Full Case:

A 79-Year-old man with Parkinson's disease was scheduled for insertion of electrodes for deep brain stimulation (OBS). He was right handed, English speaking and of normal intelligence. He had good memory function but a marked tremor. His current medications, levodopa (Sinemet), bromocriptine (Parlodel), selegiline (Eldepryl), pramipexole (Mirapex), and amantadine (Symmetrel), afforded only fair movement control. He had recently become very depressed and sertraline hydrochloride (Zoloft) had been prescribed. He also had a history of hypertension, treated with hydrochlorothiazide.

What is Parkinson's disease (PD)?

James Parkinson (1755 to 1824), an English surgeon, political radical, and paleontologist established the disease as an entity with "An Essay on the Shaking Palsy" in 1817. Sorting through several palsied conditions which he had observed, Parkinson gave the classic clinical description of the disease: "Involuntary, tremulous motion with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the sense and intellect being uninjured." Four decades later, Jean-Martin Charcot added rigidity to Parkinson's excellent description and attached the name Parkinson's disease to the syndrome. Parkinson is also noted for the earliest description in English of a case of perforated and gangrenous appendix (1812).

Parkinson's disease (PD) is a neurodegenerative condition resulting from neuronal loss in the dopaminergic substantia nigra pars compacta (SNC) (Fig 24.1). Projections from the SNC to the striatum normally allow for refined movements. Initially, the dopamine receptors in the striatum of PD patients are upregulated in response to a reduction in dopaminergic input. As increasing populations of somata are lost in the SNC, clinical symptoms begin to appear (Fig. 24.2). Dysfunction initially occurs unilaterally in the form of micrographia, hand tremor, decreased arm swing, and foot dragging. Eventually, bilateral symptoms appear as bradykinesia, resting tremor, postural instability. A therapeutic response to levodopa (L-dopa) occurs. Almost 90% of
patients with PD have significant vocal fold bowing and adduction and pharyngeal residues of solids can be found on evaluation of swallowing.


What is the underlying pathology of Parkinson's disease (PD)?

PD is a clinical diagnosis (Table 24.1), confirmed in postmortem analysis by demonstration of Lewy bodies and the loss of dopaminergic neurons in the substantia nigra pars compacta (SNC). The degeneration of SNC dopaminergic neurons, which project to the striatum as the nigrostriatal pathway, leads to a reduction in striatal dopamine content and eventually to the clinical phenotype. The genetics of PD suggest a mechanism for the presence of diagnostic Lewy bodies: oxidative stress, mitochondrial dysfunction, decreased adenosine triphosphate (ATP) production, diminished degradative action of highly energy dependent ubiquitin proteosome system (UPS), protein aggregation, and eventual disease. Administration of synthetic and endogenous proteasome inhibitors disrupts the UPS in rats causes both the clinical signs of PD (bradykinesia, rigidity, and tremor) and the pathologic findings (neuronal degeneration and Lewy body-like inclusions in the SNC and other areas similarly affected in PD patients) within 2 weeks.

Environmental factors may be involved in the pathogenesis of PD. An acute form of PD can be caused by exposure to MPTP (l-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), which is a neurotoxic by-product of the illicit synthesis of meperidine analogues. Once administered parentally, MPTP readily enters the brain and is metabolized by astrocytic monoamine oxidase B to MPP+ (l-methyl-4-phenylpyridinium). MPP+ concentrates in dopaminergic SNC neurons where it inhibits the mitochondrial electron transport chain resulting in
ATP depletion and selective cell death. Exposure to pesticides or other toxins may increase the risk of development of PD. Many studies have attempted to link PD with family history. Rocca et al. performed a historical cohort study at the Mayo Clinic on 162 PD patients and more than 1,000 first-degree relatives. In patients with early onset of PD, there was a small relative risk for first-degree relatives in developing the disorder. However, there was no increased risk for relatives of patients that had late onset PD. Approximately 20% of elderly PD patients develop a dementia similar to Alzheimer's disease, which may coexist. Also, depression occurs in approximately 40% of all patients with PD. Although this widespread comorbidity is often untreated, therapy is appropriate and must be approached cautiously because of the risks of drug interactions.


