Progressive systemic sclerosis is a chronic disease of unknown etiology characterized by widespread disturbance in connective tissue and resultant sclerosis of the skin and subcutaneous tissue, as well as alterations in various internal organs, especially the lungs, heart, gastrointestinal tract, and kidneys. This uncommon disease has a worldwide distribution but is rare in Asia, especially among the Chinese, Indians, and Malaysians. The onset of the disease is usually in the third to fifth decades, and affects women twice as often as men. Hereditary factors are not involved.

**Clinical manifestations**

**Skin.** The name scleroderma means “hard skin” and quite accurately describes the skin manifestations. Scleroderma usually begins insidiously; the first symptoms often are Raynaud’s phenomenon and symmetrical swelling or stiffness of the fingers. Raynaud’s phenomenon and sclerodactyly may precede the skin changes by months or years. In some patients, the first manifestation is pitting edema of the extremities and face.

The fingers and hands in the early stages are tightly swollen. Subsequently, the skin becomes firm, tight, waxy in appearance, and bound to the underlying subcutaneous tissue. The skin changes spread to involve the arms, face, upper part of the chest, abdomen, and back. The lower extremities are relatively spared.

The skin may become darkly pigmented even without exposure to the sun. Areas of depigmentation and numerous telangiectases often appear on the skin. Involvement of the face results in the loss of normal skin wrinkles, loss of facial expression and an inability to open the mouth fully. Mastication is sometimes hindered and there is loss of weight. When there is extensive cutaneous involvement, sweating is impaired.

**Musculoskeletal.** Generalized muscle atrophy is a common manifestation. Myositis with proximal muscle weakness and elevated levels of muscle enzymes is seen in some patients and is indistinguishable from polymyositis. Some patients who show features of scleroderma, polymyositis and systemic lupus erythematosus are considered to have mixed connective tissue disease.

**Gastrointestinal tract.** Many areas of the alimentary tract may be involved in scleroderma. Symptoms attributable to esophageal involvement and present in more than 50% of scleroderma pa-
Patients include epigastric fullness, burning pain in the epigastric or retrosternal regions and regurgitation of gastric contents. The lower two thirds of the esophagus frequently exhibit hypomotility; in advanced stages, this sometimes causes dysphagia, owing to the absence of a coordinated peristaltic wave. Peptic esophagitis frequently occurs and may eventually cause strictures and narrowing of the lower part of the esophagus.

Intestinal involvement sometimes leads to intermittent distention, vomiting, diarrhea, constipation or development of the malabsorption syndrome. Weight loss and malnutrition become significant. Barium studies show dilatation, atony and delayed gastric emptying. Atrophy and fibrous replacement of the muscularis of the large intestine result in wide-mouth diverticula or sacculations that are seen only in scleroderma (Figure 1). Complications include bowel perforation and obstruction.

Kidney. Renal failure is the leading cause of death in scleroderma, accounting for almost half of the deaths. Chronic mild proteinuria and mild hypertension are common effects of scleroderma, but the most significant renal complication is the syndrome of malignant hypertension. This syndrome causes a rapid onset of oliguric renal failure that is often fatal.

Lungs. Pulmonary involvement is present in one half to two thirds of all cases and accounts for approximately 20% of the deaths in scleroderma. Ventilatory dysfunction results from pulmonary infiltration or fibrosis (Figure 2), and to a lesser extent from impaired chest wall motion. These patients often complain of a dry cough and exertional dyspnea. Additional pulmonary problems result from aspiration pneumonia secondary to esophageal malfunction.

Heart. The cardiac involvement is the cause of death in 15% of scleroderma patients. The classic scleroderma heart is characterized by the extensive replacement of cardiac muscle with fibrous tissue, leading to arrhythmias, conduction disturbances and congestive heart failure. Scleroderma of the myocardium develops most frequently in patients with a skeletal muscle myopathy. Other causes of cardiac failure include cor pulmonale and hypertension secondary to kidney manifestations. Pericarditis is not infrequent and may be accompanied by pain, pericardial effusion, and cardiac tamponade. Echocardiography may provide evidence of pulmonary hypertension.

