CURRENT LITERATURE

Comparison of Meprobamate, Pentobarbital and Placebo as Preanaesthetic Medication for Regional Procedures *by E. I. Eger & H. H. Keasling, (1959)* : **Anaesthesiology., 20,** *1.*

The unavailability of a suitable preanaesthetic medicament is discussed. A double blind comparison of placebo, meprobamate and pentobarbital as preanaesthetic medicants for regional procedures is presented. The authors have determined the effects of each of these treatments on patient's apprehension, cooperation, drowsiness, reaction to painful stimuli, talkativeness, nausea and emesis. The anaesthetist's evaluation of the adequency of each premedicant has also been determined. Both, meprobamate and pentobarbital have been found to be more effective than placebo. The difference is well marked in younger group of patients but tends to be less marked with advancing age and may disappear in the senile group. No significant difference has been found between meprobamate and pentobarbital in doses employed.

B. N. DHAWAN

Tranquilizing Effect of "Substance P" *by P. Stern aud R. Milin. (1959)* : **Proc. Soc. Exp. Biol. and Med., 101,** *299.*

Because of synergism and certain similarities between "Substance P" on the one hand and mephenesin and meprobamate on the other, these workers have postulated that "substance P" may be a physiological tranquilizer. To verify this postulate, they have studied the effect of this substance on wild hares kept in a state of fear. This method has been previously used by them to demonstrate the sedative effect of chlorpromazine, reserpine, mephenesin and meprobamate. Substance P has also been found to exert a marked tranquilizing effect in these animals. This finding supports the view that this substance belongs to the class of biological regulators of the neuro-endocrine system.

G. P. GUPTA

Inhibition of Human Cholinesterases by Narcotic Analgesics and their Antagonists *by F. F. Foldes, E. G. Erdos, N. Baart, J. Jwartz and E. K. Zsigmond 1959* : **Arch. Int. Pharmacodepi 120,** *286*

The inhibitory effect of narcotic analgesics on cholinesterases was studied by various workers. The interest in anticholinesterase activity of narcotics increased due to the cholinergic effects of morphine and similar compounds on several organ systems and due to the potentiation of the analgesic activity of morphine by neostigmine. In this study the inhibitory effect of 8 narcotic analgesics and 2 narcotic antagonists on human plasma and red cell cholinesterase has been investigated. The allyl derivatives have a greater inhibitory effect on plasma cholinesterase but not on red cell cholinesterase, than the methyl substituted parent compounds. The morphinan derivatives are the most potent inhibitors of red cell cholinesterase. However, no correlation was found between anticholinesterase effect and analgesic activity.

G. P. GUPTA

An Anticonvulsant Effect of Monoamine oxidase Inhibitors *by D.J. Prockop, P. A. Shore and B. B. Brodie. (1959)* : **Experientia., 15,** *145.*

Three irreversible monoamine oxidase inhibitors, Iproniazid, JB 516 (phenylisopropyl-hydrazine) and JB 807 (1-[phenylisopropyl]-2-isopropyl hydrazine) have been shown to suppress the tonic extensor phase of supramaximal electroshock seizures in rats. Isoniazid, a congener of iproniazid, did not elevate brain amines and had no anticonvulsant effect. In contrast to the monoamine oxidase inhibitors, reserpine increased the response to electroshock and shortened the latent period for appearance of tonic extension. The authors suggest the possibility that a substance released by reserpine and metabolised by monoamine oxidase is involved. JB 516 and JB 807 antagonise the tonic extensor phase of convulsions evoked by intravenously administered pentylenetetrazol in mice. Diphenylhydantoin, however, has been shown to possess anticonvulsant effect in doses which do not produce a measurable rise in brain amine levels.

B. N. DHAWAN

The Metabolism of Lysergic Acid Diethylamide *by E. S. Boyd. (1959)*: **Arch. int. Pharmacodyn., 120,** *292.*

The metabolism of LSD-25 has been studied by following the distribution of radioactivity through the body of the rat after administration of Carbon-14-labelled LSD-25 (0.01, 0.1 and 1.0 mgm./kgm.). Lowest concentrations (0.01%) are seen in brain. Radioactivity can be detected in all tissues. None of the existing methods has been found to be adequate for isolating LSD-25 or its metabolites from animal tissues. About 80% of the administered radioactivity is excreted in the bile as four compounds. Two of these (M-1 and M-2) account for major part of this radioactivity. They are highly polar and appear to be only slightly modified LSD-25. Their exact chemical nature, however, is not known. Nothing is known about their psychotomimetic effects. A third compound (M-3) may be an artefact. The fourth compound (M-4) has many points of resemblance with LSD-25. All this radioactivity is excreted in the faeces in about 60 hours. About 8% of administered dose appears in urine and about 4% is exhaled as Carbon-14 dioxide.

