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ABSTRACTS

AN *in vivo* HYPOGASTRIC NERVE-SEMINAL VESICLE PREPARATION OF GUINEA-PIG. *By* **P. R. Saxena and P.V. Houwelingen**. *Pharmacology Research Department, N. V. Organon, Oss. The Netherlands.*

Isolated seminal vesicle has been only occasionally employed as a test object. Recently Naimzada (*Med. Pharmacol. Exp.*, **15**, 561, 1966) described an isolated hypogastric nerve-seminal vesicle preparation. The advantages of studying an organ *in vivo* are obvious and hence the following preparation was developed.

Male guinea-pigs (above 350 *g.*) were anaesthetised and put on artificial respiration. Blood pressure was recorded through a common carotid artery. After opening the abdomen in the mid-line, the viscera were displaced to one side to expose the seminal vesicles. The intra-seminal vesicular pressure (ISP) was recorded after introducing a small specially designed latex balloon in one of the seminal vesicles. The hypogastric nerve of the corresponding side was put on a pair of platinum electrodes about 2 *cm* from the innervated organ, and was supramaximally stimulated using a Grass S_4 stimulator. The records were traced on a Grass model 7 polygraph. Drugs were injected through a cannulated external jugular vein. Stimulation of the hypogastric nerve produced a prompt contraction of the seminal vesicle thereby increasing the ISP. The supramaximal voltage was between 5 and 15 V and the optimal frequency 30-40/sec.

Ganglion blockers (hexamethonium and BW 139C55), adrenergic neurone blockers (guanethidine, bretylium and debrisoquin), α-adrenolytics (phentolamine and phenoxybenzamine), atropine and hemicholinium reduced or completely blocked the increase in ISP due to nerve stimulation. Noradrenaline, histamine, 5-hydroxytryptamine, physostigmine and carbachol slightly potentiated these responses while this potentiation was abolished by their specific antagonists. DMPP but not McNA-343 stimulated the seminal vesicle.

The results mentioned above suggest that the stimulated fibres of the hypogastric nerve are preganglionic in nature. The postganglionic innervation is mainly adrenergic; however, some cholinergic part is also present. The inter-relationship between the adrenergic and the cholinergic components is discussed.

EFFECT OF NORADRENALINE ON CENTRAL CARDIOVASCULAR CONTROL. *By* **K.N. Dhawan, K.S. Dixit, K.M. Dhasmana, J.N. Sinha and G.P. Gupta**. *Upgraded Department of Pharmacology, K.G.'s Medical College, Lucknow.*

Noradrenaline (NA) on intracerebroventricular administration in small doses (20-33 μg)

in dogs produced a slight fall in blood pressure and bradycardia. The bradycardia was abolished by bilateral vagotomy. On repetitive administration of small doses or on administering a single large dose of NA (200-800 μg) intraventricularly there was a rise in blood pressure and tachycardia in vagotomised animals and bradycardia in nonvagotomised animals. These effects were abolished on ligating the spinal cord at C1. Topical application of NA to the floor of the 4th ventricle did not produce any effect on the blood pressure. The central pressor response was also abolished by bilateral adrenalectomy and the administration of a ganglion blocking agent. Either of these procedures alone failed to block the pressor response to NA. However, in animals where bilateral adrenalectomy was performed intraventricular administration of atropine blocked the central pressor response to NA.

AN INVESTIGATION OF FALSE ADRENERGIC NEUROTRANSMITTER HYPOTHESIS IN ISOLATED TISSUE PREPARATIONS OBTAINED FROM RESERPINE PRETREATED ANIMALS. *By* **M.L. Sherlekar, S. Y. Ringe, H.M. Parikh and O.D. Gulati.** *Department of Pharmacology, Medical College, Baroda.*

The object of this study was to see if false adrenergic transmitters and precursors thereof could restore the responses to tyramine in isolated tissue preparations obtained from animals pretreated with reserpine. For this purpose, rat ileum obtained from normal and chronically reserpinized animals (2 *mg/kg* for 8-10 days), and isolated ear and heart preparations obtained from normal and chronically reserpine treated rabbits (1 *mg/kg* i.p. every other day for 4 injections) were used.

Three to four doses of tyramine were chosen to evoke graded sympathomimetic responses. In preparations obtained from reserpinized animals tyramine failed to elicit its own characteristic sympathomimetic action. Attempts were made to restore responses to tyramine by perfusing or bathing the preparations with several alpha-methyl amino acids and their analogues.

In all the three preparations alpha-methlyl-dopa (1.0×10^{-5} to 1.0×10^{-4}) or alpha-methyl-noradrenaline (1.0×10^{-6} to 1.0×10^{-5}) restored the sympathomimetic responses to tyramine. Alpha-methyl-meta-tyrosine (1.0×10^{-4}) and metaraminol (1.0×10^{-5}) restored the vasoconstrictor responses to tyramine in the isolated rabbit ear preparations. Treatment with alpha-methyl-dopamine or alpha-methyl-paratyrosine failed to restore the responses to tyramine in rat ileum and isolated rabbit ear preparations.

When the preparations obtained from reserpine treated animals were exposed to alpha-methyl-dopa (1.0×10^{-5} to 1.0×10^{-4}) in the presence of disulphiram (1.0×10^{-6}) sympathomimetic responses to tyramine could not be restored.

STUDIES ON THE INTERACTION BETWEEN GAMMA AMINOBUTYRIC ACID AND CATECHOLAMINES. *By* **C.P. Trivedi and V.R. Dhumal.** *Department of Pharmacology, G.R. Medical College, Gwalior.*

Using different experimental preparations the interaction between Gamma aminobutyric acid (GABA) and adrenaline (A) or noradrenaline (NA) was studied. GABA in doses of 5 to 10 *mg/kg* was found to enhance the effect of A and NA on carotid blood pressure of dogs

when administered intravenously or intraventricularly. It also enhanced the action of A on the nictitating membrane of dogs. On frog's isolated heart GABA produced a depressant effect in doses of 1 to 5 *mg*. However when administered subsequent to A, GABA in doses of 1 to 2 *mg* produced a stimulant effect on frog's heart. After perfusing the frog's heart with reserpine for 30 min. GABA elicited a cardiac inhibitory effect even subsequent to the administration of A. On dog's heart *in situ* GABA enhanced the stimulant effect of A. On exposure of Finklemann's preparation to GABA (10^{-6} M) for 30 to 60 secs the intestinal relaxation induced by stimulation of superior mesenteric nerve was slightly enhanced while after exposing same preparation to GABA (10^{-6} M) for a period of 30 minutes this effect was slightly diminished. Subsequent to the exposure of this preparation to reserpine for 30 minutes the inhibitory action of GABA was considerably diminished.

Thus it appears that GABA might be sensitizing the tissues to NA and A by either releasing them or blocking their uptake.

CATECHOLAMINE RELEASE FROM RAT ADRENALS BY PHYSOSTIGMINE. *By* **C.L. Kaul and R. Singh Grewal.** *CIBA Research Centre, Goregaon East, Bombay.*

Release of catecholamines from the adrenal gland following intravenous administration of physostigmine was studied in rats anaesthetised with urethane. 0.5-0.7 *ml* of blood was collected from a cannulated adrenal vein in a cold centrifuge tube. The plasma was separated by centrifugation and was assayed for noradrenaline (NA) content on the blood pressure of a pithed rat. In control experiments the output was 0.20 $\mu g/ml$. Physostigmine, 20 μg (i.v.) produced a 3-4-fold increase in the amount of catecholamine output (0.65 $\mu g/ml$). In pithed animals no increase in catecholamine output following physostigmine injection was observed indicating a central locus of action.

The rise of blood pressure following injection of physostigmine was higher in adrenalectomised animals than in control animals. These differences in response were not due to alterations in the sensitivity of the cardiovascular system as the rise in blood pressure following injections of adrenaline (A) and NA was the same in normal and adrenalectomised rats. In these experiments the effect of physostigmine was potentiated by propranolol.

EFFECT OF SYMPATHOMIMETIC AMINES ON SUPERIOR CERVICAL GANGLIA. *By* **K.P. Gupta, Om Chandra, K.C. Singhal, S.S.A. Rizvi and P.N. Saxena.** *Department of Pharmacology, J.N. Medical College, A.M.U., Aligarh.*

It is now well established that two types of cholinoceptive receptors are present at the ganglia and acetylcholine plays an important role in ganglionic transmission. The role of catecholamines in the ganglia is still a matter of controversy although noradrenaline and dopamine have been shown to be present at the ganglionic site. In the present study therefore it was proposed to study the role of catecholamines in ganglionic transmission and the identification of adrenergic receptors in the ganglia.