What are the criteria for surgical treatment of Parkinson's disease (PD) and what types of surgery are available?

Medical therapy is palliative because drug therapy does not halt the progression of neuronal degeneration. Also, drug therapy loses its efficacy in many patients and therefore surgical strategies have been developed. Although bradykinesia may continue to respond to drug
therapy, symptoms such as dysarthria, gait disorders, and postural instability emerge, progress and respond poorly to treatment. Stereotactic surgery employs precise lesioning with the basal ganglia to dampen pathologic neuronal discharge. Procedures such as pallidotomy and thalamotomy were initially performed but are now less frequently utilized. Lesions are permanent and there is risk of severe side effects such as stroke or neurologic injury. Some years ago, experimentation with implantation of fetal neural tissue showed early promise in improving the clinical symptoms of patients with PD or MPTP (l-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-induced PD. This technique stereotactically implants fetal mesencephalic neurons or adrenal chromaffin cells into the striatum. However, any benefit from neural transplantation may be due to associated acute and reactive host brain injury. Also, the process is politically charged as it involves fetal tissue, usually collected during abortions. Recently other studies indicate that stem cells are more suitable as cellular replacements. The procedure of choice now is deep brain stimulation (DBS), which involves first the implantation of stimulatory electrodes and later placement of a generator that allows control of the electrodes. Deep brain stimulating devices are implanted in two stages: the first stage is performed with the patient awake or with minimal sedation. The second stage is performed under general anesthesia. Patients chosen for surgical implantation must be carefully evaluated for comorbidities. They should have a documented preoperative improvement from dopaminergic medication of at least 30% in the patient's Unified Parkinson's Disease Rating Scale motor disability scores. A L-dopa challenge may be needed to document the best "on" state. They should be able to lie still for several hours. Communication is essential during the procedure. Therefore they should have little or no dementia and active psychiatric disease should be treated preoperatively. Cardiorespiratory stability is also important. Hypertension should be well controlled. Patients with obstructive pulmonary disease and those who smoke must be able to lie not only supine with minimal head up position but should not have a chronic cough. Patients must be motivated with good support systems and committed to the postoperative management of DBS. As DBS techniques have also been shown to improve intractable epilepsy, cephalgias, restless legs syndrome, and other movement disorders; anesthesiologists may soon be called on to assist in many different situations and in patients with a host of pathologies.
What are the anesthetic implications of the patient's medications?

As noted in the preceding text there are many side effects associated with Parkinson's disease (PD) medications including dry mouth, orthostatic hypotension, nausea, visual disturbances, and urinary retention. Typically, in order to produce maximum effect during stimulation, the surgeon requires that no PD medications be given for several hours before surgery. Thus patients may present to the operating room with significant movement disorders. Also, if the indication for deep brain stimulation (DBS) is epilepsy, side effects of the many agents used for this disease must also be considered including hepatic enzyme induction, competitive metabolic inhibition, plasma protein level, and binding, all of which may cause drug interactions and change doses and duration of effect of other agents.
Gum hypertrophy may add to the difficulties of securing an airway emergently (Table 24.2). In addition, the anesthesiologist should not fail to inquire as to any herbal preparations that the patient may have taken as interference with clotting has been reported with gingko, ginger, garlic, and gengsing among others. Many antiepileptic drugs induce hepatic enzyme activities. If two drugs share a similar pathway for metabolism, the second drug is cleared at a faster rate due to increased hepatic enzyme activity. Phenytoin, barbiturates, and carbamazepine are potent hepatic enzyme inducers causing faster elimination of other drugs. Because antiseizure drugs increase the activity of the nonspecific drug metabolizing enzyme system, cytochrome P-450, the duration of action of muscle relaxants, narcotics or other anesthetic agents may decrease. Chronic alcoholic patients who take phenytoin can have even higher hepatic enzyme activity, which decreases the serum concentration of anesthetic agents and increases the elimination rate. The dosage of benzodiazepines or barbiturates for premedication may need to be increased. Also, induction doses of thiopental or propofol may also have to be greater. Frequent administration of muscle relaxants may be required due to increased hepatic drug metabolism.