B. N. DHAWAN

Application of Static Muscular Contraction to the Analysis of the Mechanism of Vomiting *by A. A. Sukhanov. (1958)* : **Biull. Eksptl. Biol. i. Med., 45,** *12.*

The effect of static muscular work, which consisted in holding a load on the back, on vomiting has been studied on dogs with Basov gastric fistulae and with a Thirvyvella fistula of the jejunum. Vomiting induced by apomorphine (0.03-0.05 mg./kg. subcutaneously) or potassium chloride (500 ml. of 15% solution through the gastric fistula) was inhibited. Various components of vomiting were differently inhibited. The mildest depression was found in the activity of somatic muscles (contractions of abdominal muscles and diaphragm). The autonomic component (secretion of saliva, dysponea, tachycardia, stomach contractions) was only slightly inhibited. With increase of inhibition, the changes in blood pressure and respiration were found to be the most stable components out of the whole autonomic complex of vomiting reactions. A definite sequence of various components of the act of vomiting is described in experiments without the load. New suggestions are made regarding the regulation of vomiting.

B. N. DHAWAN

Effects of Controlled Progressive Hypotension on some Spinal Reflexes in the Cat *by J. W. Kissel and E. F. Domino.* (*1959*) : **Am. J. Physiol., 196,** *59.*

The pharmacological evaluation of agents affecting the central nervous system is complicated by secon lary changes resulting from fluctuations in arterial pressure particularly in the unanaesthetised spinal animals where blood pressure is already low and neurally mediated haemodynamic compensatory mechanisms have been interrupted. In the present investigation the patellar and crossed extensor reflexes have been studied in acute unaesthetised bilaterally vagotomised spinal cats for their responses to progressive haemorrhagic reduction of blood pressure. At normotensive levels the crossed extensor reflex is considerably more variable than the patellar reflex. Both reflexes fail progressively with the fall of blood pressure but at arterial pressure of 20-40 m.m. Hg. both again become hyperexcitable and are accompanied with convulsions. The crossed extensor reflex is more affected by hypotension. Both disappear under continued severe hypotension but recover upon restoration of blood pressure. Observations on spinal and intact cats under chloralose anaesthesia indicate that patellar reflex is more affected at lower blood pressure levels in animals with an intact cerebro spinal axis. The implications of these findings have been discussed.

B. N. DHAWAN

Evidence for Reflex Control of Arterial Pressure from Abdomial Receptors with Special Reference to the Pancreas *by S.J. Sarnoff, and S.I. Yamda.* (*1959*) : **Circulation Research, 7,** *325.*

The communication describes experiments which suggest that abdominal pressoreceptors may be of significance in the regulation of arterial pressure just like contribution of afferent impulses from many special sites in the vascular bed. Twenty-four experiments have been performed in anaesthetised cats to examine the response of arterial pressure and heart rate to changing vascular pressures in the blood vessels of the abdominal viscera and more particularly of the pancreas. Hypotension in the visceral blood vessels, particularly in the pancreatic vessels produces substantial elevation of systemic arterial pressure, both in presence or absence of sino-aortic receptors. In addition tachycardia is present in most cases. Elevation of pressure in the distribution of the superior mesenteric artery has the reverse effect. The authors conclude that the receptors in this area, presumably the pacinian corpuscles, make a significant contribution to reflex cardiovascular regulation.

B. N. DHAWAN

Afferent Fibres of the Stellate Ganglion *by R. Holmes, and R. W. Torrance.* (*1959*) : **Quart J. Exp. Physiol., 44,** *271.*

The electrical activity of afferent nerve fibres passing through the stellate ganglion of the cat has been investigated. Experiments have been conducted on pentobarbitalised, bilaterally vagotomised cats. The ganglion or the nerves under study are dissected beneath liquid paraffin. The potentials are picked up with platinum or stainless steel electrodes, amplified and recorded by photographing a double beam cathode ray oscillograph. Fibres have been found which come from muscle spindles of the longus colli muscle. Another group of fibres comes from receptors in the lung root and the mediastinum dorsal to the phrenic nerve, and from receptors near to the trachea and oesophagus low in the neck. The fibres of this group respond to distortions of the tissues from which they come and some of them are even sensitive to changes in the volume of air in the lungs. Their importance in thoracic sensation and in the origin of visceral reflexes is discussed. The authors have not found any apparently vagal fibres in sympathetic nerves at the level of the stellate ganglion.

B. N. DHAWAN

The Effect of Calcium Chloride on Experimental Extrasystoles with Constant coupling *by D. Scherf, D. D. Armas, B. Garnier, W. Sullivan and M. Yildiz.* (*1959*) : **Am. Heart J., 58,** *231.*

Contradictory reports are available about the influence of calcium on cardiac arrhythmias. Extrasystoles are known to appear in man and in the experimental animal after the administration of calcium but under certain conditions they may disappear when calcium is administered. In this investigation the effect of calcium chloride has been studied on the regular extrasystolic arrhythmias produced in dogs by focal application of veratrine and inhalation of a mixture of oxygen with 20 per cent carbon-dioxide. The intravenous injection of 0.15—0.3 cc/kg of calcium chloride leads to a temporary increase in the number of extrasystoles while injection of larger doses abolishes them. This "dual action" of calcium on the heart has been discussed.