Other organ systems. Neurological involvement takes the form of peripheral or cranial neuropathy that can be ascribed to nerve compression due to thickened connective tissue around the nerve sheaths. Facial pain, or trigeminal neuralgia, may occur as a result of this process. Sjögren’s syndrome occurs occasionally with scleroderma and may cause dryness of the oral mucosa (xerostomia) and excessive dental caries.

Prognosis and treatment

In general, the course and prognosis are unpredictable. Patients with mainly skin involvement have a more gradual and favorable course than those with visceral disease, especially of the heart, kidneys and lungs. Among Caucasians, the prognosis is worse in males than in females, and it is worse in patients whose onset of disease occurs at an older age. The disease tends to be more severe in blacks, especially black females.

Unfortunately, no treatment for scleroderma has proved to be effective. Many agents have been enthusiastically proposed in the past, but none has been convincingly shown to have significant therapeutic effects. Steroids have been extensively used...
with varying but not encouraging results. Raynaud's phenomenon may respond to sympatholytic agents such as reserpine, phenoxybenzamine, methyldopa, or guanethidine. Sympathectomy has not been shown to influence the eventful course of scleroderma.\footnote{1}

Avoidance of exposure to cold is important in patients with severe Raynaud's phenomenon. Techniques of biofeedback have been used for teaching patients to control the temperature of their hands.\footnote{1} Removing causes of stress in the patient's life may be beneficial in controlling vasospasm. Skin ulcers should be kept clean. Physiotherapy may help reduce flexion deformities. Patients should be advised to dress warmly, not to smoke, and to avoid such drugs as amphetamines and ergot derivatives.

Patients with esophagitis, esophageal reflux, and stricture are treated with antacids, by elevating the head of the bed, and by esophageal dilatation if necessary. The malabsorption syndrome may respond to broad-spectrum antibiotics.\footnote{7} Patients with progressive renal failure usually require dialysis. Pulmonary infections in patients with pulmonary fibrosis require prompt treatment with antibiotics and other supportive measures. Patients with malignant hypertension require maximal medical therapy using potent antihypertensive drugs. Digitalization and diuretic agents are required for symptoms associated with congestive heart failure.

**Anesthetic considerations**

The variety of organs involved in scleroderma predisposes the patient to a number of problems that are peculiar to this disease such as esophageal stricture, reflux esophagitis, bowel and esophageal perforation, or gangrene of the digits. The scleroderma patient may also present with surgical problems unrelated to the disease itself. Therefore, it is vital that the anesthetist be aware of any and all related problems. During the anesthetic management, the anesthetist should adhere to many precautions indicated by the severity of the disease, and anesthetic agents and techniques should be modified accordingly.

It is not within the scope of this article to present a detailed discussion of all the various anesthetic complications one may encounter with scleroderma patients. Rather, a condensed diagnostic and therapeutic protocol is presented and where applicable, some of the more common problems are discussed.

**Preoperative evaluation.** In order to evaluate the operative risk and to determine the hazards at-
tending the management of scleroderma patients preoperatively, the checklist in Table I is recommended.

Skin manifestations

In order to prevent vasospastic phenomena so commonly associated with this disease, it is important to keep the operating room warm, wrap the patient's hands in towels and avoid vasoconstrictor agents such as phenylephrine, methoxamine, metaraminol and possibly dopamine. Avoid the use of anticholinergic drugs in scleroderma patients who also have Sjogren's syndrome because secretory glands are fibrosed and thus, these drugs may not be necessary. Because of the decreased sweating mechanism, the patient should be considered a likely candidate for malignant hyperpyrexia.

Lee and Atkinson warn of lack of veins and difficulty in opening the mouth wide enough for laryngoscopy. In view of these findings, one must consider an internal jugular cannulation versus venous cutdown for induction of anesthesia and IV fluid administration. If there is difficulty in opening the mouth, the blind awake nasal intubation technique or nasal intubation with the aid of a fiberoptic bronchoscope may be considered. There is also the technique reported by Manchester of establishing an orotracheal airway by introducing a 14-gauge Intracath central venous pressure (CVP) unit containing a 24-inch catheter through the cricothyroid membrane into the trachea and retrieving it from the patient's mouth. The endotracheal tube is then threaded into the trachea. If all measures fail for an awake intubation, tracheostomy must be considered for insurance of the airway during anesthesia.

