CURRENT LITERATURE

Prolongation of Chloral Hydrate Sleeping Time By 5-Hydroxytryptamine and by Certain other Drugs *by Fastier, F.N., Speden, R.N. and Hendrieka Wall (1957)* **: Brit. J. Pharmacol., 12,** *251.*

Various drugs have been tested for a capacity to prolong the hypnotic effect of chloral hydrate in mice. Amongst the compounds which when injected subcutaneously in substantial amount shortly before chloral hydrate (250 mg./kg. intraperitoneally) increased its sleeping time significantly were, adrenaline, nor-adrenaline, phenylephrine, methoxamine, 5-hydroxytryptamine (Serotonin), histamine, ergotamine, yohimbine, and atropine. The ability of these drugs to prolong chloral hydrate sleeping time can not be related to any common circulatory property but most of the active drugs are known to lower body temperature under comparable conditions. It was found that mice which have been pre-treated with 5-hydroxytryptamine or adrenaline suffer a much greater fall of body temperature when chloral hydrate is given subsequently than do mice which have been given chloral hydrate alone. It is suggested that some at least, of the drugs which prolong the effects of hypnotics do so by virtue of a hypothermic action.

Antilipaemic Agent Without Anticoagulant Action *by Basterman, E.E.M. and Evans, J. (1957)* **: Brit. Med. J., 1,** *310.*

Laminarin sulphate M and N prepared by the sulphation of Laminarin, a polysaccharide from *Laminaria cloustoni*, (containing 0.62 and 0.37 sulphate groups per glucose unit respectively), were examined for antilipaemic activity on patients with ischaemic heart disease. Samples of venous blood were submitted to paper electrophoresis. Laminarin sulphate M increased the electrophoretic mobility of lipo-proteins and altered their distribution in the same way as heparin. Antilipaemic effect persisted for 4 to 6 hours after intravenous injection of 100 mg. of Laminarin sulphate M. No effect was observed after intramuscular injection. It appears to be suitable substance for use in long term investigation of the effects of lipaemic substances on the course of atherosclerosis in man.

Ventricular Fibrillation in the Isolated Rabbit Heart *by Armitage, A.K, Burn, J. H. and Gunning, A. J. (1957),* **Brit. J. Pharmacol., 12,** *215.*

Ventricular fibrillation has been produced in the isolated and perfused rabbit heart by stimulating electrically at the rate of 500 to 700/min. When the perfusion fluid contained normal amounts of sodium, potassium and calcium, the fibrillation persisted after the stimulation was stopped in about 40 per cent of hearts. When the sodium was reduced to half, toxicity being maintained by sucrose or by choline chloride, persistent fiibrillation was observed in 100 per cent of hearts. The addition of eserine, atropine or carbachol did not alter the percentage of hearts in which fibrillation persisted. The antimalarial compounds chloroquine, mepacrine and pyrimethamine arrested persistent fibrillation, restoring a normal rhythm.

The Assay of Histamine, 5-hydroxytryptamine, Adrenaline and Noradrenaline on the blood pressure of the Fowl *by Natoff, I. L. and Mary F. Lockett (1957) :* **J. Pharm. Pharmacol., 9,** *464.*

The authors have carried out studies on blood pressure of fowls. Fowls of various breeds, weighing 1.0 to 1.6 kg. were used, aneasthetised by intramuscular injection of 1.0 ml./kg. of 6% solution of pentobarbitone sodium. Histamine and 5-hydroxytryptamine, 1 μg./kg. depress, and (−)—adrenaline and (±) nor–adrenaline 0.5 μg./kg. raise, the blood pressure of fowls under pentobarbitone anaesthesia. With each compound the response in mm.Hg. is linearly related to log dose. The authors have used these responses satisfactorily for the bioassay of these compounds.

Aspects de la Physio-pharmacologie de la Motilite Gastrique *by Malafaya-Baptista, A., Guimarais, J. A., Garrett, J. and Ossward, W. (1957) :* **Arch. int. Pharmacodyn., 111,** *191.*

The effect of some drugs on gastric motility and drug induced modifications of the responses to vagal and splanchnic stimulations were studied in 45 spinal or anaesthetised dogs. Gastric contractions were generally recorded by direct myography. The pattern of gastric muscle responses to electrical stimulation of vagus and splanchnic nervous trunks is described and in the interpretation of splanchnic motor effects emphasis is put on the adreno cholinergic character of the splanchnic nerve. Gastric motor effects of some autonomic drugs (acetylcholine, carbachol, epinephrine, nor-epinephrine, atropine, ergotamine and physostigmine) and of a few other drugs (d-tubocurarine, amobarbital, phenobarbital. succinic acid and barium chloride) have been studied and are described in detail. Some aspects concerning the mechanism of action of these drugs are discussed.

