Continuing Medical Education Article

Anaesthesia for phaeochromocytoma

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Phaeochromocytomas are functionally active catecholamine-secreting tumours of chromaffin tissue. These tumours are usually found in the adrenal medullae but may occur anywhere where chromaffin tissue exists. Chromaffin tissue occurs in association with the celiac, mesenteric, renal, adrenal, hypogastric, testicular and paravertebral sympathetic nervous plexuses. Although most phaeochromocytomas are found in the adrenal medulla (in 90 per cent of cases), they can occur anywhere in the body where paraganglion cells of the sympathetic nervous system are found. Multiple and extra-adrenal tumours are far more common in children (35 per cent) than in adults (eight per cent).[1] Although about 90 per cent are benign and surgically curable, they are of special interest because of the profound physiological effects produced by the release of large quantities of catecholamines. Phaeochromocytomas can also contain a variety of peptides including enkephalins, somatostatin, calcitonin, oxytocin and vasopressin and, rarely, can be a source of clinically important ectopic hormone production.[2]

Although these tumours account for elevated arterial pressure in only 0.1 per cent of the population with diastolic hypertension, the diagnosis should be suspected in any patient who develops hypertension at an early age, who has hypertension resistant to conventional therapy, or in anyone with a history of paroxysmal headaches, palpitations, sweating and pallor.

Phaeochromocytomas can also be part of an autosomal-dominant multiglandular neoplastic syndrome known as Multiple Endocrine Adenomatosis (Table). This syndrome can be categorized as Type II-a (Sipple's syndrome comprising medullary carcinoma of the thyroid, parathyroid adenoma/hyperplasia and phaeochromocytoma) or Type II-b (characterized by medullary carcinoma of the thyroid, Marfanoid appearance, mucosal adenomas and phaeochromocytoma). They can also be found as part of von Hippel-Lindau syndrome which includes multiple phaeochromocytomas in association with haemangioblastomas of the retinae, cerebellum and other areas of the central nervous system.[3]

Although most phaeochromocytomas are unilateral, about nine per cent occur bilaterally. Bilateral tumours also tend to be familial. Phaeochromocytomas may occur at any age, but occur with the greatest frequency in the fourth and fifth decades of life. Ten per cent of these tumours are found in children. In adults, the sex distribution of the patient population shows a slightly higher female preponderance (55–60 per cent). In children, the sex ratio is reversed since approximately 70 per cent of phaeochromocytomas occur in boys.[1]

Phaeochromocytomas can vary markedly in size, ranging in weight from 1 to 4000 g but average about 100 g in the adult population and 30 g in the paediatric population. The average size adult phaeochromocytoma is said to contain, however, the equivalent of one thousand ampoules of norepinephrine![1]

Pathophysiology

Since a phaeochromocytoma is a tumour of the sympa-

TABLE Medical syndromes of which phaeochromocytoma is a part

Multiple endocrine adenomatosis –Type II a (Sipple's syndrome)	Parathyroid adenoma/hyperplasia Medullary carcinoma of thyroid Phaeochromocytoma
Multiple endocrine adenomatosis –Type II b	Medullary carcinoma of thyroid Mucosal adenomas Marfanoid appearance Phaeochromocytoma
von Hippel-Lindau Syndrome	Haemangioblastoma of the retina, cerebellum or other parts of the CNS Phaeochromocytoma