Many clinicians believe that for these patients, regional anesthesia offers greater safety than general anesthesia. There may be prolonged sensory anesthesia resulting from infiltration and nerve block as reported by Eisele and Reitan in a patient with Raynaud's phenomenon due to scleroderma. The effect was attributed to a reduction of 30-50% in the blood flow to subcutaneous tissues of the forearm, severely impairing perfusion and possibly reducing pH. Neil, however, suggested that advantage should be taken of this prolongation of sensory anesthesia to help control postoperative pain in such a patient.

Vasospastic phenomena in scleroderma are so common that one should anticipate hemodynamic consequences following induction of anesthesia with the concomitant vasodilation. The patient may have a reduced circulating cell volume and should be treated with blood or a plasma expander. Hypotension may occur if the patient has been on prolonged steroid therapy suggesting adrenal insufficiency. The treatment, of course, is hydrocortisone intravenously.

During anesthesia, the patient's eyes may not close completely if there is tightening of the skin around the mouth and eyes. Therefore, the eyes should be lubricated and taped to prevent corneal abrasions.

Because of decreased forearm blood flow as mentioned above, the anesthetist should be aware of inaccurate blood pressures, as well as false skin temperatures. Arterial cannulation is discouraged in patients with Raynaud's phenomenon.

Musculoskeletal symptoms

Patients with musculoskeletal symptoms require careful positioning because of the frequently associated bony deformities, contractures and joint pain. There is often neck restriction and again, awake intubation or regional anesthesia may be considered.

A large majority of patients with musculoskeletal problems often take analgesics such as acetylsalicylate, phenylbutazone, and indomethacin. Gastric disturbance and occult gastrointestinal bleeding are always to be looked for in patients taking the above drugs. If the hemoglobin is below 10 gm, blood transfusion should be considered prior to elective surgery. It should be mentioned that sodium salicylate has a direct stimulant effect on metabolism and respiration and also increases prothrombin time leading to surgical ooze.

Table I
Preoperative evaluation checklist for scleroderma patients

- Examination of ability to open the mouth
- Examination of range of motion in neck
- Evidence of periodontal disease
- Pulmonary function tests
- Chest x-ray
- Skeletal x-ray (if there is limitation of joints)
- Blood gas analysis
- ECG
- Serum electrolytes, 12-test screen
- Hemoglobin
- Platelet count and bleeding and clotting time determinations
- Urinalysis
- IVP (if renal pathology is demonstrated, the patient should have a renal arteriogram)
- Previous recent general anesthetics
ing. Katz and associates state that in normal man, prolonged salicylate administration increases the sensitivity of the respiratory center to carbon dioxide.\(^1\)

It seems reasonable that patients with diminished muscle mass should require less neuromuscular relaxant drugs. Wylie and Churchill-Davidson reported evidence that such patients may have an altered sensitivity to the muscle relaxants.\(^2\) Depolarizing muscle relaxants should be administered cautiously because they may produce dangerous elevations in serum potassium levels. These patients should also be considered likely candidates for hyperpyrexia. Therefore, it is necessary to monitor temperatures.

Patients who have trigeminal neuralgia associated with Sjögren's syndrome probably should be intubated if general anesthesia is used because facial pain may be potentiated with mask anesthesia.

**Pulmonary involvement**

Regional anesthesia, when indicated, may again be preferable to general anesthesia for patients with pulmonary symptoms. If general anesthesia is used, ventilation may be difficult in patients with diffuse interstitial fibrosis as a result of altered compliance and a reduction in vital capacity. It may be necessary to increase the respiratory rate, thus ensuring an adequate minute volume. If diffusion capacity is low, it is necessary to raise the inspired oxygen tension. The narcotic-nitrous oxide-oxygen technique may be considered instead of an inhalational agent.

There is an increase in dead space from widening of the airway which also reduces resistance, causing the patient to breathe at a faster rate so as to preserve normal alveolar ventilation.\(^2\) Consequently, controlled breathing with endotracheal intubation is indicated.

