

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 and requires monitoring.

If these measures are not sufficient, additional 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 PM. Side effects include pruritus, uncomfortable piloerection, and supine hypertension, especially at higher doses. Droxidopa (Northra) for treatment of neurogenic OH associated with PAF, PD, or MSA is effective in decreasing symptoms of OH. Pyridostigmine appears to improve OH without aggravating supine hypertension by enhancing ganglionic transmission (maximal when orthostatic, minimal when supine), but with only modest clinical effects on BP. 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 or elevating the head of the bed) and reducing fludrocortisone. 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 in 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