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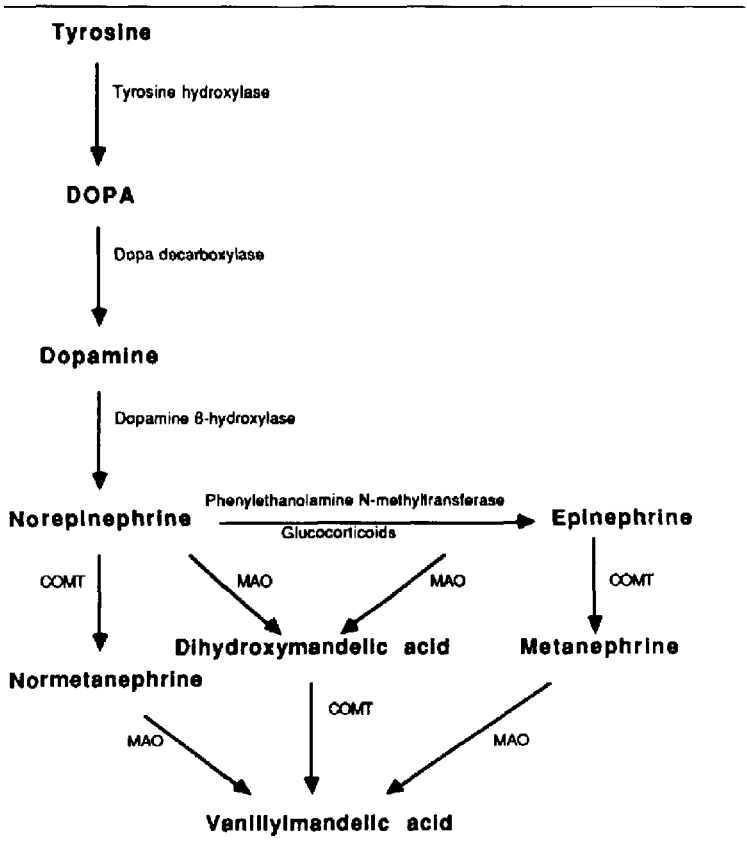

FIGURE The pathways for synthesis and breakdown of catecholamines. The rate-limiting step in catecholamine synthesis is mediated by the enzyme tyrosine hydroxylase.

thetic nervous system, a brief review of the latter is appropriate.

This system comprises two neuroendocrine systems linked together by a common group of low molecular weight substances called catecholamines which include dopamine, norepinephrine and epinephrine. Only norepinephrine is released from post-ganglionic sympathetic neurons, while both norepinephrine and epinephrine are synthesized in the chromaffin cells of the adrenal medulla and parts of the brain. Sympathetic neurons are also known as "adrenergic" neurons and the targets of their transmitters are called sympathetic or adrenergic receptors. The three general classes of these receptors include the alpha-adrenergic, beta-adrenergic and the dopaminergic receptors with subtypes for the alpha and beta receptors having been identified.

The sympathetic neuron manufactures neurotransmitters from either phenylalanine or tyrosine as is shown in the Figure. In the neuronal cytoplasm, the rate-limiting enzyme, tyrosine hydroxylase, converts tyrosine to dihydroxyphenylalanine or dopa. This is then decarboxylated to dopamine which is transported from the neuronal cytoplasm to storage granules in the axon where it is either stored unchanged or converted by another enzyme to norepinephrine. In the functional cell of the adrenal medulla, the phaeochromocyte, norepinephrine leaves the axonal granules to be methylated in the cytoplasm by an adrenal-specific enzyme called phenylethanolamine-N-methyltransferase. This forms epinephrine which is then stored in a different group of axoplasmic granules. This transformation to epinephrine requires not only this specific enzyme but also the high ambient concentration

of adrenal glucocorticoids found only in the adrenal gland. Hence, only adrenally derived phaeochromocytomas are capable of secreting epinephrine. The catecholamines epinephrine, norepinephrine and dopamine exert their physiologic effects by reversibly interacting with their appropriate receptors on target tissue. Stimulation of alpha-1 receptors on vascular smooth muscle causes vasoconstriction resulting in an increase in systemic vascular resistance and elevation of blood pressure. Alpha-2 stimulation by high concentrations of catecholamines inhibits insulin secretion of the pancreatic islet cells. Stimulation of cardiac beta-1 receptors causes the rate, contractility and automaticity of the heart to increase.

The termination of action of a catecholamine is mostly by its active reuptake by the sympathetic nerve endings. In addition, two important enzyme systems, monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT), metabolically transform the catecholamines to inactive metabolites which are excreted by the kidney. Released norepinephrine that has interacted with its receptors can be taken up again by adrenergic neurons to be stored in vesicles for reuse: any norepinephrine not retaken up can enter the systemic circulation where it is metabolized by the enzymes MAO and COMT to vanillylmandelic acid (VMA), the final common product of enzymatic breakdown. Approximately five per cent of released norepinephrine eventually appears unchanged in the urine while 95 per cent is converted to metabolic byproducts. Measurements of the urinary excretion of the metabolites of epinephrine and norepinephrine (metanephrine, normetanephrine and VMA) reflect the amount of catecholamine that has been released by adrenergic and phaeochromocytoma tissue and enzymatically degraded.