**What precautions should be made for airway management?**

Airway evaluation is especially important in these patients. As the effects of the maintenance drugs wear off, the patient may become rigid and mouth opening may be very difficult. Primary laryngospasm is a known complication of Parkinson's disease (PD) and acute withdrawal of treatment can cause airway obstruction. Dentition is often impaired in the ill, geriatric population. Patients who have been receiving Dilantin for many years may have gum hypertrophy and
loosening of teeth that may hamper placement of an airway. The head is encased in a frame and a bar crosses in front of the mouth. Also, the frame is attached to the bed making it impossible to extend the head. Not infrequently, if the procedure becomes prolonged, the degree of sedation must be increased, occasionally to general anesthesia, especially if there are intraoperative complications. Should aspiration, vomiting, or respiratory depression occur, a means to support oxygenation must be immediately available. Therefore, as well as careful preoperative assessment of the airway, the difficult airway cart should be available. Laryngeal mask and cuffed oropharyngeal airways are particularly valuable as they can be placed with little or no head movement and minimal opening of the mouth. A tracheostomy kit should also be available. It is essential that the anesthesiologist be aware preoperatively of the location of the key to the frame and know how the face piece can be immediately released should a problem occur.


**What are the anesthetic considerations in an magnetic resonance imaging (MRI) unit.**

Three types of energy in the MRI suite affect monitors and equipment and thus anesthetic delivery: a powerful static magnetic field of 1.5 Tesla (15,000 times greater than the magnetic field of the earth's surface), radiofrequency (RF) pulses that cause magnetic resonance by superenergizing cells which then emit RF signals, and time-varied magnetic field (TVMF) gradients that encode the emitted RF to produce two-dimensional and three-dimensional images. Equipment and monitors must be adaptable to the MRI suite. All devices must meet three criteria: they must function normally at the site, they must present no danger to the patient personnel, and they must not affect successful completion of the procedure or imaging. For most locations, these goals can be met by selecting commercially
available portable monitoring devices. In general, nonferromagnetic equipment must be used. Only certain metals, iron, nickel, and cobalt to name a few, are magnetic. Items made of nonmagnetic aluminum, titanium, copper, silver, and gold are safe as far as missile dangers are concerned and are among the materials used to make MR-compatible intravenous (IV) poles, fixation devices, and nonmagnetic anesthesia machines. Often one must bring into the MRI magnet room susceptible metal items such as infusion pumps for IV lines. In such cases, it is safer to position those objects securely in the magnet room before the patient enters the magnet bore. Biomedical engineers with expertise in magnetic imaging should be consulted before installation or use of any electronic devices. Implanted metals such as hip prostheses and Harrington rods are made of stainless steel, a metal usually only weakly magnetic. Information about the presence of such devices should be obtained and appropriate consultation sought from radiologists as to safety. Issues with large, weakly magnetic metal objects usually center on image degradation rather than the danger of the patient experiencing an uncontrollable magnetic force. Metals do not need to be missiles to be dangerous to the patient. Dangers from wires in epidural or pulmonary artery catheters relate to radiofrequency (RF) and the risk of burns. Systems for central wall gases (oxygen, nitrous oxide, and air) are commercially available for MRI centers and should be installed during construction. Electrical power sources for monitoring systems are usually available in the magnet room itself and consist of isolated duplex power circuits with filtered 120 V (alternating current) to prevent electrical noise artifacts from interfering with the images. Monitors plugged into these outlets should be located as far from the core of the magnet as possible, beyond the gauss line. Also, they should be free of ferromagnetic material, and RF shielded. If possible, monitors should be outside the magnet room, and an external power source used. Then cables should be passed through wave guides (used to prevent leakage of RF pulses from the magnet and interference from outside sources) in the wall to limit the effects of magnetization, RF, and TVMF on the equipment. Electrocardiography (ECG) is difficult within a static magnetic field. Maximum voltage charges are induced in any column of conducting fluid. The superimposed potentials are greatest in ST segments and T waves of leads I, II, VI, V2 and increase with field strength. Spike artifacts that mimic R waves are often produced due to the changing magnetic fields of the imaging gradients. Changes in the ECG wave
