PHEOCHROMOCYTOMA: SURGICAL AND ANESTHETIC
MANAGEMENT • †

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One of the curable forms of hypertensive cardiovascular disease is
that caused by pheochromocytoma, although the actual frequency of
these tumors is low. In a series of over 2,400 hypertensive patients
treated surgically in our clinic, only 15 have been found to have a
pheochromocytoma, an incidence of about 0.5 per cent (1). The appal-
ing fact, however, that is revealed by a review of the literature is that
pheochromocytoma is diagnosed only at autopsy in about 70 per cent
of reported cases (2). Since surgical removal is almost always fol-
lowed by cure of the disease, it is important that the index of suspicion
be high, that diagnostic points be kept clearly in mind, and that the
management of the patient before, during, and after operation be thor-
oughly understood and properly carried out. Several excellent re-
views of the subject have recently appeared in the literature (2, 3, 4).

Pheochromocytomas develop from chromaffin tissue and are thus
located wherever it is found. Ninety per cent of them are found in the
adrenal medulla, but they may also occur in the lumbar or thoracic
paravertebral spaces, in and about the great vessels of the abdomen,
in the organ of Zuckerkandl at the bifurcation of the aorta, in the celiac
ganglion, and even within the cranial cavity (2). The tumors are bi-
lateral in 10 per cent and are malignant in about 10 per cent of the
cases (3).

Pheochromocytomas secrete epinephrine and norepinephrine in
varying amounts and proportions (5). This fact has important impli-
cations with respect to the operative management of these patients, as
will be discussed in detail below.

Although the hypertension of pheochromocytoma is commonly
paroxysmal, it may be nonparoxysmal and the disease be almost indis-
tinguishable from essential hypertension. Once the lesion is suspected,
however, various measures may be employed to verify the diagnosis,
since no single test is infallible. These measures include the eliciting
of certain characteristic signs and symptoms, roentgenologic examina-
tions, the use of various test drugs, and finally operative exploration.

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Signs and Symptoms

Smithwick and his collaborators (2) in a comprehensive study of the problem have laid particular emphasis on certain signs and symptoms that occur frequently in patients with pheochromocytoma but are not usually found in patients with essential hypertension. Most of these appear to be related to the presence of epinephrine or norepinephrine in the circulating blood. They are excessive sweating, peripheral vasomotor phenomena (vasoconstriction), elevated body temperature (1 F. or more) normal cold-pressor blood pressure response, fasting blood sugar level of 120 mg. per 100 cc. or more, basal metabolic rate of 20 per cent or more, postural tachycardia and postural hypotension, glycosuria, and paroxysmal attacks of hypertension. These data are readily obtained by any physician and require no special facilities. When any of them is present, the physician should be on the alert for pheochromocytoma.

Roentgenologic Examinations

Intravenous pyelography, laminography, and perirenal air injection may be helpful in visualizing the location of a pheochromocytoma.

Tests with Drugs

Drugs that are useful in the diagnosis of pheochromocytoma fall into two categories: (1) those that precipitate attacks of hypertension, including histamine, tetra-ethyl ammonium chloride or bromide, and methylcholine hydrochloride (mecholyl), and (2) those that block the effects of the circulating pressor substances as shown by a substantial drop in blood pressure. These include piperoxan, dibenamine, and regitine®. The provocative test drugs may be dangerous unless restricted to use in patients with normal blood pressure between paroxysms. One of the blocking drugs, regitine appears to be the most useful. It is safer and more pleasant than piperoxan. Although it gives occasional falsely positive reactions, regitine intravenously does not appear to produce falsely negative reactions (6). A test is positive when the systolic blood pressure falls 35 mm. or more and the diastolic pressure falls 25 mm. or more following rapid intravenous injection of 5 mg. of the drug. An excellent report by Gifford, Roth, and Kvale (6) on the use of test drugs has recently appeared.