Diagnosis

Phaeochromocytomas have been called the "great mimics" because they are notoriously variable in their secretory activity. Their clinical manifestations may range from nil to symptoms like "nervousness" or anxiety attacks and signs such as episodic sweating, tremors, palpitations, sustained hypertension or congestive heart failure.

Generally, small tumours (<30 g) are less likely to store and metabolize catecholamines and more likely to release these active products into the circulation. As such they are generally more active clinically and also more readily diagnosed. They are also more frequently associated with other endocrinopathies and other endocrine tumours.[1] Small tumours are more likely to produce the classical intermittent hypertensive attacks with normotension between crises.

Large tumours (often weighing more than 250 g), on the other hand, usually produce sustained hypertension that would probably pass as essential hypertension in older patients. Urinary excretion shows relatively more inactive metabolites than the smaller tumours produce. Only about one-third of phaeochromocytomas present with the secretory crisis pattern that is described as "typical" for phaeochromocytomas.[4] Moreover, it is well documented that the concentration of free circulating catecholamines and associated haemodynamic conditions often have no correlation whatsoever.[5] Normal blood pressures and heart rates have been observed when the simultaneously determined plasma catecholamine levels were many times higher than normal. The reason for this discordance is not fully understood but it has been postulated that a chronic increase in circulating norepinephrine levels may cause a corresponding decrease in the concentration of alpha-2 receptors on resistance vessels leading to diminished pressor effects.[5]

Phaeochromocytomas occurring within the adrenal gland generally secrete both epinephrine and norepinephrine but norepinephrine is the predominant catecholamine liberated. Extra-adrenal tumours, as a rule, secrete only norepinephrine. In those rare cases where epinephrine is the main catecholamine produced, the patient may present with hypotension. Only one case has been reported in which dopamine was the major amine secreted.

Laboratory measurement of urinary catecholamines and their metabolites, normetanephrine, metanephrine and VMA, is helpful in the diagnosis of this condition but these laboratory tests require rigid dietary and drug restriction on the part of the patient and can consequently produce erroneous results.

Oral clonidine has been found to suppress plasma catecholamine secretion in patients with essential hypertension but not in patients with phaeochromocytomas. Thus this clonidine suppression test has been useful in distinguishing essential hypertension patients with elevated plasma norepinephrine levels from those patients with hypertension due to phaeochromocytoma.

Computerized axial tomography with or without I^{131}-labelled meta-iodobenzyl-guanidine (MIGB) is on the other hand extremely accurate in diagnosing phaeochromocytomas and should be regarded as the initial localizing procedure of choice.[6] Indeed, since the introduction of the CT scanner in our institution, arteriography as a localization technique has become exceedingly rare. If arteriography for tumour localization is contemplated, however, one should be aware that radiocontrast dyes can stimulate catecholamine release. Thus, this radiographic technique requires the presence of an anaesthetist to manage any hypertensive crises that may occur.

The importance of diagnosing a phaeochromocytoma before anaesthesia and surgery cannot be overemphasized. When an unanticipated phaeochromocytoma mani-

fests itself during even the most simple operation, operative mortality is still about 50 per cent.[7] In contrast, mortality today during removal of a known phaeochromocytoma in a well-prepared patient is of the order of 0 to 3 per cent.[8]

Preoperative preparation

The anaesthetic preparation and management of the phaeochromocytoma patient requires close communication with the internist/paediatrician and the surgeon. Practically speaking, it is the authors' opinion that it is better to involve the surgeon in the case a few days after the anaesthetist and internist have already agreed on and begun drug and fluid therapy. This way the patient isn't placed on the operative list before he/she is ready.