G. P. GUPTA

Effects of a New "Coronary Vasodilator" on the General and Coronary Hemodynamics and Myocardial Metabolism of Man *by E. Traks, D. B. Huckel, & S. M. Sancetta. (1959)* : **Ann. Int. Med. 51,** *31.*

The effect of Vasoflex (N-cinnamyl-methylamino-2-phenylpropane hydrochloride), a synthetic drug related to catechol amines has been studied on the general and coronary hemodynamics and myocardial metabolism in man by the aid of cardiac catheterization and electrocardiogram. It produces a marked increase in the coronary blood flow when given intravenously. A desirable feature is the lack of any marked alteration in the heart rate and arterial pressure. The increase in coronary flow is however accompanied by an increased cardiac output, left ventricular work and left ventricular oxygen utilization. Hence the increased flow merely balances, rather than exceeds an increased myocardial oxygen demand. The need for investigating a coronary dilator drug by objective laboratory means before a clinical evaluation is emphasized.

G. P. GUPTA

Excretion of 17-Ketosteroids in Tropical Eosinophilia *by H. S. Chakravarti and B. Mukerjee. (1958) :* **Ann. Biochem. Exptl. Med., 18,** *41.*

Twenty four hours excretion of 17–Ketosteroids in urine was estimated in twenty-one healthy adult males and in twenty cases of tropical eosinophilia before and after treatment. Normal values were 7·44 ± 2·48 mg. In cases of tropical eosinophilia the values were 4·66±1·80 mg. and rose to 6·07±2·63 mg. after treatment. The values before the treatment were significantly lower than the normal or Post-treatment values. Significance of these changes has been discussed and it is suggested that there may be some disturbance of cortico-steroidogenesis in the body during tropical eosinophilia.

B. N. DHAWAN

The Role of Hyaluronidase in the Process of Urinary Excretion *by L. N. Ivanova (1958)* : **Biull. Eksptl. Biol. i. Med., 45,** *285.*

Isolated observations are available on the role of hyaluronidase in the regulation of water-salt metabolism. In has been found in the urine of man and animals and its amount in urine has deen shown to depend on the extent of diuresis. This study has been carried out on dogs with ureters externalized in abdominal skin flaps. The hyaluronidase activity of urine has

been determined after water loading and administration of pituitrin and urea. These workers conclude that the dependence of hyaluronidase activity of urine on the extent of diuresis cannot be explained in terms of simple dilution, salt effect or change in volume of urine in which the enzyme is distributed. The urine shows high hyaluronidase activity when the animal's blood stream has a high concentration of antidiuretic hormone and when distal re-absorption of water is intense. Liberation of the hyaluronidase enzyme by renal tissue elements is related directly to the process of distal reabsorption of water and is regulated by the antidiuretic hormone of pituitary.

G. P. GUPTA

Alterations in the Pattern of Amine Excretion in Man Produced by a Monoamine Oxidase Inhibitior *by A. Sjoerdsma, W. Lorenberg, J. A. Dates, J. R. Crout, & S. Udenfriend. (1959)* : **Science, 130,** *225.*

The administration of monoamine oxidase inhibitior, 1-phenyl-2-hydrazinopropane (JB-514) produces an increase in the urinary excretion of many amines for which efficient alternate routes of metabolism are not available. These include tryptamine, paratyramine and a 'metatyramine-like' substance. The inhibitors can therefore, be used to detect previously unsuspected pathways of aminoacid decarboxylation. The finding that the excretions of norepinephrine, epinephrine, 3, 4-dihydroxyphenyl-ethylamine and possibly serotonin are not appreciably affected is consisent with previous reports of the existence of alternative metabolic routes.

G. P. GUPTA

The Mechanism of Insulin Antidiuresis *by H. V. Murdhaugh, R. R. Robinson & E. M. Doyle. (1959)* : **J. Lab. & Clin. Med. 53,** *569.*

Insulin has been shown to produce antidiuresis independent of its effect upon the blood sugar concentration. It has been suggested that this antidiuresis is due to a specific effect of insulin upon water reabsorption by the renal tubule. The present study has been conducted in normal subjects, patients with diabetes mellitus and patients with diabetes insipidus to test the hypothesis. The failure of insulin to produce antidiuresis in the patient of diabetes

insipidus and the inhibition of insulin antidiuresis in normal subjects by the administration of alcohol which inhibits the release of ADH, suggest that insulin antidiuresis is mediated through ADH and is not due to a specific effect of insulin upon the renal tubule.

G. P. GUPTA

Mechanism for the Inhibition of Gastric Secretion by Chlorpromazine in the Dog *by D. C. H. Sun and H. Shay.* (*1959*) : **J. Pharmacol. Exper. Therap. 126,** *155.*

Studies have shown an inhibitory effect of chlorpromazine on volume and acid secretion of the gastric secretion in rat and man. The present investigation has been carried out in the dogs to obtain information on the mechanism of this action. The results show that the drug inhibits output of acid and pepsin of gastric secretion induced by sham-feeding in dogs equipped with exophagostomy and a gastric fistula, but has no effect on acid or pepsin output of mecholyl induced secretion in Heidenhain pouch dogs. This supports a central rather than a peripheral site for this action of the drug.

G. P. GUPTA