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The effect of adrenaline, noradrenaline and isoprenaline was studied on the superior cervical ganglia of cat anaesthetised with pentobarbitone sodium. The drugs were injected through the lingual artery after clamping the external carotid artery. By this method the drug slowly diffuses retrogradely into the superior cervical ganglia under the pressure head of blood in the common carotid artery. Contraction of the nictitating membrane to electrical stimulation of pre- and postganglionic cervical sympathetic nerve was taken as control.

Adrenaline, noradrenaline and isoprenaline in doses of 1-10 μg. on intralingual artery administration produced no change on the resting tone of nictitating membrane. Adrenaline and noradrenaline produced potentiation of the nictitating response to preganglionic nerve stimulation without producing any change in the response to postganglionic nerve stimulation. This suggests a facilitatory role of adrenaline in the ganglionic transmission. Isoprenaline, however, did not potentiate the preganglionic response.

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A STUDY OF THE NATURE OF ANTAGONISM EXHIBITED BY GANGLION BLOCKING AGENTS. *By* **O. P. Sethi and O.D. Gulati.** *Department of Pharmacology, Medical College, Baroda.*

In view of the controversial reports regarding the nature of antagonism exhibited by ganglion blocking agents it was thought worthwhile to investigate the nature of antagonism by six ganglion blockers, i.e. hexamethonium, tetraethylammonium, mecamylamine, pempidine, chlorisondamine and pentolinium. The preparations used were isolated rabbit ileum and isolated guinea-pig hypogastric nerve vas deferens.

Isolated rabbit ileum:— Hexamethonium, tetraethylammonium, mecamylamine, pempidine, chlorisondamine and pentolinium all shifted the dose response curve to nicotine to the right. Hexamethonium and tetraethylammonium caused a parallel shift of the dose response curves to nicotine at all the dose levels studied without reduction of the maxima. Tetraethylammonium elicited a contractile response and thus for measuring the height of the contraction new base line was adopted. Mecamylamine, pempidine, chlorisondamine and pentolinium caused a parallel shift of the dose response curves to nicotine in lower doses. In higher doses the shift was not parallel and there was a reduction of the maxima.

Isolated guinea-pig hypogastric nerve vas deferens preparation:— Lower doses of the six ganglion blocking agents, hexamethonium, tetraethylammonium, mecamylamine, pempidine, chlorisondamine and pentolinium shifted the frequency response curve (constructed by taking the log of frequency of nerve stimulaton as abscissa and percentage contraction as ordinate) to right. However, in higher doses the shift was not parallel and there was a reduction of the maxima.

EXPERIENCES ON THE MEASUREMENT OF BLOOD PRESSURE IN UNANAESTHETISED DOGS. *By* **P.R. Saxena.** *Pharmacology Research Department, N.V. Organon, Oss. The Netherlands.*

Measurement of blood pressure (BP) in unanaesthetised animals is often required in many physiological and pharmacological experiments. Van Leersum (*Arch. f.d. ges. Physiol.*, **142**, 377, 1911) recorded systolic BP after exteriorizing one common carotid artery in a skin loop. Others used a cuff on the tail of dogs. Direct continuous record of BP was obtained by cannulating the aorta directly after laparatomy or by way of common carotid or femoral arteries, or by puncturing the latter vessel. Corne and Stephens (*J. Physiol.*, **188**, 9P, 1966) described a periarterial BP transducer whereas telemetry was attempted by others.

We have tried and evaluated some of the earlier-mentioned methods which have one or the other disadvantage. On the basis of the experience gained in this way, a much simpler method was developed. A mid-line incision is made on the ventral surface of the neck of an anaesthetised dog. One superior thyroid artery is dissected and a polyvinylene chloride tubing (internal diameter 0.91 *mm*, external diameter 1.52 *mm*, length 45 *cm*), obtained from Portex Limited, Hythe, Kent, England, and filled with physiological saline containing heparin (50 *U/ml*), is introduced in it. This end of the tube is directed downwards in the common *carotid* artery for 15-18 *cm* so that the tip lies in the aorta. The other end, which is closed with a tight fitting mandarin, is brought out at the dorsal side of the neck. The wound is closed and the animal is allowed to recover from anaesthesia. BP is recorded by a transducer. The catheter remains satisfactory for several months and if the registration of BP is done every 2-3 days, no heparin is usually needed in the catheter.

A STUDY OF ELECTRO-CARDIOGRAPHIC, RESPIRATORY AND BLOOD PRESSURE CHANGES IN DOGS AFTER INJECTING SALINE/BLOOD IN THE CEREBELLUM OF DOGS. *By* **N.K. Misra, J.N. Prasad and T.C. Gupta.** *Department of Physiology, J.N. Medical College, Aligarh.*

Changes in electro-cardiographic patterns subsequent to cerebrovascular accidents and encephalopathy have been described by Martin and Sheehan (1941), Byer *et al.* (1947), Levine (1953), Papar (1955), Anand and Dua (1956), Wasserman (1956), Beard *et al.* (1959), Burch *et al.* (1960). The present work is a part of an extensive experimental study of electro-cardiographic patterns, blood pressure and respiratory changes in dogs after saline/blood injection in different parts of brain, in an effort to simulate the clinical haemorrhage or exudation. Two groups of 10 dogs each were made for the present study. In one group isotonic saline 5 c.c. and in the other blood 5 c.c. of the same dog were injected in cerebellum and electro-cardiographic, respiratory and blood pressure changes were recorded at intervals of 15, 30, 60 and 90 minutes. Almost identical changes were noted in both the groups.

A significant decrease in heart rate was noted. Appearance of sinus arrhythmia and atrial extra-systoles were also observed subsequent to injection. Significant changes in polarity and amplitude of the P-wave were observed. Peculiar changes in Intrinsicoid deflection were recorded. A decrease in the duration of QRS interval was highly significant. Appearance of

*Department of Physiology, Medical College, Darbhanga.

Q waves in 7 out of 20 dogs like that of ischaemic heart disease was very interesting. All the 20 dogs showed an initial rise in R wave followed by a subsequent fall in V1. In 3 dogs typical covplane S—T segment was recorded in Lead III and a VF. Significant changes in S—T segment in one or other lead were observed in 17 out of 20 dogs just 15 minutes after injection. In all the 20 dogs changes in the polarity of T wave were noted in one or other lead after injection at variable intervals. A rise in amplitude of T wave was noted in 17 out of 20 dogs in one or other lead after variable intervals. The rate and depth of respiration were markedly increased after injection. The respiration became irregular and Cheyne Stoke's type in most of the dogs. No uniform pattern of blood pressure changes was recorded. It however showed an inconsistent slight increase at varying intervals after injection.

EFFECTS OF CAROTID SINUS REFLEX ON VENOMOTOR TONE. *By* **N.V. Jog and S.K. Manchanda**. *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Conflicting reports have appeared in the literature regarding the role of capacitance vessels in the carotid sinus reflex. This study was therefore undertaken to decipher the comparative importance of changes in the venomotor tone and the resistance vessels, i. e. arterioles, in bringing about reflex changes in blood pressure when carotid sinus was stimulated.

In these preliminary studies dogs weighing between 7 and 10 *kg* were anaesthetised with chloralose. Venous and arterial pressures in the lower limb were recorded from the branches of femoral vein and artery. Circulation to the limb was then blocked with high pressure occlusion at the level of the inguinal region. When the pressures after occlusion of the vessels became stabilised, the carotid reflex was elicited by either Moissejeff's technique or by balloon preparation. The results obtained indicated that when sinus pressure was suddenly raised from a level of 100 to 250 *mm* Hg, the venous pressure invariably registered a fall suggesting a decrease in the venous tone.

On the other hand when pressure in the carotid sinuses was reduced by bilateral occlusion of the common carotid arteries, the venous tone registered either an increase or a decrease. It is not yet possible to analyse these effects of carotid sinus reflex.

PHYSIOLOGICAL STUDY OF HAEMORRHAGIC SHOCK. *By* **V. Dutt Mullick, S.H. Singh and O.P. Bagga**. *Department of Physiology and Biochemistry, Lady Hardinge Medical College, New Delhi.*

As the basic physiological defect in shock is inadequate tissue perfusion, a quantitative index of the extent of inadequate perfusion of tissues may be a better judge of the severity of shock than blood pressure, which has traditionally been index of shock. Inadequate perfusion may lead to permanent cellular damage. Hence blood lactate levels may give a better picture of the severity of shock than blood pressure.

Healthy mongrel dogs were subjected to haemorrhagic shock by reducing the arterial pressure to 30-35 *mm* of Hg by bleeding them in less than 15 minutes. The arterial pressure was maintained at this level by further withdrawal or re-infusion of small amounts till physio-

logical compensation failed. After the physiological compensation had failed, they were re-transfused to judge the reversibility of shock. Blood lactate, pyruvate and glucose levels were estimated.