The anaesthetist should be familiar with the patient's history and be especially careful in assessing the extent and severity of any end-organ damage. The nature and the severity of the hypertension should be documented and any possible complications arising from it (such as catecholamine cardiomyopathy with failure) should be documented.

Clinically significant cardiomyopathy has been found to occur in about 58 per cent of patients with phaeochromocytoma and when this occurs, mortality is high.[9] The clinical manifestations of this cardiomyopathy are variable and non-specific and may include disturbances of cardiac rhythm or congestive heart failure with acute pulmonary oedema. ECG's should be done preoperatively on all patients since such examinations may reveal evidence of ventricular hypertrophy, dysrhythmias, ischaemia or infarction. M-mode echocardiography is useful in assessing left ventricular function in those patients suspected of a cardiomyopathy.

A fasting serum glucose level should be measured in all phaeochromocytoma patients to establish a baseline. Fully 60 per cent of adult patients have hyperglycaemia preoperatively but insulin is seldom required.

It is also necessary to assess renal function prior to surgery. In addition to measuring the patient's plasma creatinine level, a scintigraphic renal scan is useful in establishing bilateral renal function and measuring the patient's GFR. This is especially important in the rare event a nephrectomy may be necessary to completely remove a phaeochromocytoma.

A chest *x*-ray may reveal the presence of congestive failure, in addition to screening for the rare intrathoracic tumour.

The circulating blood volume is usually diminished due to a catecholamine-induced vasoconstriction: a haematocrit greater than 45 per cent is a clue that the blood volume is significantly contracted. Serial monitoring of the haematocrit is a simple way of evaluating the adequacy of volume expansion and satisfactory alpha-blockade is implied if an absolute drop in the haematocrit of about five per cent is achieved.

Hypercalcaemia found preoperatively is a clue, along with a positive family history, that the phaeochromocytoma may be a part of a multiple endocrine adenomatosis (Type II). A patient with co-existing hyperparathyroidism, if not causing serious hypercalcaemia, should usually have the phaeochromocytoma excised before a parathyroidectomy is planned.

The surgical preparation of the patient not only involves assessment and treatment of end-organ damage but also adequate alpha-adrenergic blockade, blood volume re-expansion and the treatment of any dysrhythmias. Preoperatively, the patient is started on oral phenoxybenzamine; still the mainstay of pharmacologic therapy. This drug irreversibly alkylates alpha-1 adrenergic receptors on vascular smooth muscle and renders them nonfunctional, thereby causing vasodilation. Phenoxybenzamine at a dose of 10 mg bid PO is usually started one to two weeks before surgery and is increased every one to two days, not only until the hypertension is controlled, but until some orthostatic drop in blood pressure occurs. It may take 24–36 hours for phenoxybenzamine to produce any effect: the duration of action of a single dose approximates its 24 hour half-life. During this vascular volume re-expansion period, it is important not to cause too precipitous a drop in the blood pressure; a high salt intake and/or isotonic fluid administered intravenously may be necessary to ensure this. Aside from postural hypotension, other side effects of phenoxybenzamine may include reflex tachycardia, pupillary constriction, nausea, sedation, weakness, gastric irritation and nasal stuffiness.

Phentolamine, another alpha-blocking drug, has little place in the preoperative management of these patients aside from treating acute hypertensive crises when they arise. The drug can also cause pronounced gastric upset or alarming tachycardia.

Whether it is advisable to continue phenoxybenzamine right up to the day of operation is still moot. In some centres, phenoxybenzamine is discontinued 24 hours preoperatively to ensure that the patient is only partially alpha-blocked. During surgery on these partially blocked patients, surgical manipulation for the tumour can cause a hypertensive spike that supposedly aids the surgeon in tumour localization. It is currently our feeling, however, that patients should be as completely alpha-blocked as is possible. The various provocative tests for phaeochromocytoma are potentially dangerous and unnecessary in today's era of computerized axial tomography and we do not believe that withholding phenoxybenzamine to allow a patient to develop hypertensive spikes in the operating

room is a useful tumour-localizing exercise. Practically speaking, it has also been our clinical experience that, despite the most aggressive pharmacologic loading with phenoxybenzamine, these patients will still develop some degree of hypertension during surgical manipulation of the tumour.