form are present even in filtered systems designed for MRI use and make it impossible to reliably monitor for ischemia or to interpret arrhythmias. Plethysmography can be used as cardiac monitor, but is not useful for ischemia detection. Telemetry units have been used with low magnetic fields (0.6T), but their use may interfere with the RF needed for imaging. In patients highly susceptible to ischemia, a 12-lead ECG pre- and post-MRI is recommended. Several MRI compatible ECG systems are currently available, and use ECG electrodes made of carbon graphite to lower resistance, eliminate ferromagnetism and minimize RF interference. The skin must be adequately prepared (dried or abraded). ECG cables are coaxialized to avoid any coils and subsequent burning of the skin. A small towel is folded and placed on the patient's chest, to avoid contact with the skin as an extra precaution. Automated oscillometric blood pressure monitoring, based on pneumatic principles, eliminates the problems of electromagnetic interference. Units should be placed away from the magnet's core, and the tubing extended to accommodate this distance using plastic connectors as necessary. A conventional noninvasive blood pressure unit is not shielded from either RF or the magnetic field and uses a 120 V electrical outlet. Consequently, there is usually some interference with RF during scanning. Manual mercury sphygmomanometers have been adapted in for use in MRI by replacing all ferromagnetic hardware with brass or aluminum pieces. Invasive blood pressure monitoring in the MRI center has certain practical limitations. Conventional disposable transducers may function adequately outside of the gauss line, although their accuracy should be determined by a biomedical engineer. Because disposable transducers have a predictably high natural frequency, a modest addition of tubing to move the transducers away from the patient is unlikely to cause damping. Self-contained multiple-monitor systems designed for MRI suites are now built with modes for invasive monitoring (Magnetic Resonance Equipment, Bay Shore, NY). Because of the length of the tube, it is usually impossible to visualize the patient's face and chest for adequacy of ventilation during scanning. Alternative techniques include respiratory capnography, available in both conventional systems placed beyond the gauss line and MR-compatible systems. Should general anesthesia be required and in deeply sedated, spontaneously breathing patients the Jackson Rees circuit can be attached to either the endotracheal tube or a tight-fitting mask (using a mask strap). When the circuit is placed on the chest, visualization of bag movement
outside of the magnet indicates adequacy of ventilation. Direct visualization of the airway by observing the scan image is also useful to confirm airway patency. Acoustic noise produced by the rapidly changing electric current pulsing through a static magnetic field makes useful auscultation during scanning impossible. Alternative monitoring techniques for confirmation of heart rate and ventilation include a system for remote auscultatory monitoring using microphones. The sounds are transmitted to a remote receiver and headphone set as infrared light, which does not interfere with imaging. Many commercially available pulse oximeters function well in the magnet but burns to extremities have been caused by the induction of current within a loop of wire in the presence of magnetic flux with resultant heating of the wires. MR-specific pulse oximeters use heavy fiberoptic cables, which do not overheat and cannot be looped. These cables are expensive and easily damaged. If conventional oximeter(s) are used, burns can usually be avoided by placing the sensor on the extremity distal to the magnet, keeping the sensor wires free of coils and protecting the digits with clear plastic wrap.

Quench monitors are usually present within each MRI suite. The magnet superconductors are kept cool in liquid nitrogen. Should this coolant evaporate due to leaky housing ("quench") the ambient oxygen supply of the room can drop precipitously causing hypoxia and the potential for cryo injury.

By replacing the machine's ferromagnetic components of the anesthetic machine with brass, aluminum, and plastic, the ferromagnetic content can be reduced to less than 2% of the total weight. One such machine, the Excel-210 MRI (Ohmeda, Madison, WI) is 99.8% stainless steel, brass, aluminum, and plastic. A similar model has recently been marketed by Drager (Doylesstown, PA). The position of the machine in the scanner suite should be determined by a biomedical engineer. Medical gas cylinders constructed from aluminum should be used exclusively. Vaporizers, however, are affected little by the powerful magnetic field, and function accurately.

Plastic battery-operated laryngoscopes should be available. Batteries last longer if shielded with a paper casing or if plastic coated. If MRI compatible laryngoscopes are not available, the airway must be secured outside the magnet room using conventional ferromagnetic laryngoscopes.