There may be respiratory insufficiency associated with progressive weakening of intercostal and diaphragm muscles. There may also be aspiration pneumonia due to the weakness of the muscles involved in swallowing. The patient should be observed closely in the recovery room and should be left intubated and ventilated mechanically until adequate tidal volume is returned.

**Gastrointestinal involvement**

When there is gastrointestinal involvement, there is an increased incidence of esophageal reflux and regurgitation and the patient must be considered a potential aspiration victim. A very important step is to explain to the patient the modal-

ities to be undertaken prior to the actual induction of anesthesia, since many procedures are done while the patient is in the awake and responsive state. Decompression of the viscus with a nasogastric tube should be done with the patient awake and only minimally premedicated. If there is a significant esophageal stricture, insertion may be difficult and should not be forcefully done because esophageal perforation can occur.

There is no guarantee that regional anesthesia will prevent aspiration, but it is logical that the chance of its occurrence will be lessened with this technique when properly administered. If general anesthesia is used, awake endotracheal intubation may again be the preferred method of securing an airway and preventing soilage of the lungs. The technique of rapid intubation, if selected, should be well known to all clinicians and should be correctly practiced. The patient with the high potential for aspiration should receive the utmost expertise of the clinician.

The problems associated with malabsorption states are many and deserve special anesthesia consideration. They are weight loss, diarrhea, electrolyte imbalance, hypokalemia, hyperprothrombinemia, tetany and osteomalacia, anemia, hypovolemia and protein deficiency. The pathophysiologic changes that disorders of the gastrointestinal system cause have multiple effects on almost all organ systems.

**Renal involvement**

In the presence of advanced renal disease, the action of drugs may be altered owing to anemia, serum protein and electrolyte abnormalities, body fluid relocation, and abnormal cell membrane activity. Great caution should be exercised when administering any therapeutic agents because their levels are sustained for prolonged periods of time. Drugs which are metabolized and then excreted such as morphine are presumed to be more suitable for administration in the patient with impaired renal function. Drugs which are eliminated unchanged via the kidney alone such as gallamine are contraindicated.

Premedication for sedation may not be necessary, depending on the degree of obtundation present. Atropine is normally 50% excreted unchanged by the kidney. Scopolamine is almost completely metabolized prior to excretion and is preferable if a drying agent is indicated. The anuric patient often has dry, friable mucous membranes, so antispasmodics may not be necessary.

Spinal anesthesia is contraindicated because of anemia and hyperprothrombinemia that often occur with renal disease.
Thiopental's activity decreases by redistribution through the body, rather than by renal excretion. Still, with 70% normally binding to albumin, a given dose of thiopental will have a greater central nervous system effect in renal failure if hypalbuminemia is present.

Fixed agents such as morphine, meperidine, fentanyl, droperidol, diazepam and ketamine do not depend on renal excretion and may be used. Doses should be reduced in debilitated patients.

Although most inhalation anesthetic agents are biotransformed to some extent and the products of metabolism are often eliminated by the kidney, these drugs do not rely on renal excretion for reversal of their therapeutic effects, but rather, are terminated by exhalation. Methoxyflurane is nephrotoxic when exposure and concentration are extended. It is recommended that this agent be avoided in the presence of renal failure.

Enflurane, isoflurane, and fluoroxyne pose a potential hazard in a patient with compromised renal function. There is concern that using these agents may lead to increased fluoride levels and possible nephrotoxicity.

In the uremic patient, hyperkalemia, hypocalcemia and acidosis may cause increased myocardial irritability. Therefore, agents that sensitize the heart to catecholamines such as cyclopropane or halothane, or agents that cause their release such as ether, should be administered with great caution. Hypercarbia may be particularly dangerous in patients predisposed to cardiac irregularities, so hypoventilation must be avoided. Nitrous oxide concentrations should not exceed 50% because of decreased oxygen-carrying capacity associated with the anemia and increased intrapulmonary shunting that occurs during general anesthesia. Fluid administration must be monitored closely and insertion of a central venous line may be useful.

In a patient with no kidney function, d-Tubocurarine is probably the muscle relaxant of choice. Although curare-induced paralysis is terminated by redistribution, with more than 70-80% of the drug excreted unchanged by the kidney, it has an excretion pathway in the bile, thus apparently accounting for its safe use in reduced dosages.