Prazosin (Minipress®), a competitive alpha-1 blocker has been used preoperatively to alpha-block patients but has been criticized due to its failure to prevent adequately perioperative hypertensive episodes.[10]

The use of competitive alpha-blockers has not met with much success in controlling blood pressure intraoperatively. It would appear that the vast amounts of catecholamines liberated by a surgeon squeezing a phaeochromocytoma can easily overwhelm any competitive agent that reversibly occupies the alpha receptors. It requires irreversible alkylation, not just competitive inhibition, to ensure that alpha receptors will not respond to the high plasma concentrations of norepinephrine and epinephrine caused by tumour manipulation.

Many patients in the literature have received beta-adrenergic blockers like propanolol or metoprolol but it is important to appreciate that beta blockers can only be given after patients are well into their course of phenoxybenzamine.[1] Use of beta-blockers without the prior use of alpha-blockers can cause severe hypertension due to unopposed alpha-stimulation of vascular smooth muscle. Extreme caution is also advised in the use of beta-blocking drugs in patients with a history of catecholamine cardiomyopathy. Beta-blockade in these patients may cause congestive failure that is refractory to therapy.

Labetalol (Trandate®), a mixed alpha- and beta-blocking drug, has been used in phaeochromocytoma patients. The beta-blockade is qualitatively similar to that of propanolol but the alpha-blockade is about 1/10th as potent as that of phentolamine.[11] Labetalol alone, however, is not able to control arterial pressure if large quantities of norepinephrine are released from the tumour.[12] Indeed, since labetalol is a weaker alpha-blocker than a beta-blocker, it may cause an increase in blood pressure.

It is the authors' view that generally beta-blockade of phaeochromocytoma patients is indicated only in those situations where significant cardiac dysrhythmias and/or tachycardia are present.

Regardless of how alpha-blockade is achieved, the benefits of preoperative alpha-blockade are dramatic. In 1951 the perioperative mortality of patients with phaeochromocytoma having elective resection of their tumour was over 50 per cent:[13] this has dropped to 0–3 per cent with the introduction of the alpha-blocking drugs in 1967.[8]

If bilateral adrenalectomy is expected, glucocorticoid and mineralocorticoid coverage is mandatory, but the details of the appropriate regimen are no different than for similar surgical procedures that render a patient Addisonian.

Premedication is based primarily on the preference of the anaesthetist but in general we feel that the patient should be sedated prior to arrival in the operating room to allay anxiety which can cause release of catecholamines. In the paediatric age group, both pentobarbital sodium 2 $mg \cdot kg^{-1}$ per rectum or diazepam 0.3 $mg \cdot kg^{-1}$ PO two hours preop has been used with success. Morphine is undesirable on the more theoretical grounds that it can release histamine, a potent inducer of catecholamine release.

Atropine premedication, if it is to be given at all, should be given with caution to paediatric phaeochromocytoma patients. It causes a sympathetic preponderance with tachycardia and can cause severe hypertension. In the authors' opinion, atropine is indicated during the anaesthetic induction only if a bradycardia develops that is accompanied by significant hypotension.

Intraoperative management

The times of significant intraoperative danger to the patient are: (1) during the anaesthetic intubation, (2) during tumour manipulation, and (3) immediately following ligation of the tumour's venous drainage.

The following are essential for the safe anaesthetic management of the surgical resection of a phaeochromocytoma: a large bore intravenous line, an indwelling radial artery catheter for direct pressure measurement and blood sampling, an ECG monitor, a urinary catheter, a temperature probe and a central venous pressure line. If the patient is suspected of having compromised left ventricular function due to a catecholamine cardiomyopathy, it is better (if the patient's size allows it) to use a Swan-Ganz catheter rather than a CVP catheter. The pulmonary wedge pressure determined by the Swan-Ganz is a more accurate reflection of left-sided filling pressures than the right atrial pressure measured by the CVP line, especially in a patient with abnormal left ventricular function.