The Hypothalamus as an Intermediary for Pituitary Adrenal Activation by Aspirin *by George, R. and Way, E. L. (1957) :* **J. Pharm. & Exper. Therap., 119,** *311.*

The authors studied the effect of aspirin on adrenal ascorbic acid in rats with hypothalmic lesions. Lesions of the median eminence completely blocked the adrenal ascorbic acid depletion which normally occurs within one hour following the administration of aspirin (150 mg./kg.). Partial lesions of the anterior median eminence, as well as lesions placed anterior and dorsal to the median eminence, did not alter the normal response to aspirin. The significance of these findings is discussed.

The Assay of Acetylcholine on the Superfused Frog Rectus Muscle *by Ahmad, A. and Taylor, N. R. W. (1957).* **J. Pharm. Pharmacol., 9,** *536.*

A method of superfusion for assaying acetylcholine on the eserinised frog rectus muscle applying each dose in a volume of 0.2 ml. is described. The sensitivity of the superfused preparation is compared with that of the preparation in a 5 ml. bath and the former is 10-20 times more sensitive than the bath preparation. Statistical evidence from the results in 10 parallel assays (2+2) is adduced to show that the method of superfusion and bath method are of equal accuracy when used under comparable conditions. They conclude that the method of superfusion gives a reliable and accurate assay of acetylcholine.

Modification of the Pharmacology of Reserpine and Serotonin by Iproniazid *by Chessin, M., Kramer, C. R. and Scott. C. C, (1957) :* **J. Pharm. & Exper. Therap., 19,** *453.*

Mice, pretreated with iproniazid, respond to reserpine administration with marked excitation instead of usual depression. This excitation is effectively blocked or inhibited by chlorpromazine. Similar excitatory effects of reserpine are seen in rats, guinea pigs and rabbits pretreated with iproniazid. In cats and dogs the onset of reserpine depression is delayed by iproniazid. Serotonin administered intracerebrally or 5-hydroxytryptophan administered intravenously induce stimulation in iproniazid-pretreated mice which differs from that seen with reserpine. Iproniazid also reduces the mortality rate of insoluble reserpine administered to mice. Effect of reserpine on blood pressure of dogs and cats pretreated with iproniazid is also described.

Ecchymotic Skin Lesions in Patients Receiving Prednisone *by Denko, C. W. and Schroeder, L. R. (1957)* : **J. Amer. Med. Ass., 164,** *41.*

The authors noted the occurence of purpura, ecchymotic skin lesions, and easy bruising in 20 per cent of a group of 75 patients receiving prednisone for a variety of rheumatological disorders. The incidence of these side effects was only 2-5 per cent in patients maintained on cortisone, hydro-cortisone and ACTH. Investigations made on the coagulating mechanism in evaluating this bleeding tendency indicated, consistently disturbed normal capillary function and decreased capillary resistance. Alteration in platelets or capillary physiology due to prednisteroids was thought to be due to derangement involving ascorbic acid and some interferrence in fibrinogen synthesis, since ascorbic acid 50 mg. twice daily was found valuable in some cases, while the remainder improved on discontinuance of therapy. Ecchymoses were observed as early as seventeen days after initiation of prednisteroid therapy and as late as seven months after, and occured in patients receiving as little as 5 mg. per day.

A Method for Measurement of Analgesic Activity on Inflamed Tissue *by Randall, O. L. and Solitto, J. J. (1957):* **Arch. int. Pharmacodyn., 111,** *409.*

A new method for measuring analgesic activity in rat has been developed based on the principle that inflammation increases sensitivity to pain. Salicylate, phenylbutazone, and R02-5383 raise the pain threshold of both normal and inflammed tissue. This procedure therefore, differentiates analgesics of the salicylate type from the central antipyretics of the amino-pyrine type and the central narcotics.

Effect of epinephrine, norepinephrine and isopropylarterenol on the isolated auricles of four mammalian species *by Penna, S. G. and Gauz, A. (1956)* : **Amer. J. Physiol., 185,** *332.*

The authors tested epinephrine, norepinephrine and isopropylarterenol on the amplitude of contraction and rate of the auricles of the rat, guineapig, rabbit and cat. The auricles were suspended in Lock's solution at 29°C. In some of the cats left and right auricles were separated and the two auricles were attached to separated isotonic writing levers. Isopropylanterenol was much more potent in all species particularly in rats. Nor-epinephrine was least effective. Right auricle was more sensitive.

Antifoam Agents in Pulmonary oedema *by Balagot, R. C., Reyes, R. M. and Sadove, M. S. (1957) :* **J. Amer. Med. Ass., 163,** *630.*

A new compound, No.5507 which consisted of silicon 0.01 per cent, Superinone (polyhydric alcohol) 0.75 per cent, potassium carbonate 1 per cent, glycerol 1 per cent, was tested for its ability to suppress foam in adrenaline-induced pulmonary oedema in rabbits. It was found superior to octly alcohol and 10 and 20 per cent ethanol. The drug is safe and without any depressant effect on central nervous system. It was tried clinically in 8 patients suffering from pulmonary oedema with almost immediate suppression of foam.