Both circle and rebreathing anesthesia systems can be used for ventilation but may require additional lengths of tubing.
Nonferromagnetic ventilators powered by compressed oxygen are commercially available for use with MRI (Omnivent, Topeka, KS). Standard ventilators on anesthesia machines can be modified by reducing the ferromagnetic content. A standard Air Shields Venti meter Controller II (Hatboro, PA) has been used successfully at a distance of 12 ft from the core of the magnet at the 70 gauss line. The difficulties of administering general anesthesia with an anesthesia machine can be avoided by using total intravenous anesthesia with a continuous infusion of propofol. However, all commercially available infusion pumps contain ferromagnetic circuitry which can be damaged and malfunction in the presence of a high magnetic field. Several pumps are accurate in the MR environment outside the gauss line including the IVAC 530 33(R), the 1M ED 960/960A 35, and the Medfusion 2010 (also see Chapter 61 Questions CA, C.5, and C.6).


The surgeon wants to implant electrodes. What are the anesthetic implications?

A surgical team consisting of a neurosurgeon, an electrophysiologist, and a neurologist adjust measurements such as pulse, amplitude, and electrical port to optimally inhibit subthalamic nuclei (STN) output to the thalamus. After the experience in the magnetic resonance imaging (MRI) unit, the patient usually does not experience pain as much anxiety. With the return to the operating room, the anesthesiologist can now utilize all familiar equipment. Essential monitors are applied.
Before further injection by the surgeon around the operative site, a small dose of midazolam (1 to 1.5 mg) and/or fentanyl (25 to 50 /Lg) is appropriate. If necessary, a bolus injection of propofol (20 to 30 mg) may be used. Thereafter, a propofol infusion of 10 to 20 /Lg/kg/minute allows sedation with consciousness.

As the surgeon places the electrodes, communication is essential both with the operator and the patient. Movement by the latter may seriously compromise precise placement. Until cooperation has been achieved, a patient attitude must be maintained.

The surgeon asks that the patient become more responsive. What would you do?

Depending on the medications that have been used for sedation, naloxone or flumazenil may be given to reverse narcotic and benzodiazepine effects. Naloxone should be given in increments of 0.1 mg as sudden reversal of analgesia may cause the patient to move unduly and cause scalp tearing. Even if it has been necessary to place a laryngeal mask airway (LMA), patients can still be awakened and tolerate the airway, especially if lidocaine 50 mg has been given intravenously. Intelligible sounds can be appreciated through an LMA.

The patient is complaining of pain. What would you do?

Small doses of remifentanil 0.01 to 0.05 Jig/kg/minute for 3 to 5 minutes combined with propofol 15 Jig/kg/minute have been shown to be effective in relieving pain during conscious sedation. Onset of action of fentanyl is longer than that of remifentanil, making it less useful. Fentanyl is also cumulative. However, in doses of 25 t-tg the drug may be beneficial. Alfentanil offers no particular advantage.


About 1 hour into the postoperative period, the patient becomes comatose. What should be done?
The patient has most likely sustained a seizure. During a convulsion, the patient must be protected from injuring him/herself. If vital signs, especially oxygen saturation, are stable and if the seizure stops within seconds spontaneously, it may not be necessary to intubate. Rather, close observation is indicated. The dosing schedule of the patient's anticonvulsant drugs should be reviewed, serum levels obtained and a dose of Dilantin given. Should the patient not recover promptly, computed tomography (CT) scan is indicated. Intracranial hemorrhage and cerebral edema are included in the differential diagnosis. Serum electrolytes should be evaluated as hyponatremia is associated with diminished consciousness. The anesthetic agents given should also be reviewed, especially as to the use of reversal agents during periods of stimulation. Flumazenil, a benzodiazepines antagonist that involves the receptor site on the GABA receptor–GABA channel complex has been implicated in neuroexcitatory phenomena, especially seizures. Also, the duration of action of flumazenil is shorter than that of midazolam or diazepam. Therefore, the sedative effects of these latter drugs may resurface in the postoperative period, especially in older patients in whom the half-life of the benzodiazepines is extended.