The patient should be transferred gently onto the operating table to avoid undue straining that may cause catecholamine release. Once on the table, a precordial stethoscope, blood pressure cuff with doppler and ECG leads are attached to the patient. The patient must have a functioning large bore intravenous line in place prior to the induction and, if necessary, this line is started in the operating room with local infiltration of the skin with lidocaine. At this point sedation with 1–2 $\mu g \cdot kg^{-1}$ of fentanyl is useful in allowing cannulation of the patient's radial artery with a 22- or 20-gauge catheter under local anaesthesia. The ability to continuously monitor blood

pressure even prior to the actual induction is critically important because of the probable occurrence of marked increases in blood pressure. A "sleep dose" of sodium thiopental is then given and the patient is allowed to breathe increasing concentrations of isoflurane in nitrous oxide and oxygen until clinically deep enough for intubation. Two minutes prior to the actual intubation, an injection of 1.5 $\mu g \cdot kg^{-1}$ lidocaine is given intravenously to minimize the sympathetic response to laryngoscopy. The patient can then be paralyzed for the intubation and the anaesthetic is maintained with N_2O/O_2/isoflurane with fentanyl either by bolus or infusion. Succinylcholine is theoretically undesirable for tracheal intubation because of its stimulating effect on postganglionic sympathetic neurons and because fasciculations may cause raised intra-abdominal pressure sufficient to mechanically squeeze the tumour of some of its catecholamines.

Isoflurane is preferred because it provides adequate analgesia with good muscle relaxation without sensitization of the heart to catecholamines. Despite its use in the past we feel that the use of halothane can no longer be recommended for these cases because this vapour is dysrhythmogenic in the presence of large concentrations of catecholamines. Continuous end-tidal CO_2 and O_2 saturation monitoring is useful but results should always be checked by frequent measurement of arterial blood gases.

Induction doses of pancuronium can cause severe hypertension due to the drug's stimulant action on the sympathetic nervous system of which the adrenal medulla is a part.[14] The use of curare for relaxation is also not recommended because of its potential for histamine and hence catecholamine release. Atracurium and vecuronium, although causing no sympathetic stimulation, are short acting and require either frequent injections or an infusion. For intraoperative relaxation, vecuronium seems to be the drug of choice, at least on a theoretical basis, since it is free of histamine release.

However, it should be noted that metocurine, atracurium and curare have all been used successfully in the past despite having the potential of histamine release to varying degrees[15] and there have been many clinical reports documenting the safe use of pancuronium in these patients.

The intraoperative use of droperidol for these patients is still contentious but evidence is mounting in its disfavour. Bittar[16] has reported a series of seven cases in which the injection of Innovar® precipitated a massive hypertensive response. In one of these patients, droperidol was reported to be the active agent. Montiel *et al.*,[17] in an elegant study, has shown that intraoperative hypertension may be due to droperidol's occupying the presynaptic dopaminergic receptors of chromaffin cells that would normally inhibit release of catecholamines. Thus the presence of droperidol can disinhibit these chromaffin cells and encourage catecholamine release. In light of this information, droperidol should be used intraoperatively with extreme caution.

As was mentioned earlier, many different anaesthetic techniques and drugs have been used successfully in the intraoperative management of phaeochromocytoma patients. Roizen *et al.*[15] determined that phaeochromocytoma patients can be managed successfully with regional anaesthesia, isoflurane, enflurane, halothane or nitrous oxide with narcotics and that the choice of technique was not the crucial factor determining outcome after resection of the tumour.

A 0.01 per cent solution of sodium nitroprusside should be immediately available to treat any intraoperative hypertension that may occur. Intermittent boluses of 1–5 mg of phentolamine have been used successfully but nitroprusside is our preferred agent because it acts more quickly, lasts only one to two minutes and causes little reflex tachycardia or tachyphylaxis. Cyanide toxicity is not a problem because of the small quantities of nitroprusside used. It is our experience that intravenous phentolamine works a little too slowly and lasts a little too long to be easily controllable in the operating room. Nitroglycerine has been used successfully but large doses are required to achieve the desired effect.[18] Cardiac dysrhythmias that occur during tumour manipulation can be treated with lidocaine or propanolol. Propranolol's action following its intravenous administration is approximately 30–45 minutes and may persist following the removal of the tumour causing hypotension or myocardial depression that can result in intraoperative pulmonary oedema.[19] When it becomes available in Canada, a better choice than propranolol may be esmolol. It has a rapid onset, is very short acting and thus could be titrated more precisely.

