BRIEFS FROM THE LITERATURE

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Briefs were submitted by Drs. C. M. Ballinger, Lee S. Binder, John P. Bunker, M. T. Clarke, R. A. Devloo, D. W. Eastwood, J. E. Eckenhoff, Martin Helrich, J. R. Householder, S. J. Martin, R. E. Ponath, Alan D. Randall, R. W. Ridley, and H. S. Rottenstein. Briefs appearing elsewhere in this issue are a part of this column.

MONOAMINE OXIDASE INHIBITOR

Central nervous system stimulants are found in compounds such as: (1) sympathomimetics, particularly the phenylalkylamines (ephedrine, amphetamine, methamphetamine), and the newer phenethylamines (pipradol, methylphenidate, phenmetrazin); (2) variations of certain antihistaminic structures which have yielded both tranquilizers and central stimulants (phenyltoloxamine); (3) anticholinergic cogeners of atropine (benactyzine); (4) local anesthetics; and (5) ganglionic stimulants (nicotine, lobeline). However, the majority of these central stimulants have certain structural features contained in norepinephrine, acetylcholine, histamine and serotonin. The replacement of an amino group by a hydrazine moiety in a series of sympathomimetic amines has yielded a number of potent central stimulants which produce their effect both by direct stimulation of the central nervous system (amphetaminelike), and by monoamine oxidase inhibition in the brain. This prevents metabolic destruction of endogenous central excitatory amines (norepinephrine and dopamine). (*Biel, J. H., Nuhfer, P. A., and Conway, A. C.: Structure and Activity Relationships of Monoamine Oxidase Inhibitors, Ann. New York Acad. Sc. 80: 568 (Sept. 17) 1959.*)

MONOAMINE OXIDASE INHIBITORS

Side effects associated with chronic use of monoamine oxidase inhibitors are: orthostatic hypotension, periorbital and dependent edema, subclinical and possibly clinical jaundice, constipation, delayed micturition, impotence (and its opposite), pruritis, gastritis, anemia, and in one instance, uremia. In roughly 70 per cent of psychiatric patients, a recrudescence of psychopathology occurs accompanied by hyperactivity, irritability, agitation and assaultiveness. Neuromuscular systoms include flaccidity, paresthesias and twiching. (*Bailey, S. d'A, and others: Comparison of Iproniazid with other Amine Oxidase Inhibitors, Including W-1544, JB-516, RO 4-1018, and RO 5-0700, Bull. New York Acad. Sc. 80: 652 (Sept. 17) 1959.*)

MONOAMINE OXIDASE INHIBITORS

The histological changes in the liver of patients who developed jaundice following the intake of iproniazid represent different stages and degrees of a diffuse hepatic parenchymal disease, the picture being similar to that considered characteristic for viral hepatitis. The main difference is the higher incidence of more severe alterations in the iproniazed group. (*Popper, H.: Hepatic Injury in Patients Who Have Received Iproniazid, Bull. New York Acad. Sc. 80: 928 (Sept. 17) 1959.*)

MONOAMINE OXIDASE INHIBITORS

Monoamine oxidase inhibitors in large doses led to a decrease in hemoglobin and in the number of red cells observed. Histological examination revealed other signs of erythrocyte destruction: hemosiderosis of spleen, liver and kidney; increased cellularity of bone marrow; and hyperemia of the spleen. Some compounds were also hepatotoxic, including severe swelling, fatty infiltration, and necrosis of the liver. Liver damage was usually accompanied by some degenerative changes and fatty infiltration of the kidneys. Prolonged treatment with therapeutic doses produced no changes in reproductive organs of rats. Higher doses, however, caused

atrophy of the testicles and impairment of spermatogenesis. No obvious relationship of the monoamine oxidase-inhibiting activity of the compounds to any of these changes could be detected. (*Zbinden, G., and Studer, A.: Experimental Pathology of Iproniazid and Related Compounds, Bull. New York Acad. Sc. 80: 873 (Sept. 17) 1959.*)

ANTICONVULSANT Monoamine oxidase inhibitors have a pronounced anticonvulsant effect in animals which is closely associated with elevation of brain 5-hydroxytryptamine and norepinephrine, while reserpine enhances convulsions. The association between changes in physiologically active brain amines and enhancement of or protection against experimental seizures raises a possibility that certain types of epilepsy may involve a localized dysfunction in the formation, release, or metabolism of known or unknown amines. (*Prockop, D. J., Shore, P. A. and Brodie, B. B.: Anticonvulsant Properties of Monoamine Oxidase Inhibitors, Bull. New York Acad. Sc. 80: 643 (Sept. 17) 1959.*)

PRESSOR AMINES Sympathomimetic amines can be divided into 3 main classes on the basis of their action after norepinephrine infusion. Class I contains derivatives of catecholamine. Their pressor action is diminished by prior infusion of norepinephrine (N). Class II contains some derivates of ethanolamine rather closely related to N chemically. Their pressor action is less diminished by prior infusion of N. Class III contains other derivatives of ethanolamine and derivatives of phenylethylamine. Their pressor action is markedly enhanced by a prior infusion of N. Aramine, vasoxyl and propadrine, derivatives of phenylethylamine, were found to belong to class II. Methedrine, mephine and vonedrine, derivatives of phenylethylamine, acted like class III agents with mephine having the most marked action. During an infusion of N this agent is stored in the vessel wall from which it is slowly released. It is postulated that the large amount of stored N blocks the pressor action of circulating N in some way. Class III agents appear to act by liberating N from the vessel wall. Class II agents act in this way in part, but also have a direct action on the vessel wall as do class I agents. It is suggested that the most effective means of supporting the pressor action of an N infusion which is gradually failing is to give a class III agent. Class II agents would be less effective. (*Burn, J. H. and Rand, M. J.: Fall of Blood Pressure After Noradrenaline Infusion and Its Treatment by Pressor Agents, Brit. M. J. 1: 394 (Feb. 14) 1959.*)

NOREPINEPHRINE The response to norepinephrine in 8 patients with aortic regurgitation was studied and contrasted with findings in 7 normals. A disparity of response between the two groups was most manifest in the pulmonary "capillary" and artery pressure alterations, a nearly fourfold rise to pulmonary congestion levels in the aortic regurgitation group contrasted with a 5 mm. Hg rise occurring in the normal. This small increment of left ventricular filling pressure was associated with a sizable stroke work increase in the normal, but no significant change in the aortic regurgitant group. Bradycardia and increased pulmonary arteriolar resistance, present in the normals, were absent in the aortic regurgitation group. Displacement of blood from the peripheral venous system seems the predominant if not the sole mechanism in the induction of pulmonary congestion and diminished left ventricular performance. Data acquired in four patients during peripheral venous occlusion by tourniquet supported this interpretation. Here, the pulmonary "capillary" pressure increment and the stroke work response after norepinephrine were of the same order exhibited in the normal. (*Regan, T. J., and others: Norepinephrine Induced Pulmonary Congestion in Patients with Aortic Valve Regurgitation, J. Clin. Invest. 38: 1564 (Sept.) 1959.*)

LEVARTERENOL Use of levarterenol in treatment of shock is sometimes complicated by extravasation sloughs of skin and subcutaneous tissue. Treatment has been by infiltration of the local areas of ischemia by 5–10 mg. phentolamine methane sulfonate (Regitin) with reversal of vasoconstrictive ischemic effects in 5–7 minutes. This treatment is effective only if the extravasation is discovered and treated promptly. Studies have shown mix-