It was observed that as compared to the control animals, in the group in which haemorrhagic shock was produced, there was progressive and statistically significant increase in arterial lactate level. Those which had lactate levels above 77 *mg*/100 *ml* went into irreversible stage, while those with lower lactate levels were in reversible stage. Blood pyruvate and glucose levels also showed an increase during haemorrhagic hypotension. Lactate/pyruvate ratio was higher in irreversible shock. Electrocardiograms were indicative of myocardial ischaemia during haemorrhagic hypotension.

PHARMACOLOGICAL ACTIONS OF TETANUS TOXIN ON THE CARDIOVASCULAR SYSTEM. *By* **G. Choudhury, R.S. Jaya Singh, A.N. Mehrotra and H. Vaishnava.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

The effect of injections of graded doses of the tetanus toxin (Haffkine) were studied on the cardiovascular system. The toxin produced a depressor response which was, at times, preceded by a pressor phase. Low doses of the toxin produced stimulation of the isolated frog or rabbit heart, but higher doses produced cardiac depression and a reduction in coronary flow. An increase in peripheral resistance was observed after the toxin was infused into the peripheral blood vessels of the hind limb of the rat.

THE DISTRIBUTION OF SEROTONIN AND HISTAMINE IN VARIOUS TISSUES OF THE INDIAN TOADS (BUFO. MELANOSTICTUS). *By* **S.K. Gupta and M. Singh.** *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

The present work was designed to evaluate histamine and 5-HT contents of various tissues in the Indian toad (*Bufo. melanostictus*). Besides these amines, on the evidence that skin of toad has been administered for the treatment of dropsy in the past years, the study of its cardio-active principle was also undertaken. The experimental data reveals the histamine contents in terms of histamine acid phosphate in various tissues.

Histamine levels in the stomach of the toad ranged between 0.83 and 10.0 *mcg/gm* with a mean value of 4.37 ± 0.64 *mcg/gm.*

Thigh muscles content of histamine ranged between 1.5 and 6.45 *mcg/gm* with a mean of 3.00 ± 0.119 *mcg/g*. Histamine content of the lung tissue was found to range between 0.75 and 7.64 *mcg/gm* with a mean of 2.94 ± 0.18 *mcg/g*.

No detectable amount of histamine was, however, found in the skin of the toad.

The study further revealed the contents of 5-HT as creatinine sulphate in the following tissues. The levels of 5-HT in the skin ranged between 1.0 and 5.0 *mcg.* with a mean of 2.31 ± 0.28 *mcg/g.* of the tissue. The range of 5-HT levels in the intestine was between 0.06

and 2.80 *mcg/g.* with a mean value of 0.924±0.317 *mcg/g.* 5-HT contents of thigh muscles ranged between 0.35 and 2.50 *mcg/g.* with a mean of 0.77±0.18 *mcg/gm* of the tissue. The 5-HT levels of heart ranged between 0.25 and 6.20 with a mean of 1.19±0.533 *mcg.*

Specific antagonists were used to demonstrate the accuracy and specificity of the procedure. In this connection mepyramine was used at the end of every histamine assay. It was found that 1 *mcg.* of mepyramine per 8 *ml.* bath fluid partially blocked the action of histamine and tissue extracts. Two *mcg* of mepyramine could completely block these effects. The recovery of the tissues from mepyramine was rapid and complete.

The specificity of 5-HT assay was checked by the use of antagonist dihydroergotamine (DHE). It was observed that 2 *mcg.* of DHE in 8 *ml* of bath fluid partially antagonised the uterine contraction produced by 5-HT and tissue extracts. However 5 *mcg.* of DHE in the bath fluid completely blocked their actions. In case of DHE the antagonism lasted for more than 60 minutes.

Skin extract of toad was found to possess a significant cardiotonic activity.

SPONTANEOUS CEREBELLAR ELECTRICAL ACTIVITY IN ANAESTHETISED, CONSCIOUS AND MID-COLLICULAR CATS. *By* **Baldev Singh and G.S. Chhina**. *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Fourteen cats were studied in states of anaesthesia, consciousness and deafferentation (mid-collicular). Bipolar EEG recordings were made from lateral lobes of the cerebellum (13 cats) and from vermis (1 cat), through implanted electrodes. Also effects of changes in blood glucose, and of photic and gustatory stimuli were observed on cerebellar activity in mid-collicular preparations.

Both in conscious and in anaesthetised preparations, the EEG activity recorded from cerebellum followed three distinct patterns, i.e. (i) low voltage (25 to 40 μV) fast (55/sec.); (*ii*) slow activity (2 to 6/sec.) with variable amplitude; and (*iii*) spindle like activity (70 μV, 14/sec.). In anaesthetised animals the slow activity was more preponderant.

In mid-collicular preparations on the other hand cerebellar recordings in addition to showing low voltage fast activity, and slow activity, also frequently showed high voltage (100 to 150 μV) fast (60 to 70/sec.) activity, but no spindles. The high voltage fast activity showed periods of waxing and waning.

When the mid-collicular preparations were exposed to increased glucose utilization induced by glucose injection, the cerebellar activity increased either in frequency or in amplitude. On the other hand when glucose utilization was decreased with insulin, the amplitude of cerebellar activity decreased and in some animals was even completely inhibited to isoelectric line. The photic and gustatory stimuli however did not affect the cerebellar activity in the mid-collicular preparations, as these afferents could not project into the cerebellum. In conclusion the cerebellar activity changed in response to deafferentation and was also influenced by the level of glucose utilization.

MODE OF ACTION OF GLUCOSE UTILIZATION ON THE ELECTRICAL ACTIVITY OF HYPOTHALAMIC FEEDING CENTRES. *By* **B.K. Anand and G.S. Chhina**. *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Previous studies have shown that when glucose utilization in the body is increased the activity of "satiety" neurones is increased, while that of "feeding" neurones is decreased. As it is not clear whether this level of glucose utilization is "sensed" at the periphery or in the central nervous system, experiments were planned to study this after making mid-collicular brain-stem sections and thus removing the effects of the peripheral afferents. In twenty-five cats with brain-stem cuts EEG and single neurone unit activities of hypothalamic centres were recorded and the effects on them of glucose and insulin injections were observed. With decreased glucose utilization produced by insulin EEG activity of the 'feeding' centre was increased in voltage and frequency, while that of 'satiety' centre was slowed with some increase in voltage. Opposite type of EEG changes were produced on increasing glucose utilization by glucose infusion. EEG recordings from other areas of hypothalamus, limbic system, and neocortex did not show any specific change.

Similarly decrease in glucose utilization with insulin produced increase in the spike frequency of 3 of the 4 feeding centre units, and slowing of all the 3 satiety centre units. Increased glucose utilization produced by glucose injection, on the other hand, produced reverse type of changes in their unit activities. The posterior hypothalamic unit did not show any significant change. The present study showed that the activity of the hypothalamic feeding centres was influenced by the glucose sensitive mechanisms present in the nervous system and was not due to peripheral sensing mechanism.

EFFECT OF FENFLURAMINE (PONDRAX) ON THE BLOOD GLUCOSE AND ELECTRICAL ACTIVITY OF HYPOTHALAMIC FEEDING CENTRES. *By* **S. Khanna, U. Nayar and B.K. Anand**. *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

It was demonstrated previously that changes in the electrical activity of the hypothalamic feeding centres were produced due to an alteration in the blood glucose utilization. Some of the drugs which were found to change the appetite had their primary effect on glucose utilization. The effect of fenfluramine, an amphetamine-like drug, on the arteriovenous differences in blood glucose (glucose, utilization) was determined. Subsequently, the effects of fenfluramine on the electrical activity of the feeding centres were examined.

Experiments were conducted in cats under Nembutal anaesthesia. Blood samples from the femoral artery and vein were analysed for blood sugar level every 2, 4, 6, 8 and 10 hr following the injection. The results of 8 acute preparations indicated an increase in the glucose utilization which appeared between 2 and 8 hr after the injection of the drug.

The electrical activity was recorded in these acute preparations from the ventromedial nucleus of the hypothalamus and the cortex. Selective changes in the activity of feeding centres were observed.

HYPOTHALAMIC INFLUENCE ON THE ACTIVITY OF RETICULO-ENDOTHELIAL SYSTEM OF CAT. *By* **P.K. Thakur and S. K. Manchanda.** *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

The activity of the reticulo-endothelial system (RES) was measured by using the carbon clearance technique. The stimulating effect of 17-beta oestradiol was measured in 10 male cats in doses ranging between 0.25 *mg* and 2.0 *mg* daily for 7 days. Noradrenaline (NA) in high doses grossly depressed the RES activity while in very low doses slight increase in the RES activity was observed. This effect of NA could be due to changes in the blood flow of various organs especially liver and spleen.

Since hypothalamus exercises an important influence on the levels both of oestrogens and NA the possbility of its role in changing the RES activity was investigated with the help of classical neurophysiological techniques. Lesions placed in different hypothalamic areas decreased the RES activity to a marked degree. Lesions in the middle and posterior hypothalamus produced a slightly greater decrease than the lesions in anterior hypothalamus. Lesions in the left cingulate gyrus in one cat produced no effect on the phagocytosis of carbon particles.