The Extra Cardiac Hypotensive Effect of Veratrum *by Rose, C. J. and Lazaro, E. J. (1956)* : **J. Pharm. & Exper. Therap., 117,** *461.*

When veratrum was administered to dogs maintained with mechanical left ventricle of constant output, it produced a hypotensive response. This indicates that hypotension produced by veratum occurs independantly of any alteration in Cardiac function. Together with the studies of Wand, (1952) which demonstrated the absence of a hypotensive effect when the drug was excluded from the coronary and pulmonary circulations this work tend to confirm previous work indicating that a reflex producing hypotension independantly of bradycardia is initiated in the chest.

A Delayed Slow Contracting Effect of Serum and Plasma Due to the Release of a Substance Resembling Kallidin and Bradykinin *by Schachter, M. (1956) :* **Brit. J. Pharmacol., 11,** *111.*

Dilution of ox, guinea-pig, rat, dog, cat and human serum or plasma releases a smooth muscle stimulating agent resembling kallidin and bradykinin. The release of this substance is demonstrable when dilution occurs in test bath, but incubation of dilute serum increase the release. The release of this substance by dilution of ox or guineapig serum is greatly reduced or abolished in the presence of soya bean trypsin inhibitor or by heating the serum at 56°C for 3 hours to destroy kallikreinogen. This substance resembles kallidin and bradykinin in that it contracts guinea pig, cat, and dog intestine, and guinea, pig, rat and cat uterus. The hypothesis is suggested that dilution of serum releases kallidin through activation of kallikreinogen.

The influence of Lesions in the Anterior and Postetior Hypothalamus on the Tonic and Phasic Autonomic Reactions *by Gellhorn, E., Nakao, H., and Redgate, E. S. (1956) :* **J. Physiol., 131,** *402.*

Experiments performed on lightly anaesthetised cats are reported in which the influence of lesions restricted to either the anterior or the posterior hypothalamus on autonomic reactions was studied. The slowing of heart rate during nor-adrenaline induced rise of blood pressure was used as a test for parasympathetic system, whereas the return of the blood pressure from a drug induced hypotension (with acetyl choline, mecholyl, or histamine) and other sympathetic effects served as indicators for the excitability of the sympathetic system. Lesions of the anterior hypothalamus lead to a considerable decrease of the nor-adrenaline-induced (i.e. parasympathetic) reflex while lesions of the posterior hypothalamus lead to an aggravation of the drug induced hypotension with a lessened sympathetic response of the heart and the nictitating membrane. In addition lesions of the anterior hypothalamus produce signs of release of posterior sympathetic hypothalamus and vice versa. The principle of reciprocal innervation seems to be valid for the hypothalamus according to them. They conclude on the basis of these observations that tonic sympathetic and parasympathetic discharges originate in the posterior and anterior division of the hypothalamus respectively.

Dynamics of Complete Right Ventricular Failure in Dogs Maintained With an Extracorporeal left Ventriclc *by Rose, J. C,, Lazaro, E. J. and Broida, H. P. (1956) :* **Circulation Research, 5,** *173.*

The authors produced acute isolated right ventricular failure in dogs maintained with a mechanical left ventricle of controlled output. They observed (1) An immediate and marked elevation of central venous pressure simultaneously with uptake of large quantities of fluid from the pump reservoir (2) In the abscence of right ventricular contractions, the venous pressure became a linear function of left heart output (3) The intravascular volume became passively expanded when right heart failure was induced (4) Edema formation was acclerated by right heart failure, hypervolemia and venous hypertension. These observations elucidate the role of normal right ventricular function in the maintenance of the central venous pressure within physiologic ranges, and they also lend support to the theory that venous hypertension directly results from right ventricular failure. The authors also conclude that hypervolemia is a necessary accompaniment of cardiac incompetence.

Effect of Anaesthetics on Systemic Baroreceptors *by Robertson, J. D., Swan, A. A. B. and Whitteridge, D. (1956) :* **J. Physiol., 131,** *483.*

Inhalation of ether, chloroform or trichloroethylene but not cyclopropane increases the sensitivity of carotid sinus and aortic baroreceptors in cats. The effect has been observed in single units from the perfused carotid sinus, where mechanical factors, such as changes in the form of the pressure pulse wave, can be excluded. The authors have also found that receptors in the perfused carotid sinus show an increased discharge in conditions in which contraction of smooth muscle of the arterial wall has been shown by others to decrease the discharge. The role of sensitisation of baroreceptors in the vasomotor response of the intact animal during induction of anaesthesia with volatile anaesthetics is discussed.

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