pain is diffuse, spontaneous, and either burning, throbbing, or aching in quality. The involved extremity is warm and edematous, and the joints are tender. Increased sweating and hair growth develop. In phase II (3–6 months after onset), thin, shiny, cool skin appears. After an additional 3–6 months (phase III), atrophy of the skin and subcutaneous tissue plus flexion contractures complete the clinical picture. Autonomic testing or bone scans are occasionally useful when the diagnosis is in doubt.

The natural history of typical CRPS may be more benign and more variable than previously recognized. A variety of surgical and medical treatments have been developed, with conflicting reports of efficacy. Clinical trials suggest that early mobilization with physical therapy or a brief course of glucocorticoids may be helpful for CRPS type I or II. Other medical treatments include the use of adrenergic blockers, nonsteroidal anti-inflammatory drugs, calcium channel blockers, phenytoin, opioids, and calcitonin. Stellate ganglion blockade is a commonly used invasive technique that often provides temporary pain relief, but the efficacy of repetitive blocks is uncertain.

TREATMENT AUTONOMIC FAILURE

Management of autonomic failure is aimed at specific treatment of the cause and alleviation of symptoms. Of particular importance is the removal of drugs or amelioration of underlying conditions that cause or aggravate the autonomic symptoms, especially in the elderly. For example, OH can be caused or aggravated by angiotensin-converting enzyme inhibitors, calcium channel-blocking agents, tricyclic antidepressants, levodopa, alcohol, or insulin. A summary of drugs that can cause OH by class, putative mechanism, and magnitude of the BP drop is shown in Table 454-6.

PATIENT EDUCATION

Only a minority of patients with OH require drug treatment. All patients should be taught the mechanisms of postural normotension (volume status, resistance and capacitance bed, autoregulation) and the nature of orthostatic stressors (time of day and the influence of meals, heat, standing, and exercise). Patients should learn to recognize orthostatic symptoms early (especially subtle cognitive symptoms, weakness, and fatigue) and to modify or avoid activities that provoke episodes. Other helpful measures may include keeping a BP log and dietary education (salt/fluids). Learning physical counter-maneuvers that reduce standing OH and practicing postural and resistance training are helpful measures.

SYMPTOMATIC TREATMENT

Nonpharmacologic approaches are summarized in **Table 454-9**. Adequate intake of salt and fluids to produce a voiding volume between 1.5 and 2.5 L of urine (containing >170 meq/L of Na^+) each 24 h is essential. Sleeping with the head of the bed elevated will minimize the effects of supine nocturnal hypertension. Prolonged recumbency should be avoided when possible. Patients are advised to sit with legs dangling over the edge of the bed for several minutes before attempting to stand in the morning; other postural stresses should be similarly approached in a gradual manner. One maneuver that can reduce OH is leg-crossing with maintained contraction of leg muscles for 30 s; this compresses leg veins and increases systemic resistance. Compressive garments, such as compression stockings or abdominal binders, are helpful on occasion but uncomfortable for many patients. For transient worsening of OH, drinking two 250-mL (8-oz) glasses of water can raise standing BP 20–30 mmHg for about 2 h, beginning ~20 min after the fluid load. The patient can increase intake of salt and fluids (bouillon treatment), increase use of physical counter-maneuvers (elevate the legs when supine), or temporarily resort to a full-body stocking (compression pressure 30–40 mmHg).

TABLE 454-9 INITIAL TREATMENT OF ORTHOSTATIC HYPOTENSION (OH)

Patient education: mechanisms and stressors of OH
High-salt diet (10–20 g/d)
High-fluid intake (2 L/d)
Elevate head of bed 10 cm (4 in.) to minimize supine hypertension
Maintain postural stimuli
Learn physical counter-maneuvers
Compression garments
Correct anemia

Anemia should be corrected with erythropoietin, administered subcutaneously at doses of 25–75 U/kg three times per week. The hematocrit increases after 2–6 weeks. A weekly maintenance dose is usually necessary. However, the increased intravascular volume that accompanies the rise in hematocrit can exacerbate supine hypertension.

If these measures are not sufficient, pharmacologic treatment may be necessary. Midodrine, a directly acting α_1-agonist that does not cross the blood-brain barrier, is effective. It has a duration of action of 2–4 h. The usual dose is 5–10 mg orally tid, but some patients respond best to a decremental dose (e.g., 15 mg on awakening, 10 mg at noon, and 5 mg in the afternoon). Midodrine should not be taken after 6:00 P.M. Side effects include pruritus, uncomfortable piloerection, and supine hypertension especially at higher doses. Droxidopa (Northera) was recently approved by the FDA for treatment of neurogenic OH associated with PAF, PD, or MSA; oral droxidopa is converted to NE and in short-term clinical trails was effective in decreasing symptoms of OH. Pyridostigmine (Mestinon) appears to improve OH without aggravating supine hypertension by enhancing ganglionic transmission (maximal when orthostatic, minimal when supine). Fludrocortisone will reduce OH but aggravates supine hypertension. At doses between 0.1 mg/d and 0.3 mg bid orally, it enhances renal sodium conservation and increases the sensitivity of arterioles to NE. Susceptible patients may develop fluid overload, congestive heart failure, supine hypertension, or hypokalemia. Potassium supplements are often necessary with chronic administration of fludrocortisone. Sustained elevations of supine BP >180/110 mmHg should be avoided. Supine hypertension (>180/110 mmHg) can be self-treated by avoiding the supine position (e.g., sleeping in a recumbent chair) and reducing fludrocortisone. A daily glass of wine, if requested by the patient, can be taken shortly before bedtime. If these simple measures are not adequate, drugs to be considered include oral hydralazine (25 mg qhs), oral nifedipine (Procardia; 10 mg qhs), or a nitroglycerin patch.

A promising drug combination (atomoxetine and yohimbine) has been studied for use in human subjects with severe OH not responsive to other agents, as can occur is some patients with diabetes and severe autonomic neuropathy not responsive to other medications. The atomoxetine blocks the NE reuptake transporter, and yohimbine blocks α_2 receptors that mediate the sympathetic feedback loop for downregulation of BP in response to atomoxetine. The result is a dramatic increase in BP and standing tolerance. This combination is not FDA approved for this purpose. It is possible that the limited drug duration of action can be used to withdraw drug treatment when the patient anticipates becoming supine (e.g., before sleep).

Postprandial OH may respond to several measures. Frequent, small, low-carbohydrate meals may diminish splanchnic shunting of blood after meals and reduce postprandial OH. Prostaglandin inhibitors (ibuprofen or indomethacin) taken with meals or midodrine (10 mg with the meal) can be helpful. The somatostatin analogue octreotide can be useful in the treatment of postprandial syncope by inhibiting the release of GI peptides that have vasodilator and hypotensive effects. The subcutaneous dose ranges from 25 μg bid to 200 μg tid.