Within seconds of ligation of the venous drainage of a solitary phaeochromocytoma, the high concentration of circulating norepinephrine usually falls. It is possible that if volume replacement has been inadequate up to this point the blood pressure may fall. Indeed in the past some have taken the position that a fall in blood pressure at the time of venous ligation of the tumour is proof that no other tumours are present. We do not feel that this is always true. Aggressive volume replacement can cope with a dilating vascular tree at the time of venous ligation to the extent that *no* significant blood pressure fall may be observed. Also, fully 50 per cent of phaeochromocytoma patients will remain hypertensive for days postoperatively even if only one tumour was present. Plasma catecholamine levels may remain above normal in some patients for up to 72 hours even when there is no reason to suspect another tumour.[4] A precipitous drop in blood pressure is

treated with a rapid infusion of blood or crystalloid but in the rare instance when the blood pressure cannot be raised quickly enough, an infusion of a vasopressor (phenylephrine or norepinephrine) may be started as a stop-gap measure until the newly dilated vascular space is filled.

Postoperative management

The anaesthetist would ideally like to have the patient fully awake and breathing spontaneously at the end of the operation. In the recovery room, the patient should be closely monitored for blood pressure, heart rate and rhythm, central venous pressure, urine output and level of consciousness.

The three important postoperative complications to watch for are: hypertension, hypotension and hypoglycaemia.

Hypertension may be caused by pain at the operative site, hypoxia, hypercarbia, urinary retention or the presence of another as-yet-undiagnosed phaeochromocytoma. Appropriate measures should be taken to: alleviate pain, ensure that ventilation and oxygenation are adequate, drain the bladder and pharmacologically control any excess catecholamine effects should another tumour be suspected.

Significant hypotension is a rare occurrence in patients who have been alpha-blocked and adequately volume-expanded preoperatively but if it develops, it is treated by volume administration. An acute fall in blood pressure in the recovery room may indicate intra-abdominal bleeding necessitating reoperation.

The majority of phaeochromocytoma patients have some degree of hyperglycaemia and glucosuria both preoperatively and intraoperatively because circulating catecholamines act on the alpha-receptors of the pancreatic beta-cells to suppress insulin release. The catecholamines also increase glycogenolysis and free fatty acid levels in the blood and as a consequence, provide alternate energy substrates and decrease glucose clearance from the blood. Within minutes of tumour removal, the suppression of beta-cell function disappears and plasma insulin levels rise. Postoperative hypoglycaemia may follow and cause loss of consciousness and respiratory arrest.[20] Also, the classic symptoms of hypoglycaemia may be masked in a postoperative phaeochromocytoma patient and who has been receiving analgesics and who may have residual beta-blockade. Consequently, switching to a glucose-containing intravenous fluid at the time of tumour removal and monitoring blood glucose levels frequently for the first 24 hours postoperatively is prudent.

Phaeochromocytomas are malignant in about ten per cent of cases and some are not resectable. Nevertheless, the surgeon should attempt to remove as much tumour tissue as possible. Reduction in the amount of catecholamine-secreting tissue will facilitate pharmacologic control of the remaining catecholamine excess. Chemotherapy and radiotherapy are of little benefit but the biochemical effects of unresectable phaeochromocytomas can be treated with adrenergic antagonists. A tyrosine hydroxylase inhibitor, alpha-methyl-para-tyrosine, has been used clinically, effecting a 70–80 per cent reduction in the urinary excretion of catecholamines and their metabolites.[21] It can, however, cause side-effects including postural hypotension, central nervous system dysfunction and renal damage. Streptozotocin has had both failures and successes but can lead to diabetes mellitus.

The clinical course of patients with metastatic phaeochromocytomas is quite variable and the five-year survival rate averages 45 per cent.[1]

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