Surgical Management

In this clinic, surgical approach to the adrenal gland is made through the Smithwick incision for thoracolumbar splanchnicectomy (7). The twelfth rib or eleventh and twelfth ribs are removed, the diaphragm is divided, and a retropleural, retroperitoneal dissection carried out. The kidney and adrenal gland are fully exposed. The entire lumbar
paravertebral region can be explored if the tumor is in the extra-adrenal location or if the question of multiple tumors arises. Bilateral exposure is easily and safely done at one stage. We believe that the posterior approach facilitates removal of pheochromocytoma. If no tumor is found in the usual locations but tests indicate the presence of an actively functioning pheochromocytoma, laparotomy or rarely even thoracotomy may be necessary to locate the tumor. Utmost gentleness is necessary in the removal of these tumors in order not to precipitate a paroxysm of hypertension. The blood supply to the mass should be secured as quickly as possible to aid still further in this regard. Squeezing the tumor must be avoided. Short-acting blocking drugs such as regitine must be on hand in case the blood pressure does rise to alarming levels.

**Anesthetic Management**

The dangerous reactions that occur during the removal of pheochromocytoma are similar to those manifested by patients with essential hypertension undergoing splanchnicectomy, except that they are likely to be exaggerated. Therefore, in our clinic the principles and techniques which have been found to be successful in the latter situation have been applied to the former.

The hazards to be avoided result from extreme fluctuations in blood pressure caused by excessive amounts of epinephrine and norepinephrine in the circulating blood during the first part of the procedure and by the abrupt decrease in secretion of these substances when the tumor is removed. Very high levels are frequently recorded during the immediate preoperative period when the patient is being prepared and transported to the operating room. Especial care in moving the patient must be exercised to avoid pressure over the tumor. Pentobarbital in amounts adequate to insure sleep is ordered for the night preceding operation. Preoperative medication consists usually of suitable doses of pentobarbital two hours and of morphine sulfate and scopalamine one hour before operation. When patients are extremely excited or apprehensive, anesthesia is induced in their own rooms using a drip of thiopental sodium, 0.3 per cent, and they are then transported to the operating room. If this has not been done, an intravenous infusion of 5 per cent dextrose in water is started upon arrival in the operating room and then induction is accomplished by slow intravenous injection of a mixture of sodium pentobarbital, 50 mg., and thiopental sodium, 150 mg., to the point where the patient barely fails to respond. Inhalation anesthesia is then started with nitrous oxide-oxygen-ether and intubation is done as soon as the level of anesthesia is adequate. The patient is turned to the prone position, great care being exercised to avoid pressure over the abdomen either during the moving or after the patient is in position. Fluctuations in blood pressure are likely to occur during the induction. A fall in pressure often results from in-
jection of the barbiturate and following intubation and change of position. The pressure usually rises during the early periods of inhalation anesthesia.

The changes in pressure may be minimized by gentle handling and slow administration of agents. Hypotension, which does not respond to lightening of the anesthesia, is treated by the intravenous infusion of a solution of dextrose in water containing either phenylephrine (neosynephrine®), 10 mg. per liter, or 1-norepinephrine, 4 mg. per liter. Transfusion of whole blood is begun as soon as the patient is placed in position. It is usually necessary to assist respiration during the time the patient is in the prone position in order to maintain adequate oxygenation. During manipulation of the tumor the blood pressure may
rise to extreme heights. We have preferred to control this complication by asking the surgeon to desist while the anesthesia is deepened with ether. Regitine is kept at hand for use if the crisis becomes alarming, but so far we have not found it necessary to use it.

When the tumor is removed there is an immediate profound fall in blood pressure. It is essential that (1) adequate circulating blood volume be provided by transfusion, and (2) peripheral vasoconstriction be maintained until the patient becomes adjusted.

The blood loss is usually fairly small but it is our experience that

![Graph showing blood pressure and pulse](image)

**Fig. 2.** Record of blood pressure and pulse following patient's return to recovery room, showing decrease in pulse rate when neosynephrin was substituted for epinephrine in the infused fluid.
at least 500 cc. of blood should have been transfused by the time the tumor is removed, and that transfusion should be continued until a total of 1 liter is given. Continuous infusion of a vasoconstrictor agent is necessary during the operation and for a variable period thereafter. In our early cases epinephrine, 1:100,000, was used for this purpose. Both l-norepinephrine and phenylephrine are satisfactory, and have less cardiac effect than epinephrine. Figures 1 and 2 illustrate the operative and immediate postoperative course of a 26 year old woman from whom a pheochromocytoma was removed.

