Preparation for Anaesthesia - Pheochromocytoma

Fewer than 0.1 percent of all cases of hypertension are caused by pheochromocytomas, catecholamine-producing tumors derived from chromaffin tissue. [143] Nevertheless, these tumors are clearly important to the anesthetist, as 25 to 50 percent of hospital deaths in patients with pheochromocytomas occur during induction of anesthesia or during operative procedures for other causes. [144] Although usually found in the adrenal medulla, these vascular tumors can occur anywhere, such as in the right atrium, the spleen, the broad ligament of the ovary, or the organs of Zuckerkandl at the bifurcation of the aorta. Malignant spread, which occurs in fewer than 15 percent of pheochromocytomas, usually proceeds to venous and lymphatic channels with a predisposition for the liver. This tumor is occasionally familial and/or part of the pluriglandular-neoplastic syndrome known as multiple endocrine adenoma type IIa or type IIb, manifesting as an autosomal dominant trait on chromosome 10. Type IIa consists of medullary carcinoma of the thyroid, and parathyroid adenoma or hyperplasia and pheochromocytomas. Often, bilateral tumors are found in the familial form. Localization of tumors can be done with magnetic resonance imaging (MRI) or computed tomography (CT) scans, metaiodobenzylguanidine nuclear scanning, ultrasonography, or intravenous pyelography studies (in decreasing order of combined sensitivity and specificity).

Symptoms and signs that may be solicited preoperatively and that are suggestive of pheochromocytoma are excessive sweating; headache; hypertension; orthostatic hypotension; previous hypertensive or arrhythmic response to induction of anesthesia or to abdominal examination; paroxysmal attacks of sweating, headache, tachycardia, and hypertension; glucose intolerance; polycythemia; weight loss; and psychological abnormalities. In fact, the occurrence of combined symptoms of paroxysmal headache, sweating, and hypertension is probably a more sensitive and specific indicator than any one biochemical test for pheochromocytoma [143, 145, 146] (Table 25–9). Despite more than 2,000 articles in the literature about pheochromocytomas, little is known about what factors in care affect perioperative morbidity. [147, 148, 149]

TABLE 25–9. Characteristics of Tests for Pheochromocytoma

			LIKELIHOOD RATIO	
TEST/SYMPTOMS	**SENSITIVITY (%)**	**SPECIFICITY (%)**	***POSITIVE RESULT*[a]**	***NEGATIVE RESULT*[b]**
Vanillylmandelic acid excretion	81	97	27.0	0.20
Catecholamine excretion	82	95	16.4	0.19
Metanephrine excretion	83	95	16.6	0.18
Abdominal computed tomography scan	92	80	4.6	0.10

Concurrent paroxysmal hypertension, headache, sweating, and tachycardia[c]	90	95	18.0	0.10

[a]Ratio representing the likelihood of a positive result is obtained by dividing sensitivity by 1 and then subtracting specificity.

[b]Ratio representing the likelihood of a negative result is obtained by subtracting sensitivity from 1 and then dividing by specificity.

[c]Data for concurrent paroxysmal symptoms are best estimates from available data.

Modified from Pauker and Kopelman[145]

Although no controlled, randomized, prospective clinical studies have studied the value of preoperative use of adrenergic receptor–blocking drugs, the use of such drugs is generally recommended before surgery. These drugs probably reduce the complications of hypertensive crisis, the wide blood pressure fluctuations during manipulation of the tumor (especially until venous drainage is obliterated), and the myocardial dysfunction that occur perioperatively. The reduction in mortality associated with resection of pheochromocytoma (from 40–60% to the current 0–6%) occurred when a-adrenergic receptor blockade was introduced as preoperative preparatory therapy for such patients [146, 147, 148, 149, 150, 151]

TABLE 25–10. Preoperative Mortality Associated With Resectioning of Pheochromocytoma[a]

YEAR OF SERIES	STUDY	MORTALITY (%)	PATIENTS IN SERIES (n)
1951	Apgar (review)	45.0	91
1951	Apgar	33.0	12
1963	Stackpole	13.0	100
Earlier than 1960	Mayo Clinic	0.0–26.0	101 (?)
Later than 1960	Mayo Clinic	2.9 (?)	44 (?)
Earlier than 1967	Modlin (without a blockade)	18.0	17
Later than 1967	Modlin (with;a blockade)	2.0	41

TABLE 25–10. Preoperative Mortality Associated With Resectioning of Pheochromocytoma[a]			
YEAR OF SERIES	**STUDY**	**MORTALITY (%)**	**PATIENTS IN SERIES (n)**
1976–1993	Scott	3.0	33
1976–1993	Roizen	0.0	56
1974–1994	Lucon	2.0	50
[a]Data were abstracted from studies discussed in Roizen et al[149] and include more recent patient information.			

a-Adrenergic receptor blockade with prazosin or phenoxybenzamine restores plasma volume by counteracting the vasoconstrictive effects of high levels of catecholamines. This re-expansion of fluid volume is often followed by a decrease in hematocrit. Because some patients may be very sensitive to the effects of phenoxybenzamine, it should initially be given in doses of 20 to 30 mg/70 kg orally once or twice a day. Most patients usually require 60 to 250 mg/d. Efficacy of therapy should be judged by a reduction in symptoms (especially sweating) and a stabilization of blood pressure. For patients who have carbohydrate intolerance because of inhibition of insulin release mediated by a-adrenergic receptor stimulation, a-adrenergic receptor blockade may reduce fasting blood sugar levels. For patients who exhibit ST-T changes on ECG, long-term preoperative a-adrenergic receptor blockade (1–6 months) has produced ECG and clinical resolution of catecholamine-induced myocarditis. [147, 148, 149, 150, 151, 152]

b-Adrenergic receptor blockade with propranolol is suggested for patients who have persistent arrhythmias or tachycardia, [147, 148, 149, 150, 151, 152] because these conditions can be precipitated or aggravated by a-adrenergic receptor blockade. b-Adrenergic receptor blockade should not be used without concomitant a-adrenergic receptor blockade, lest the vasoconstrictive effects of the latter go unopposed, thereby increasing the risk of dangerous hypertension.

