recklinghausen's disease during the surgical removal of a left adrenal pheochromocytoma. This patient was given phentolamine, 50 mg. every six hours. However, a complete adrenergic block was not sought because the tumor had not been accurately localized preoperatively.

In patient 16, an 18 year old man with von Recklinghausen's disease, we avoided complete blockade with phentolamine because the tumor had not been outlined prior to surgical exploration and because of the possibility of multiple tumors. Aortography, pyelograms and presacral oxygen insufflation combined with tomograms had failed to reveal a tumor and the patient did not have significantly increased amounts of epinephrine in urine or plasma. Norepinephrine excretion was 1,000 μg. in 24 hours and the plasma level varied between 9 and 12 μg./liter. Seven blood specimens were obtained at various levels in the vena cava and right atrium. Except for the elevation noted in the adrenal region (16.1 and 0.5 μg. of norepinephrine and epinephrine per liter of plasma) concentrations were not significantly different from those in the antecubital vein. Since little epinephrine was found in the sample obtained at the adrenal level, the increase could not be attributed to normal adrenal medullary secretion which is predominantly epinephrine. Fluctuations in blood pressure during the operation were greater in this patient but never dangerously so. However, it was possible to elevate the pressure by manipulating a small mass in the left adrenal which proved to be pheochromocytoma, weighing 8.5 g. Figure 3 shows changes in the pulse and blood pressure in this patient.

Postoperative Course and Prognosis

The postoperative problems in these patients, once the blood pressure has become stabilized, are not very different from those in other hypertensive patients undergoing comparable procedures. Occasionally it is difficult to establish the absence of additional tumors or metastases from a malignant pheochromocytoma. None of the tumors removed from patients in table 1 have been found to be malignant, although reviews of the literature indicate that 7–10 per cent of these metastasize. If a fall in blood pressure does not follow the removal of a pheochromocytoma, the presence of additional tumor tissue is suggested. Under these circumstances, histamine and phentolamine have been used to substantiate such a suspicion. More commonly, the question is raised when a secondary elevation of blood pressure occurs during the first few days postoperatively. This occurred in 5 of the 9 of our patients with persistent hypertension. This elevation continued for only two weeks in one patient and as long as three years in another. The second patient, in fact, has not had a pressure lower than 140/80 mm. of mercury and has, under stress, exhibited pressures up to 180/100 mm. of mercury. There are patients with underlying esential hypertension in whom the blood pressure is not materially altered by removal of a tumor. Renal hypertension may also occur in these patients. In a patient previously reported [12] the hypertension was not ameliorated until removal of an ischemic kidney. In a majority of the patients, the blood pressure will return to normal in a period of weeks or months. However, repetition of diagnostic studies during or after the immediate postoperative period may be required. Symptoms may recur later because of a second tumor or metastases, and the physician must continue to follow the patient with this in mind.

Summary

Pheochromocytoma should always be considered as a possible cause of a variety of paroxysmal disorders or of hypertension, particularly when asociated with hypermetabolism, glycosuria, weight loss, severe sweating, postural hypotension or neurocutaneous syndromes. The prognosis in patients treated for pheochromocytoma is excellent when the diagnosis is established before permanent cardiac damage and cerebrovascular disturbances occur. In these patients, the risk of surgical removal of these tumors is small after suitable preoperative preparation, followed by good anesthetic and surgical management. However, when such patients are subjected to unrelated surgical procedures without the diagnosis of pheochromocytoma having been suspected, the mortality rate is estimated to be as high as 50 per cent. Thus, the prognosis depends upon the establishment of the diagnosis of the tumor. The presence of a functioning pheochromocytoma can be confirmed or negated in the great majority of patients by intelligent use of methods for measuring the catecholamines and their metabolites in plasma and urine.

Preoperatively, serious pathologic disturb-

ances, such as hypertension, hypermetabolism, and hypovolemia, can be controlled by oral doses of phentolamine given in sufficient quantities. Studies to localize the tumor can then be accomplished with greater ease and safety. If plasma and red cell volumes return to normal during this period or are restored by transfusion, oral phentolamine administered to the patients, up to and at the time of their being anesthetized, reduces or eliminates the need for intravenous injections to prevent hypertensive crises during the operation, and reduces the need for norepinephrine to prevent vascular collapse after the tumor has been removed.

Anesthetic management of these patients has been handled successfully by using various types of anesthesia, including nitrous oxide, halothane, ether, and epidural block in combination with muscle relaxants following thiopental induction.

Supported in part by U.S.P.H.S. Grants H-6285 and A-4426.

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