EFFECT OF NITRAZEPAM ON EEG AROUSAL AND EVOKED POTENTIALS IN THE MIDBRAIN RETICULAR FORMATION OF CATS. *By* **J. David and R.S. Grewal,** *CIBA Research Centre, Goregaon East, Bombay.*

The effect of Nitrazepam (Mogadon) was investigated on patterns of electroencephalographic (EEG) and behavioural arousal induced by intrareticular stimulation in anaesthetized and in unanaesthetized cats with electrodes permanently implanted in the midbrain (MRF) and pontine reticular formation (PRF). In acute experiments, on artificially respired cats, immobilized with gallamine triethiodide or in encephale isole preparations, intravenous administration of Nitrazepam (0.5-10 *mg/kg*), induced the appearance of periodic bursts of synchronized, high voltage slow waves, 9 to 14 cps, within 30 to 50 seconds. The spindling activity persisted for 3 to 4 hours. Intrareticular high frequency stimulation of the MRF and PRF at threshold voltages of 0.8-3 volts evoked EEG desynchronization, which was abolished by low doses (0.5-1 *mg/kg* i.v.) of Nitrazepam. However, on increasing the threshold voltage two-fold, the EEG activation response reappeared but was significantly reduced in duration. Higher doses of Nitrazepam (5-10 *mg/kg* i.v.) did not induce further depression of the reticular threshold. In unrestrained cats with electrodes chronically implanted in the MRF and PRF, stable patterns of sleep and behavioural arousal, elicited by low and high frequency stimulation respectively, were established.

Nitrazepam (5-25 *mg/kg* i.p.) produced ataxia, hypotonia but no behavioural sleep, while the EEG showed a fast synchronized activity without spindling. EEG and behavioural responses to low frequency stimulation were abolished at all dose levels but responses to high frequency stimulation remained unaltered.

The effect of Nitrazepam was further investigated on the amplitudes and latencies of potentials recorded from the MRF, evoked by stimulation of the PRF, and the sciatic nerve.

Single shocks to the sciatic nerve elicited 'fast' and 'slow' potentials with latencies of 20 and 50 milliseconds respectively, indicating them as extralemniscal potentials. With doses of 0.5-5 *mg/kg* i.v., the evoked potential increased in amplitude and its latency was prolonged. Larger doses of 7.5 to 10 *mg/kg* i.v. induced a similar prolongation of the latency but diminished the amplitude, though complete abolition was never observed. On the other hand, intrareticularly evoked potentials showed a prolongation of latency without a concomitant enhancement of the amplitude.

STUDIES ON SOME HETEROCYCLIC QUATERNARY OXIMES. *By* **V.N. Sharma, R.L. Mital and H.L. Sharma.** *Department of Pharmacology and Experimental Therapeutics, S.M.S. Medical College, Jaipur.*

A view strongly upheld by several workers is that there is an equilibrium within the brain between the two groups of biogenic amines, serotonin catecholamine on one hand, and acetylcholine-histamine on the other. Parkinsonism is characterised by an imbalance between these two systems and can be corrected by increasing the neurohormonal content of one system or by decreasing that of the other. One feasible way to reduce the Parkinsonism liability is to increase the anti-acetylcholine like action of drugs. Since oximes are well known as antidotes for organophosphorus poisoning, it was thought that anti cholinergic quaternary oximes of phenothiazine drugs could provide a tranquillizer with lesser liability of extrapyramidal reaction. Such a study is also likely to furnish certain clues for the inter-relationship of these two actions, one desirable and the other unwanted.

With this aim in view, certain heterocyclic quaternary oximes were synthesized. These compounds were assessed for their CNS depressant properties, and the results were compared with their parent drugs, employing a battery of tests: spontaneous motor activity, potentiation of pentobarbitone hypnosis, influence on the fighting behaviour in paired mice, conditioned avoidance response in trained rats and protection against amphetamine toxicity in aggregated mice. The scoring of the intensity of the cataleptic reaction in rats was also undertaken. Some experiments were also performed employing cats and monkeys to study the action of these drugs as tranquillizers and also for their liability to involve the extrapyramidal system. Our studies show that it is possible to decrease Parkinsonism liability greatly, with little loss of tranquillizing activity. Some of these compounds seem promising as possible tranquillizing agents.

MODIFICATION OF THE EFFECTS OF DRUGS ON BODY TEMPERATURE BY ELECTROCONVULSIONS. *By* **G.P. Gupta and K.N. Dhawan.** *Upgraded Department of Pharmacology, K.G.'s Medical College Lucknow.*

The present study deals with the modification by electroconvulsions of the effects of certain drugs on body temperature of rabbits. Electroconvulsions produced for seven days in rabbits blocked the hypothermic effect of chlorpromazine and hydroxyzine but did not alter the pyretic effect of LSD-25. The pyrexia produced by TAB vaccine or pheniprazine and reserpine administration was reduced in animals subjected to electroconvulsions for 7 days. The pyrexia produced by intracerebroventricular administration of adrenaline was enhanced by electroconvulsions.

THE ANTIHISTAMINIC ACTION OF MEPYRAMINE, DIPHENHYDRAMINE AND PROMETHAZINE AS DETERMINED BY SEVERAL pA VALUES*. *By* **M. B. Gharpure.** *Department of Pharmacology, Medical College, Aurangabad.*

The antihistaminic action of 3 compounds has been determined by the modified Schild's pA method, employing isolated guinea-pig ileum as the test object. The 17 different pA values that have been determined are given in Table I.

TABLE I

Series	a	b	c	d	e	*Remarks*
I	2	11	101	1,001	10,001	Each higher value is 10 times the lower one.
II	2	6	51	501	5,001	Value b is 5 times the value a; other values: Each higher value is 10 times the lower one.
III	2	3.5	26	251	2,501	Value b is 2.5 times the value a; other values: Each higher value is 10 times the lower one.
IV	2	3	5	9	17	Each higher value is 2 times the lower one.

Results :

The comparison of pA_2 and pA_{11} values shows that all the three compounds antagonize histamine competitively. However, the comparison of higher values shows that while mepyramine is competitive upto the highest value determined namely pA_{10001}, diphenhydramine and promethazine cease to be competitive beyond the pA_{1001} value.

CONCLUSION

It is recommended that to describe an antagonist completely, the following procedure should be adopted :—

(1) First determine its pA_2 value.

(2) Then further determine several such pA values that each succeeding value differs from the previous one by a factor of 10. This should be followed till

(*a*) Some practical difficulty prevents the determination of the next higher value.

or

(*b*) Three consecutive values are "not-competitive".

(3) Next, with a view to determine accurately the concentration at which the antagonist turns to be "not-competitive", work out some pA values between highest competitive value and the lowest "not-competitive" value. These should be such that the suc-

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ceeding value differs from the previous one by a suitable factor which is smaller than 10.

THE ANTIHISTAMINE AND ANTIACETYLCHOLINE EFFECTS OF METHAQUALONE AND SOME TETRAZOLIUM DERIVATIVES—A QUANTITATIVE STUDY. *By* **V. K. Sharma, S. Sangiah, P. K. Gujral, T. J. Singh and R.B. Arora.** *Department of Pharmacology, A.I.I. of Medical Sciences, New Delhi.*

The antihistamine and antiacetylcholine potencies of methaqualone, tetrazolium red, tetrazolium blue and neotetrazolium were determined using the method described by Schild (1947). pA_2 values were determined for contact periods of 2 and 14 *min.* The experiments were carried out on the isolated guinea-pig ileum.

Methaqualone was found to possess a weak antihistamine as well as antiacetylcholine activity. Our observations show that methaqualone is a non-specific antagonist.

For the antiacetylcholine effect the order of potency was: atropine > tetrazolium blue > neotetrazolium ⩾ tetrazolium red. Likewise, for the antihistamine effect the order of potency was: mepyramine > neotetrazolium ⩾ tetrazolium red > tetrazolium blue. The quantitative data are summarised below.

Active drug	*Antagonist*	pA_2 2 *min.*	pA_2 14 *min.*
Acetylcholine	Atropine	8.4	8.6
	Tetrazolium blue	7.8	7.7
	Neotetrazolium	6.7	6.7
	Tetrazolium red	6.7	6.3
	Methaqualone	3.4	3.2
Histamine	Mepyramine	8.4	9.8
	Neotetrazolium	6.4	6.6
	Tetrazolium red	6.3	6.9
	Tetrazolium blue	3.9	3.9
	Methaqualone	3.9	4.4

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MECHANISM OF 1-(5-METHYL-1-PHENYL-4-PYRAZOLYL)-3-[4-(O-TOLYL)-1-PIPERAZINYL]-1-PROPANONE HYDROCHLORIDE (Go. 1002) INDUCED ADRENALINE REVERSAL. *By* **R. Singh Grewal and C.L. Kaul.** *CIBA Research Centre, Goregaon East, Bombay.*

Go. 1002 (0.5 *mg/kg* i.v.) produced a reversal of the pressor response to adrenaline (A)

but did not diminish the pressor response to noradrenaline (NA) in the cat and the dog. Propranolol (400 $\mu g/kg$ i.v.) given either before or after Go. 1002 reverted the depressor response to A to a pressor response. Drugs like cocaine, imipramine and hexamethonium, that interfere with catecholamine uptake either blocked the depressor response or converted it to a pressor response. Go. 1002 potentiated the effects of A and isoprenaline on the rat uterus and this effect was blocked by propranolol. The results of the experiments suggested that Go. 1002 sensitized the beta-receptors to the vasodilator action of A and thus produced a reversal of its pressor effect.