The optimal duration of preoperative therapy with phenoxybenzamine has not been studied. Most patients require 10 to 14 days, as judged by the time needed to stabilize blood pressure and to ameliorate symptoms. On the basis of my experience, this is a minimal period. [148, 149, 152] Because the tumor spreads slowly, little is lost by waiting until medical therapy has optimized the patient's preoperative condition. Accordingly, I recommend using the following criteria:

1. No in-hospital blood pressure reading higher than 165/90 mm Hg should be evident for 48 hours before surgery. We often measure arterial blood pressure every minute for 1 hour in a stressful environment (our postanesthesia care unit). If no blood pressure reading is greater than 165/90, this criterion is considered satisfied.
2. Orthostatic hypotension should be present, but blood pressure on standing should not be lower than 80/45mm Hg.
3. The ECG should be free of ST-T changes that are not permanent.
4. No more than one premature ventricular contraction should occur every 5 minutes.

Other drugs, including prazocin, calcium channel–blocking drugs, clonidine, and magnesium, have also been used to achieve suitable degrees of a-adrenergic blockade prior to surgery.

Although specific anesthetic drugs have been recommended, I believe that optimal preoperative preparation, a gentle induction of anesthesia, and good communication between surgeon and anesthesiologist are most important. Virtually all anesthetic agents and techniques (including isoflurane, sevoflurane, sufentanil, remifentanil, fentanyl, and regional anesthesia) have been used with success. In fact, all agents studied are associated with a high rate of transient intraoperative arrhythmias [148] (Table 25–11). I have avoided halothane because it sensitizes the myocardium and may increase arrhythmogenic frequency, and desflurane, because it may precipitate nonneurogenic catecholamine release. No good data indicate these biases are appropriate.

TABLE 25–11. Incidence of Perioperative Complications in a Randomized Study of Patients Undergoing Resectioning of Pheochromocytoma Under One of Four Anesthetic Techniques

	ANESTHETIC[a]			
	ENFLURANE (6)	***HALOTHANE (6)***	***DROPERIDOL AND FENTANYL (7)***	***REGIONAL (5)***
Ventricular tachycardia				
Needing no treatment	5	5	6	5
Needing treatment	0	1	1	0
Vasodilator needed				
Intraoperatively	6	6	7	5
Postoperatively	0	1[b]	1[b]	0
Vasopressor needed				
Intraoperatively	0	1	1	0
Postoperatively	0	0	0	0
Myocardial infarction[c]	0	0	0	0
Renal failure[c]	0	0	0	0
Congestive heart failure[c]	0	1	1	1

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	ANESTHETIC[a]			
	ENFLURANE (6)	***HALOTHANE (6)***	***DROPERIDOL AND FENTANYL (7)***	***REGIONAL (5)***
Stroke[c]	0	0	0	0
Death[c]	0	0	0	0

[a]Number of patients shown in parentheses

[b]Not all the abnormally secreting tumor tissue was removed from the patient.

[c]Occurring postoperatively

Data from Roizen et al[148]

Because of ease of use, the author prefers to give phenylephrine hydrochloride (Neo-Synephrine) or dopamine for hypotension and nitroprusside for hypertension. Phentolamine (Regitine) has too long an onset and duration of action. Occasionally (five times in >50 pheochromocytoma resections) I have used a b-adrenergic blocking agent (esmolol is now the preferred one) for severe tachycardia without hypertension or volume depletion. Painful or stressful events such as intubation often cause an exaggerated stress response in less than perfectly anesthetized patients who have a pheochromocytoma. This response is caused by release of catecholamines from nerve endings that are “loaded” by the reuptake process. Such stresses may cause catecholamine levels of 200 to 2,000 pg/mL in normal patients. For the patient with pheochromocytoma, even simple stresses can lead to blood catecholamine levels of 2,000 to 20,000 pg/mL. However, infarction of a tumor, with release of products onto peritoneal surfaces, or surgical pressure causing release of products, can result in blood levels of 200,000 to 1,000,000 pg/mL—a situation that should be anticipated and avoided. (Ask for a temporary stay of surgery, if at all possible, while the rate of nitroprusside infusion is increased.) Once the venous supply is secured, and if intravascular volume is normal (as measured by pulmonary wedge pressure), normal blood pressure usually results. However, some patients become hypotensive, occasionally requiring massive infusions of catecholamines. On rare occasions, patients remain hypertensive intraoperatively. Postoperatively, about 50 percent remain hypertensive for 1 to 3 days—and initially have markedly elevated but declining plasma catecholamine levels—at which time all but 25 percent become normotensive. It is important to interview other family members and perhaps advise them to inform their future anesthetist about the potential for such familial disease.