Gallamine and decamethonium rely almost entirely on urinary excretion for termination of their action. Therefore, their use in patients with decreased renal function should be avoided.

Pancuronium has been used with minimal complications in debilitated patients. Termination of action is thought to depend upon redistribution and hepatic metabolism. As with d-Tubocurarine, the dosage should be reduced and its effect monitored with a peripheral nerve stimulator.

Succinylcholine is metabolized by plasma cholinesterase and does not require intact renal function to terminate its action. Plasma cholinesterase activity is, however, reduced with renal failure. Succinylcholine is known to cause a rapid but transient rise in serum potassium which may be particularly dangerous in the uremic patient in whom pre-existing hyperkalemia, hypocalcemia, acidosis and diminished ability to excrete potassium tend to produce ventricular arrhythmias. For this reason its use is relatively contraindicated.

Patients with severe renal disease are frequently taking antihypertensive medication, most commonly thiazide diuretics, methyldopa, reserpine and guanethidine. Anesthesia in these patients must be induced slowly and with smaller dosages of anesthetic agents, otherwise, profound hypotension may occur. If a vasopressor is necessary, direct alpha adrenergic stimulators such as phenylephrine are effective but because of their interference with renal circulation, they should not be administered over long periods of time. Intropin® may be the drug of choice because it induces renal vasodilation, thereby enhancing renal blood flow, glomerular filtration rate, urine flow and sodium excretion. Intropin® (dopamine) and phenylephrine are contraindicated in the presence of Raynaud's phenomenon because of the pronounced effects of vasoconstriction.

Methyldopa and reserpine, which reduce both central and peripheral norepinephrine levels, are known to interact with anesthetic agents in a dose related fashion, covering the minimal alveolar concentration (MAC) of anesthetic agents. Guanethidine reduces norepinephrine peripherally but not centrally and it does not alter MAC.

Cooling must be prevented because of the decrease in renal blood flow. Cooling may be used for this purpose but care must be taken in regulating the temperature in order to prevent burning parts of the body where there are existing skin manifestations of this disease.

Cardiac manifestations

Preoxygenation should be done followed by a slow induction to maintain cardiovascular homeostasis. Depolarizing muscle relaxants should be given cautiously in the digitalized patient to prevent the dangerous arrhythmias which can occur. The oxygen concentration should be at least 50%. Balanced anesthesia results in minimal cardiovascular disturbance.

The patient with advanced cardiac involvement may arrive in the operating room with pericarditis and may exhibit symptoms associated with pericardial effusion and cardiac tamponade, a life-

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threatening situation. Anesthesia management must be selected to preserve venous pressure, stroke volume, heart rate and myocardial contractility. All the inhalational anesthetics are known myocardial depressants, and most of them are peripheral vasodilators as well and, therefore, should be avoided. Kaplan and associates recommend local anesthesia until the tamponade is removed; this is then followed by general endotracheal anesthesia if necessary. If required, mild sedation with fentanyl or ketamine in subdissociative doses (0.25 mg/kg) has proven to be successful with minimal hemodynamic effects.

Postoperative care
Careful monitoring must continue into the postoperative period. It should be remembered that narcotics in the postoperative period are as much a potential source for respiratory difficulty as the general anesthetic. The patient must be able to demonstrate adequate respiratory reserve and ability to handle secretions before leaving the recovery room. If any of these criteria are not met, postoperative ventilation with endotracheal intubation should be instituted. If prolonged ventilation is required, a tracheostomy should be considered.

Summary
The anesthetist must be aware of the organs involved, the severity of the disease, and the associated anesthetic considerations and potential risks in order to safely and skillfully manage the patient with scleroderma. Therefore, a thorough understanding of anatomic and physiologic derangements is a necessity.

A detailed preoperative assessment is necessary. Regional anesthesia, when indicated, is considered preferable over general anesthesia in patients with scleroderma.

Knowledge of the pharmacokinetics of drugs that the patient is receiving is important in order to treat any untoward effects that may occur during anesthesia.

REFERENCES

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