STRUCTURE ACTIVITY RELATIONSHIP OF VERATRUM ALKALOIDS PRODUCING THE VERATRINE RESPONSE.

By **P.K. Gujral and R.C. Sharma.** *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

Protoverine di- and triacetate (PDA, PTA) and protoverine acetonide di- and triacetate (PADA, PATA) produced a veratrine response (VR) of the 'brief' type upon the isolated frog sartorius muscle (mean duration of contraction rose from 63 to 150 msec). Protoverine penta- (PPA), isopenta- (PIPA) and hexacetates (PHA) produced a VR of the 'prolonged' type (mean duration of contraction rose from 63 to 563 msec). PTA, PPA and PHA exerted powerful veratrinic effects upon the mammalian skeletal muscle (cat gastrocnemius-soleus). The order of their potencies was PPA > PTA > PHA. The mean ED_{50} values were 3.56 *mg/kg*; 7.15 *mg/kg* and 18.25 *mg/kg* respectively.

These observations and the data available for the muscular effects of some other veratrum alkaloids e.g. veratridine, germine acetates, protoveratrine A and protoveratrine B lead to the following generalizations regarding their SAR.

1. Two types of VR were observed, i.e. 'brief' or 'prolonged'. A transition from the 'brief' to 'prolonged' type of VR occurred when the number of acetate esters on the protoverine nucleus was more than three.

2. High veratrinic activity was associated with esterification at C_3 and C_{16}.

3. PTA, PPA and PHA produced a qualitatively similar action upon the mammalian skeletal muscle; however, quantitatively these effects differed. PPA was the most potent in the series. PADA and PATA did not elicit any VR. Since PTA was quite active and differs from PATA with regard to a molecule of acetone at $C_{14,15}$ it is evident that acetonide formation resulted in loss of veratrinic activity.

4. PPA differed from PHA only with regard to an acetate group at C_4. Likewise protoverine isopenta-acetate (PIPA) differed from PPA in having an acetate group at C_4 and lacking an acetate group at C_{16}. Since PPA was approximately 5 times as potent as PHA and PIPA was inactive, it seemed reasonable effect upon the VR whereas esterification at C_{16} was associated with high veratrinic activity.

PRELIMINARY REPORT OF EXPERIMENTAL STUDIES ON THE INTERACTIONS OF TETANUS TOXOID AND TOXIN. *By* **R.S. Jaya Singh, S.N. Dutta, R.K. Sanyal and H. Vaishnava.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

The prior injection of tetanus toxoid annulled the effects of the tetanus toxin on the frog heart, the rat hind limb, rat phrenic nerve-diaphragm and the dog gastrocnemius-sciatic nerve preparations but not on the isolated rabbit heart preparation. Higher doses of the toxin could, however, produce some effects. The results suggested a competitive type of antagonism.

ROLE OF THE SYMPATHETIC NERVES IN CARDIAC ACCELERATOR MECHANISMS OF ANGIOTENSIN. *By* **K.K. Janardhanan, K.P. Skandhan, P. Gopinath, M.G. Amin, J.P. Saxena and S.D. Nishith.** *Department of Physiology, Medical College, Baroda.*

The mechanism of cardiac accelerator action of angiotensin was studied in dogs under chloralose anaesthesia. The baroreceptor reflexes are not affected by chloralose anaesthesia.

Following rapid intravenous injections of 10μg of angiotensin heart rate first decreased and then increased. After sinoaortic denervation the initial decrease in heart rate was absent but the subsequent increase in heart rate was marked. The decrease in heart rate could be mediated through sinoaortic reflexes. The cardiac accelerator effect of angiotensin could be due either to a release of catecholamines from the adrenal medulla or a release of catecholamines from the sympathetic supply to the heart or a stimulation of S-A node directly.

The role of adrenal medulla in the mediation of cardiac accelerator action of angiotensin (10 μg) has been excluded in an earlier study. After the administration of sympathetic blockers the cardiac accelerator action of angiotensin has very much reduced. The cardiac accelerator action of angiotensin was also very much reduced after the blockade of beta cells of sinoauricular node. This indicated that in doses of 10 μg, angiotensin acted via the release of catecholamines from the sympathetic supply to the heart.

STUDY OF SINOAORTIC REFLEX AT NORMAL TEMPERATURE AND DURING HYPOTHERMIA. *By* **A.R. Biswas, M.G. Amin, M.N. Saha, S.D. Nishith and J.P. Saxena.** *Department of Physiology, Medical College, Baroda.*

Nineteen healthy mongrel dogs of either sex were cooled by immersion hypothermia. Injection of noradrenaline (8 expts) and histamine (6 expts) revealed that at a low temperature of 25° C the sinoaortic mechanism was reflexly modulating the heart rate although the reflex fall or rise in heart rate was depressed at hypothermic temperatures. Probably hypothermia along with the reduction of general metabolism also reduced the metabolism of centres and sinoaortic receptors. This contention was confirmed by the complete surgical denervation of the heart to abolish the sinoaortic mechanism (5 expts), when it was found that the sinoaortic mechanism was ineffective at normo and hypothermic temperatures.

ANTIVERATRINIC AND CARDIOTONIC ACTIONS OF PERUVOSIDE AS COMPARED WITH OUABAIN. *By* **O.P. Gupta, P.K. Gujral, N. Bagchi and R.B. Arora.** *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

The present study was undertaken to investigate the antiveratrinic and cardiotonic actions of peruvoside, a new cardiac glycoside, and compare it with ouabain. Both antiveratrinic and cardiotonic effects were studied in the frog. Antiveratrinic action was studied under isometric conditions using the method described by Gujral and Flacke (1965).

Male frogs, R. tigrina, weighing between 50 and 70 *g.* were used. Both sartorii were dissected out and mounted in identical muscle baths of 10 *ml.* volume containing bicarbonate buffer solution which was bubbled continuously with oxygen. Both muscles were stimulated supramaximally, every two minutes using a Grass Model S4 stimulator. Tension was recorded isometrically using either an isometric lever or a transducer coupled to direct writing oscillograph. For the antiveratrinic effect two types of experiments were performed. In one series of experiments the veratrine response (VR) was allowed to fully develop in both muscles. The glycoside was then added to one muscle, the other serving as a control. In the second series of experiments one muscle was first pretreated with the glycoside for fourteen minutes (*i.e.* seven stimuli). Thereafter veratridine was added to both the control and pretreated muscle. The VR was elicited by veratridine 10^{-7}w/v.

In the first series of experiments, peruvoside 2×10^{-7}w/v exhibited an immediate antiveratrinic effect and the VR was completely antagonized 30 to 40 minutes after addition of peruvoside. After the VR was antagonized by peruvoside, it was not possible to re-elicit the VR. Similar results were obtained with ouabain 10^{-6}w/v.

In the second series of experiments, pretreatment of muscle with peruvoside had no effect on development of VR. However, while in the control muscle the intensity of the VR was maintained, the antiveratrinic action of peruvoside became noticeable 16 minutes after the exposure of muscle to veratridine and the normal twitch was restored 42 minutes after veratridine. Similar results have been reported by Arora (1953) with other cardiac glycosides.

In the isolated straub heart made hypodynamic by reducing the calcium content of the ringer to 1/4, both peruvoside and ouabain (concentration: 2×10^{-6}w/v and 10^{-5}w/v respectively) produced a positive inotropic effect which was followed by a negative inotropic and chronotropic effect with the heart stopping in systole.

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ACTION OF BETHANIDINE UPON THE ISOLATED MAMMALIAN HEART. *By* **P.K. Gujral.** *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

The effect of bethanidine was studied in the heart-lung preparation of normal and reserpine pretreated dogs. In the normal heart, injection of bethanidine (0.1 to 30 *mg*) evoked a positive chronotropic effect which lasted for more than 2 hr. The dose response curve was steep and the ED_{50} was 0.46 *mg*. In the reserpine pretreated dogs (0.5 *mg/kg* reserpine given s.c. 24 and 48 hr. prior to the isolation of the heart), bethanidine in doses upto 6 *mg* had very little or no effect on heart rate. The dose of 6 *mg* caused a twenty-fold increase in the sensitivity of the pace-maker to administered noradrenaline compared to a ten-fold increase seen with guanethidine.