One death occurred in our series of 14 cases. The patient was a 55 year old woman who had a twelve year history of hypertension with paroxysmal attacks and symptoms characteristic of pheochromocytoma. Operation was undertaken although it was realized that the risk was serious. Premedication and induction were conducted in the manner previously described. The injection of barbiturate for induction was followed by a precipitous drop in blood pressure to 80 mm. systolic and 50 mm. diastolic. Infusion of l-norepinephrine resulted in restoration of the pressure to 260 mm. systolic and 120 mm. diastolic. Inhalation anesthesia with nitrous oxide-oxygen-ether was started and an endotracheal tube inserted as soon as relaxation was adequate. The blood pressure continued to be very labile, but could be maintained at levels between 200 to 140 mm. systolic and 110 to 100 mm. diastolic. The patient was placed in the prone position, transfusion started and operation performed. Although the patient was obese, ventilation was satisfactory and the blood appeared to be well oxygenated. Technical difficulties with the intravenous apparatus rendered it impossible to administer the blood is rapidly as was desirable and an increasing pulse rate caused some apprehension. However, blood pressure was well maintained except for an episode of about five minutes during manipulation for exposure of the tumor, when it was promptly controlled by increased infusion of l-norepinephrine. The expected fall occurred when the large tumor was removed, but the pressure was again restored by more rapid infusion of l-norepinephrine. At the close of operation, the pulse was 120 per minute, and of fair quality, the blood pressure was 90 mm. systolic and 60 mm. diastolic, and the patient was breathing well. When she was turned from the prone position to her back, cessation of respiration and cardiac activity occurred. The heart was immediately exposed—not more than ninety seconds elapsed—and found to be in standstill. All efforts at resuscitation were unsuccessful.

In retrospect, it appears that inadequate blood replacement may have been a large factor in this fatality.

Results of Surgical Treatment

The total experience in our clinic has been with 15 patients having pheochromocytoma. One of these was moribund upon admission and was not operated upon. Another was seriously ill; she had had a re-
cent subarachnoid hemorrhage and died of cardiac arrest immediately after operation (see above). The other 13 have had their tumors removed and are all living and well, with normal or near normal blood pressures up to eight years after operation. These patients are being reported in detail by Smithwick et al. (2). Figure 3 shows the blood pressure data on all but our most recent case.

**Comment**

In our experience with operations on hypertensive patients having either essential hypertension or pheochromocytoma, serious accidents occur more frequently from failure to cope with episodes of hypotension than from hypertension. For this reason we avoid preparation of pa-

**PHEOCHROMOCYTOMA — A CURABLE DISEASE**

**POSTOPERATIVE FOLLOW-UP STUDIES**

![Graph showing blood pressure changes over time](image)

**FIG. 3.**


tients for operation with blocking agents and the use of these agents to reduce pressure during operation. In the event that other measures to reduce dangerous blood pressure levels are unsuccessful and it becomes necessary to employ a blocking agent, regitine is preferred because of the short duration of its action.

We agree with Apgar and Papper (8) that the selection of anesthesia is perhaps less important than understanding of the physiologic principles underlying management. The circulation must be supported. Adequate ventilation must be maintained. Endotracheal intubation is obligatory. Spinal anesthesia and cyclopropane are best avoided, the former because of the danger of circulatory collapse and the latter because it sensitizes the heart to epinephrine and norepinephrine. Rapid induction with a mixture of thiopental sodium and a muscle relaxant may precipitate a dangerous vascular collapse. Muscle
relaxing agents have not been employed for this group of patients except in one or 2 cases in which mytolon chloride was administered to facilitate intubation when splanchnicectomy was the proposed operation, and the pheochromocytoma not previously diagnosed was discovered in the course of operation. No untoward effects were noted following the use of this drug. We have noted no serious effects which could be ascribed to the sympathomimetic effects of ether.

Summary

Pheochromocytoma is a curable form of hypertensive cardiovascular disease.

Certain characteristic signs and symptoms occur in patients with pheochromocytoma that should arouse suspicion of the diagnosis.

The use of test drugs as an aid in diagnosis has been outlined briefly.

Surgical approach through an incision employed for posterior thoracolumbar splanchnicectomy is the preferred route of exposure in our clinic.

Anesthetic management of the patient before, during, and after removal of the tumor is of the utmost importance and is given in detail.

Results of surgical treatment in 13 successful cases are reported.

REFERENCES

1. Smithwick, R. H.; Personal Communication to the authors.

AUSTRALIA PLANS JOURNAL

Preliminary arrangements for the publication of a Journal by the Australian Society of Anaesthetists are well under way. An invitation from that Society for anesthetists throughout the World to submit contributions for their Journal has been extended.