

### ***Adverse Effects of Antihypertensive Drugs***

**THERE** are few things in this world that are a completely unmixed blessing. Therapeutic results obtained with the newer antihypertensive agents have

been encouraging and as a result they are enjoying more widespread use. These preparations, however, are by no means innocuous. All can produce side effects occasionally with serious consequences. It behooves us, therefore, when embarking on a pro-

gram of chemotherapy to be cognizant fully of their inherent dangers as well as anticipated benefits.

The oldest of the newer hypotensive drugs are the Veratrum alkaloids (Vertavis, Veriloid, Vergitryl, Provell Maleate, Veralba, Unitensen). They also are among the safest. No deaths and no sensitization or chronic cumulative reactions have been recorded from their use. Nevertheless, they are notorious for producing disturbing acute reactions characterized by vomiting, bradycardia, hiccough or severe hypotension in dosages only slightly in excess of the therapeutic dose. The hypotension can be reversed by giving ephedrine, 50 mg. intramuscularly, and the vomiting and bradycardia are eased by atropine in doses of 0.5 to 1 mg. intramuscularly. When Veratrum is given intravenously it always should be administered slowly in dilute solution with continuous checking of the blood pressure in order to avoid profound hypotension. The infusion must be stopped as soon as the blood pressure falls significantly.

The ganglionic blocking agents (Bistrium, Hexameton, Esomid, Methium, Ansolysen) also produce only acute side effects. These are secondary to the inhibition of impulses through all autonomic ganglia—parasympathetic as well as sympathetic. The resulting side effects include postural hypotension, paralysis of visual accommodation due to failure of reflex constriction of the pupil, dryness of the mouth caused by loss of salivary secretion, atony of the gastrointestinal tract leading to constipation and even paralytic ileus, failure of contraction of the urinary bladder and impotence. All of these will disappear when the drug is discontinued. However, even though transient, marked hypotension and particularly paralytic ileus can be dangerous. Deaths have been reported especially from the latter.

Extreme hypotension with collapse with these agents is best treated by placing the patient in the head-down (Trendelenburg) position. Epinephrine should not be used although norepinephrine (Levophed) by slow intravenous drip can be given if the blood pressure is checked continuously.

Because of the extreme potency of these agents, recordings of blood pressure several times daily by the patient or a member of his family are essential at all times even after the initial dosage adjustment period. Severe salt restrictions should not be imposed except in cardiacs, as this intensifies the degree of postural hypotension. Parasympathomimetic agents have been helpful, particularly oral pilocarpine nitrate (3 to 6 mg. t.i.d.) to combat dry-

ness of the mouth, urinary retention and failure of visual accommodation. Ansolysen is more effective and better tolerated by the oral route of administration than are the other ganglionic blocking drugs. Despite the frequency of side effects, Ansolysen usually is an extremely effective drug for controlling the blood pressure when other methods fail.

Apresoline produces not only acute effects but also sensitization phenomena on long-term administration. The acute side effects consist of headache, palpitation and tachycardia and can be minimized by elevating the dosages gradually. Dependent edema is common and does not mean that the patient has developed cardiac failure, but may necessitate discontinuing the drug. The sensitization phenomena occur after long-term use and include fever, dermatitis, arthritis and anemia. The most serious is a lupus erythematosus-like syndrome. Most of these severe reactions occur when the daily dosages are above 300 mg. per day. When they occur the drug should be discontinued immediately.

Rauwolfia serpentina and its derivatives (Rau-dixin, Rauwiloid, Serpasil, Reserpoid) have been widely advertised as "persistently pleasant drugs" and "tranquilizers." It is becoming apparent, however, that the emotional reaction is not always pleasant. Some patients complain of lassitude and depression which is to them decidedly unpleasant. Others may experience no adverse psychic effects until after several months of treatment when a severe depression gradually develops. Six such cases have been observed in our clinic; in two of these suicidal thoughts were entertained. The nasal congestion which occurs with the Rauwolfia alkaloids also has been considered to be of minor consequence, but we have encountered two cases of severe epistaxis which could not be controlled until the drug was discontinued.

These comments are not meant to discourage the physician from using antihypertensive agents since they seem to be valuable in selected cases, for example, Rauwolfia in the anxious, labile hypertensive and Ansolysen plus Rauwolfia in the patient with sustained hypertension who is developing organic damage therefrom. It should be realized clearly however that the goal of uniformly effective, easily regulated nontoxic antihypertensive drug therapy has not yet been achieved. In the meantime, a knowledge of the side effects produced by the presently available compounds will increase our alertness to their occurrence and prevent more serious developments.

—EDWARD D. FREIS, M.D.