THE EFFECT OF NEWER NOR-CAMPHANE DERIVATIVES ON CORONARY FLOW. *By* **P. Sen, S.L. Kapoor and H. Kaur.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

During preliminary investigations with a new compound 2-ethylamino-3-phenyl nor-camphane hydrochloride (Merck, H-610), Sanyal (personal communication) observed a profound increase in the coronary flow in the rabbit Langendorff preparation. The effects of this and four allied compounds were therefore studied in the rabbit and guinea-pig Langendorff preparations, and *in vivo* in the dog. All the compounds produced vasodilatation in the isolated hearts. The parent compound was a potent coronary vasodilator *in vivo* experiments in the dog; the effects of the other compounds were insignificant. However, the compound H-610 was a vasodepressor and produced a marked stimulation of the central nervous system. This reduces its potentiality as a coronary vasodilator.

A STUDY OF THE CNS EFFECTS OF ISATIN—AN ANTICONVULSANT COMPOUND. *By* **T.J. Singh, P.K. Gujral and V.K. Sharma.** *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

Isatin (30 *mg/kg* i.p.) significantly reduced the spontaneous motor activity (SMA) in mice. The reduction in SMA is dose-dependent. Higher doses, i.e. upto 0.2 *g/kg* given orally, produced drowsiness and depression. Still higher doses (between 0.8 and 1.0 *g/kg*) led to immobility, loss of righting reflex and deep sleep. These effects were reversible in 6 to 8 hours.

Isatin potentiates hexobarbitone sleeping time. It is about 30 times less potent than chlorpromazine (CPZ). A reduction in body temperature which became maximal (100 *mg/kg* i.p.) in 30 minutes was also observed.

The anticonvulsant effect of isatin which has earlier been described by Kohli *et al.* (1962) was confirmed.

Isatin resembles CPZ with regard to its effects upon SMA, potentiation of hexabarbitone sleeping time and reduction in body temperature. However, it differs from CPZ in two important aspects :

1. With CPZ or other tranquilizers it is possible to awaken sleeping animals with stimuli of an intensity sufficient to awaken untreated animals. With large doses of isatin it is not possible to arouse the animals by the stimuli described.

2. Unlike CPZ and other tranquilizers isatin has an anticonvulsant effect.

On the basis of these experiments, it seems probable that isatin is a general central nervous system depressant.

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A COMPARATIVE STUDY OF 3-AMINO-6-7-BENZOQUINAZOLONE-4-ONE, CHLORDIAZEPOXIDE AND PLACEBO ON NORMAL HUMAN VOLUNTEERS BY DOUBLE BLIND PROCEDURE*. *By.* **J. N. Sharma, C.R. Prasad and B.N. Dhawan.** *Pharmacology Division, Central Drug Research Institute, Lucknow.*

3-Amino-6-7-benzoquinazolone-4-one is a chlordiazepoxide type of tranquilizer whose pharmacological activity has been reported earlier (Sharma and Prasad, *Ind. J. Physiol. Pharmacol.* **12**, 4, 1968). It has later been found to be safe in chronic toxicity studies. This communication reports the activity of the compound in eighteen healthy human volunteers (age 24-45 years). Physical examination (blood pressure, respiration, pulse rate, muscular tone, muscular power, co-ordination in limbs, response to sensory stimuli), and psychomotor test (mental, arithmetic, reading, etc.) were done in all subjects. They were kept in a quiet room and physical examination and psychomotor tests were repeated every hour over a period of 4 hr. Subjective and objective observations were made during the course of experimentation. The volunteers were again interviewed and examined next morning.

The trials were carried out by the cross-over technique where each individual received 20 *mg* of the compound, same dose of chlordiazepoxide and placebo at intervals of at least a week. The order was determined by using the possible permutations of the 3 agents but the subjects were randomly allotted.

In most cases the investigators and volunteers could correctly differentiate between the effects of the compound and the placebo. They made more errors in differentiating between chlordiazepoxide and placebo and maximum mistakes were made in differentiating the drug from chlordiazepoxide. The effects of 20 *mg* of the compound were more pronounced than those of an equivalent dose of chlordiazepoxide though both were almost equiactive in animal experiments. The subjects had no hangover the next day. There was no marked effects on blood pressure, pulse rate, respiration, etc.

ANTIDEPRESSANT AND ANTICONVULSANT PROPERTIES OF SOME DERIVATIVES OF 4-N-PHENYLPIPERAZINE-3-AMINO PYRIDINE. *By* **A. Ahmad.** *Department of Pharmacology, College of Veterinary Science and Animal Husbandry (JNKVV), Jabalpur.*

4-N-Phenylpiperazine-3-amino pyridine (I) was found to possess marked central and vasodepressor actions (1). In view of the interesting activity of the compound I, certain selected variations were made in different parts of the molecule of the compound to study the structure

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activity relationship. The phenyl ring seems to be essential for anticonvulsant and antidepressant activities, which disappeared when it was replaced by an alkyl group. Therefore, compounds with various substitutions on phenyl ring were studied for antireserpine and anticonvulsant actions. Compound I showed anti-electroshock property, blocked polysynaptic reflexes and antagonised reserpine syndrome. Any alteration in compound I decreased or abolished antireserpine activity. Compound I was, therefore, studied in a little detail with respect to its antireserpine action and compared with imipramine. Compound I (15 *mg/kg*, i.p. in mice and 2.5 *mg/kg*, i.v. in rabbits) markedly reduced reserpine induced ptosis, sedation and hypothermia. Substitution of 'Cl' and 'CF3' at meta position of the phenyl ring markedly enhanced anticonvulsant effect. These substituted compounds are effective in mice both by i.p. and oral routes against electroshock seizure (oral ED_{50} 17.5 and 12.6 *mg/kg* respectively). The anticonvulsant property of the compound with 'CF3' at the meta position of the phenyl ring compares favourably with that of the diphenyl-hydantoin sodium.

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EXPERIENCE OF HYPNOSIS WITH MEDICAL STUDENTS AS SUBJECTS. *By* **Dr. H. Jana.** *Municipal Medical College, Ahmedabad.*

About 100 medical students of both sexes were the subjects of this experiment on medical hypnosis. They were hypnotised by combination of visual and auditory stimulation and test suggestions. Their responsiveness to trance, experience during and after the trance and the effect of suggestions on them were studied and compared with those of western workers. The salient findings are :—

1. Preliminary talks with subjects are of prime importance for trance induction, because it helps the development of rapport and gives a correct picture of hypnosis removing misconceptions.
2. Morning sessions are more effective in inducing trance than evening sessions.
3. Our subjects are more susceptible to hypnosis; sex difference is negligible. Difficult subjects respond better after they witness good subjects being hypnotised.
4. 'Sleep' suggestion during induction is likely to give rise to trance alternating with sleep.
5. Amnesia is not a characteristic of the trance state.
6. Subjective version both during and after trance about his experience in trance is one of the more reliable guides to assess its depth. Psychodelic experiences like 'absence of a limb', 'floating beneath the roof', 'living in the land of fairies among the clouds', etc. have been reported.

7. Suggestions can command motor responses, produce alteration in sensory perception including anaesthesia and cardic acceleration. Touch sensation is invariably present when loss of all sensations is suggested in trance.

8. Duration of trance should not be cut short and dehypnotisation should preferably be a more and more gradual process in case of deep-trance subjects to avoid headache, heaviness and such other unpleasant ailments.

9. Hypnosis offers a nice tool for the study of emotions. Recollection of previous birth has been reported in two hypnotised subjects.

10. Trance is not only comfortable, but it helps the students in increasing their motivation and concentration to studies also.

11. Hypnosis is useful in the treatment of dysmenorrhoea, stammering and functional dysphagia.

VALIDITY OF ANTAGONISM OF CERTAIN EFFECTS OF RESERPINE FOR ASSESSING ANTIDEPRESSANT ACTIVITY. *By* **B.P. Jaju, G.P. Gupta and K.N. Dhawan.** *Department of Pharmacology and Therapeutics, K.G.'s Medical College, Lucknow.*

A reliable test of antidepressant activity should demonstrate the antidepressant activity not only of drugs but of other procedures like electroconvulsions as well. It was, therefore, thought of interest to study the effect of electroconvulsions on various actions of reserpine. The sedative, ptotic, hypothermic and conditioned-avoidance response blocking effects of reserpine were studied in normal rats and in rats subjected to electroconvulsions for five days. Prior exposure to electroconvulsions blocked only the hypothermic response to reserpine.

EFFECTS OF SEX HORMONES ON HEXOBARBITAL INDUCED HYPNOSIS. *By* **V.S. Murthy, R. Vijayvargiya, I.S. Gandhi and C.B. Seth.** *Department of Pharmacology, M.G.M. Medical College, Indore.*

The effect of sex and sex hormones was studied on the hexobarbital induced hypnosis in rats. Male rats were found less susceptible to the hypnotic action of hexobarbital than female rats. When this difference was studied in relation to age, the sensitivity of male rats showed a steady reduction from 6 weeks of age onwards.

Orchidectomized rats as well as oophorectomized rats were observed to be more susceptible than the male and female rats to hexobarbital though this increase in susceptibility was more marked after orchidectomy.

When the effect of chronic sex hormone administration was studied, testosterone was found to lower the sensitivity in normal male, female, orchidectomized and oophorectomized rats. While oestrogen and progesterone treatments caused prolongation of the hexobarbital induced hypnosis in male but not in female, orchidectomized and oophorectomized rats. Oestrogen and progesterone treatment in these animals reduced the sensitivity for the hypnotic.

Acute administration of hormones to rats alters the sensitivity in a different way. Progesterone was found to be the most potent in prolonging the hexobarbital induced hypnosis, while testosterone was less effective. Same was observed with acute administration, on the spontaneous motor activity in mice indicating a direct action of sex hormones on the CNS.

STUDIES ON THE MECHANISM OF ACTION OF PHYSOSTIGMINE ON TISSUE GLYCOGEN. *By* **R.S. Rathor and P.K. Das.** *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

In anaesthetised guinea-pigs physostigmine significantly increased the glycogen content of auricle, ventricle and skeletal muscle. But the liver glycogen was not significantly altered. The action of physostigmine in the heart was reduced by pretreatment with pentolinium and was blocked in the heart and liver by pretreatment with atropine. Gallamine (150 μg/100 g i.v.) caused generalised glycogenolysis which was significant in auricle, ventricle and liver. The action of physostigmine on skeletal muscle and liver glycogen was completely blocked by pretreatment with gallamine.

SEASONAL VARIATIONS IN TISSUE GLYCOGEN AND ACETYLCHOLINE CONTENTS IN FROG. *By* **R.S. Rathor and P.K. Das.** *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

Analysis of the glycogen and acetylcholine contents of auricle, ventricle, liver and skeletal muscle in frog were conducted every month for two consecutive years. Rainfall and ambient temperature at the time of experiments were also recorded. The glycogen content of the liver was found to be the highest, that of the auricle to be lowest, and that of the ventricle and the sketetal muscle to be intermediate. The acetylcholine content, on the other hand, was greater in the auricle than in the ventricle. The glycogen content of all the tissues was lowest in summer and highest in winter. On the other hand the acetylcholine content of the heart was lowest in winter and highest in summer.

Physostigmine in the dose of 0.1 *mg/kg.* did not affect significantly the glycogen content of auricle, ventricle and skeletal muscle throughout the year. On the other hand physostigmine raised the glycogen content of the liver during March to June, had no effect during July to September and January to February, and lowered it during October to December. Physostigmine raised the acetylcholine content of both the auricles and the ventricles throughout the year but the increase was more marked in summer than in winter.

PHARMACOLOGICAL STUDIES WITH AN INDOLE ALKYLAMINE ISOLATED FROM ARUNDO DONAX L. *By* **A.K. Sanyal, S.K. Bhattacharya, R. Pandit and R. Lal.** *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

Chemical studies of the aerial parts and rhizomes of *Arundo donax* L. (Hindi—Narkat) revealed the presence of a few indole-3-alkylamine bases viz. N,N-dimethyltryptamine, 5-methoxy-N-methyltryptamine, gramine and its N-oxide, bufotemine and bufotenidine. The yield of bufotenidine, obtained from the rhizomes, was maximum i.e. 3.7 *gm* from 700 *gm* of the crude

extract (Dutta and Ghoshal, 1967). As few pharmacological studies have been made with this substance, a detailed investigation was undertaken. It showed characteristic response on dog's B.P., skeletal muscle, and smooth muscles. It has no significant action on other systems.

Dog's B.P.—The drug (0.5 *mg/kg* i.v.) showed acute hypotensive response of prolonged duration (one to one and half hours). Repeated doses produced tachyphylaxis, which could be reversed by prior slow perfusion of histamine (5 *mcg/ml/mt.* for 30 mts.). It also blocked or reduced the hypotensive response of a known histamine liberator (tubocurarine—0.2 *mg/kg* i.v.). The studies indicate that hypotensive response might be due to histamine liberation.

Skeletal muscle—The drug in 10 *mg/kg* dose administered i.p. or orally in mice and rats respectively, produced ataxia in all the animals. Death due to respiratory failure resulted in all the mice. The drug also blocked the Ach (5 *mcg/ml*) response in frog's rectus abdominis muscle without effecting KCl induced spasms. ED_{50} of the drug, as an anti-Ach agent on frog's rectus muscle, was determined as 1.45 *mcg/ml*, as against 1.05 *mcg/ml* ED_{50} of tubocurarine. The drug also produced the characteristic head drop in rabbits. However, it was 6-10 times weaker than tubocurarine *in vivo*.

Smooth muscle—On isolated intestine of guinea-pig the drug blocked the action of Ach, histamine and $BaCl_2$, with no spasmodic effect of its own. However, it produced spasm of the intestine *in situ* of dog and of related rat and guinea-pig uterus. The latter effects were observed only upto a certain dosage (10-30 *mcg/ml*). Tachyphylaxis was not seen in isolated uterus but did occur in dog intestine *in situ*.

ACKNOWLEDGEMENT

Chemical studies leading to isolation and characterization of bufotenidine have been done by Dr. S. Ghosal of the Department of Pharmaceutics, B.H.U.

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HYPOTENSIVE STUDY WITH A FEW SYNTHETIC QUINOLINES AND QUINOZOLINES. *By* **A.K. Sanyal, R. Pandit and S.K. Bhattacharya.** *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

Two quinoline and fourteen quinozoline ethers were synthesized to study their hypotensive effects. Quinozolines produced either a very transitory hypotensive response or no response at all in normotensive dogs anaesthetised with pentobarbitone (35 *mg/kg* i.p.) or chloralose (80 *mg/kg*, i.v.). One of the two quinoline ethers, however, elicited a prolonged hypotensive response ($1\frac{1}{2}$ to 3 hr) in a dose of 2 to 5 *mg/kg* (i.v.). Further pharmacological studies with this substance showed that the drug potentiated the responses to catecholamines on dog blood pressure and intestine *in situ*; produced spasm of intestine of dog *in situ*, and of isolated intestine and uterus of guinea-pig. The drug had no effect on perfused frog heart. The drug was not acutely toxic to albino rats upto 50 *mg/kg* (i.p.).

UTEROTONIC ACTIVITY OF GOSSYPIUM ARBOREUM. *By* **K. Kadambari and G. Santhakumari.** *Department of Pharmacology, Medical College, Trivandrum.*

The uterotonic activites of *Gossypium arboreum* Linn. a plant belonging to Malvaceae family was studied using the aqueous extracts of the whole plant, leaves, seeds, root bark and stem bark. It was observed that all the extracts exhibited uterine stimulant action, the most potent being the aqueous extract of the leaves. The selective extracts of the leaves had no effect. The active extract revealed stimulant action on the uteri of albino rat, rabbit, guinea-pig, dog, cat and human in both *in vitro* and *in vivo* studies. The effect was immediate, reaching a peak in 60-75 secs and lasting for 5-6 mins. The drug behaved more like oxytocin than Ergometrine, the only difference being the gradual increase in tone. One gram of the crude drug was found to be equipotent to 0.108 units of syntocinon. The stimulant effects of the drug were blocked completely by papaverine hydrochloride (0.1 *mg/ml*) and partly blocked in descending order by Adrenaline, Noradrenaline, Isoxuprine and Atropine. The uterotonic activity of the drug seemed to be due to a direct stimulant action.

PROTECTIVE ACTION OF ASCORBIC ACID AGAINST LETHAL EFFECT OF STRYCHNINE. *By* **P.K. Dey.** *Department of Physiology and Biochemistry, College of Medical Sciences, Banaras Hindu University, Varanasi.*

The author observed incidentally that incubation of strychnine sulphate solution with lemon juice at 37° was attended with the complete loss of lethal and convulsive actions of the same. It was the amount of ascorbic acid in lemon juice which was responsible for annulling lethal action of strychnine. Therefore, further experiment was carried out with ascorbic acid soln *per se*. The dose-response and time-response relationships between ascorbic acid and strychnine showed that the antagonism between the two was competitive in nature and was directly related to the plasma ascorbic acid level.

It has also been observed that ascorbic acid only possesses protection against strychnine and not its oxidised product, diketogulonic acid. The vitamin failed to show any protective action against other convulsive agents like picrotoxin and metrazol, therefore indicating that protective function of vitamin was specific to strychnine. Other organic acids like citric acid, pyruvic acid, lactic acid, etc. are devoid of such protective action.

Certain pentose sugars like D-xylose and hexose sugars like D-glucose and D-fructose also exhibited marked protection against strychnine. Xylose shows equivalent potency like vitamin C in annulling the lethal action of strychnine. On the other hand, D-arabinose and disaccharides are not effective in this respect. Meanwhile it was found also that SH-group containing compounds like cysteine and reduced glutathione exhibit marked protection; but cystine and oxidised glutathione lacked this property. It is interesting to note that cysteine, when administered *in vivo*, is incapable of exhibiting protective effect against strychnine, but when cysteine is mixed with strychnine sulphate soln *in vitro* and then administered in the body, there is a complete loss of toxic action of strychnine.

It was tentatively suggested that the mechanism of action of strychnine in the central nervous system might be related with the involvement of SH-radical which might be the active site of neuronal receptors, and the function of vitamin C and other effective reducing sugars is to competitively antagonize SH-receptor-strychnine binding.

LOCAL ANAESTHETIC ACTIVITY, IRRITANCY AND TOXICITY OF SEVEN NEW SYNTHETIC LIGNOCAINE ANALOGUES. *By* **M.A. Patel**. *Drugs Laboratory, Laboratory of the Drugs Control Administration, Gujarat State, Baroda.*

Seven new lignocaine analogues were studied for their local anaesthetic activity, irritancy and toxicity. All the compounds exhibited significant degree and duration of local anaesthesia but compound 'G' [N(*p*-4'-chlorobenzylexy phenyl)-*o*(-diethenolamine propinoamide hydrochloride] and compound 'L' [N(*p*-benzylexy phenyl)-*o*(-diethylamine propinoamide hydrochloride] were found to be the most potent as surface and block anaesthetic. All the compounds were found to be atoxic in concentrations used for producing local anaesthesia. Acute toxicity studies have shown that compounds G and L though most potent local anaesthetics are less toxic than other tested compounds including reference drugs. Compounds G and L thus hold promise as future most potent, non-irritant and less toxic local anaesthetic compounds.

PHARMACOLOGICAL ACTIONS OF OXIMES OF ACETOPHENONE. *By* **B.K. Jain, R. Vijayvargiya, V.S. Murthy and C.B. Seth.** *Department of Pharmacology, M.G.M. Medical College, Indore.*

Two oximes of acetophenone and *p*-aminoacetophenone were synthesized in our laboratory and screened for pharmacological properties. Both the oximes potentiated the action of acetylcholine on the isolated rectus abdominis muscle of frog in doses of 0.25, 0.5 and 1.0 *mg/ml*. When compared with 2-PAM, acetophenone oxime was found to be about half as potent while *p*-aminoacetophenone oxime was only one-tenth as potent as 2-PAM in doses of 1 *mg/ml*. On phrenic nerve diaphragm preparation acetophenone oxime in doses of 100 *mcg/ml* caused increase in the amplitude of directly as well as indirectly stimulated twitch responses but produced marked lowering of tetanic threshold. While with doses of 500 *mcg/ml* all the three responses were depressed markedly, *p*-aminoacetophenone oxime was found less potent than acetophenone oxime in this action. When studied on carotid B.P. of dog, both oximes produced a fall in B.P. of the magnitude of 20 to 30 *mm* of Hg when given in doses of 5 *mg/kg*. This hypotensive response was blocked by atropine. In doses of 100 *mcg/kg* acetophenone oxime produced potentiation of acetylcholine induced hypotensive responses. In view of the above findings the effect of oximes was studied on rat's brain cholinesterase. Acetophenone oxime was found to be half as potent while *p*-aminoacetophenone oxime was one fourth as potent as 2-PAM in inhibiting cholinesterase activity of rat brain.

The findings are suggestive of anticholinesterase activity of the synthesized oximes.

STUDY OF THE EFFECT OF 1, 4-BENZODIAZEPINE DERIVATIVES ON D-AMPHETAMINE INDUCED TOXICITY IN MICE. *By* **B.P. Mukherjee and S.R. Dasgupta.** *Department of Pharmacology, Institute of Basic Medical Sciences, University College of Medicine, Calcutta University, Calcutta.*

Recently, the 1, 4-benzodiazepine derivatives viz. chlordiazepoxide, diazepam and nitrazepam have been reported to possess significant anti-stress and anti-anxiety properties (1-4). In view of the anti-stress activity of these derivatives, the present work was undertaken to examine if premedication with chlordiazepoxide and nitrazepam would afford any protection to D-amphetamine treated mice kept in a group. Aggregation of mice in a cage is possibly responsible for creating a stressful condition for the mice making them more susceptible to amphetamine toxicity. A significant decrease in mortality in the CDP(100*mg*/*kg* i.p.)-premediated and aggregated mice was observed. Nitrazepam(2.5*mg*/*kg*,i.p.) however failed to afford any such protection in the doses used. The anti-stress property of CDP, in addition to its tranquillizing activity probably played some role in diminishing the toxicity of D-amphetamine in aggregated mice. Nitrazepam has been reported to cause marked hyperactivity at doses below that caused sedation (5). This may explain the effects observed following premedication with this drug.

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PHOTOLYSIS OF DL-CITRULLINE. *By* **Mohammad Asif, Rashid Ali and Intisar Husain.** *Department of Biochemistry, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.*

Samples of aqueous solutions of citrulline of 1, 2 and 5 mM concentrations at *p*H 7.0, were irradiated by ultraviolet rays (high pressure mercury vapour lamp) for 1, 2, 3, 4 and 6 hrs. This resulted in the decomposition of citrulline producing ammonia and urea. The amounts of ammonia and urea liberated were found to be directly dependent upon the concentration of citrulline and the time of irradiation. The irradiated samples were chromatographed using water saturated phenol and butanol-acetic acid-water. No other ninhydrin positive spot was detected except that of citrulline.

However, when citrulline solutions of the above concentrations were irradiated in the presence of hydrogen peroxide, larger quantities of ammonia and urea were formed even for lesser period of irradiation. The formation of ammonia and urea was also found to be dependent upon the concentration of hydrogen peroxide. The effective concentration of hydrogen peroxide was found to be almost directly proportional to the concentration of the amino acid. Hydrogen peroxide *per se* was ineffective.

When irradiated citrulline (5 mM, 2 hrs. irradiated sample in the presence of hydrogen peroxide) was subjected to paper chromatography using water saturated phenol as the developing solvent, six ninhydrin positive spots were detected with no trace of citrulline. The amino acids identified were arginine, aspartic acid, glutamic acid and glycine. Two spots of Rf 0.05 and 0.22 are still to be identified.

EFFECTS OF ULTRAVIOLET RAYS UPON AQUEOUS SOLUTIONS OF ARGININE. *By* **Rashid Ali and Intisar Husain**. *Department of Biochemistry, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.*

Aqueous solutions of arginine of 100, 200 and 500μM concentrations at *p*H 7.0 were exposed to ultraviolet light (high pressure mercury vapour lamp) resulting in the formation of urea and ammonia. The amount of ammonia and urea liberated as a result of irradiation was found to be directly dependent upon the concentration of amino acid and period of irradiation. The amount of urea formed was found to be equivalent to the loss of arginine. A change in the absorption spectra of the solution was noted following irradiation. Complete degradation of arginine was noted when irradiation was carried out in the presence of hydrogen peroxide.

PHOTO-OXIDATION OF DOPA AND TYROSINE IN THE PRESENCE OF PSORALEN. *By* **Rashid Ali and Intisar Husain**. *Department of Biochemistry, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.*

Inspite of a large number of clinical investigations on psoralens some confusion still exists regarding their mechanism of action. In dark, psoralen *per se* did not bring about any appreciable oxidation of DOPA and tyrosine whereas together with psoralen, considerable oxidation and then formation of melanin was noted. The absorption spectra of the oxidized product of DOPA and tyrosine exhibited a peak at 460 mμ which was identical to the peak obtained with standard dopachrome.

The increase in the concentration of psoralen upto a certain limit was found to bring about increased oxidation of both DOPA and tyrosine. Further increase in psoralen concentration was observed to decrease the extent of oxidation and thus pigment formation. Copper ions were found to stimulate the formation of dopachrome from tyrosine and DOPA. Glutathione, cysteine and thiourea considerably inhibited the oxidation process.

It could be concluded from these studies that the mechanism by which psoralen may stimulate the sun-tanning process could possibly be due to its accumulation in the melanocytes where it would photo-oxidize the available DOPA and tyrosine to excessive formation of melanin.

INFLUENCE OF CERTAIN SUBCORTICAL STRUCTURES ON THE MONOSYNAPTIC REFLEX RESPONSES. *By* **U. Nayar, G.S. Chhina and B.K. Anand**. *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Experiments were conducted in 33 cats under anaesthesia. Monosynaptic reflex response was recorded either from the sciatic nerve or a branch of the sciatic nerve entering the muscle. The distal ends of the nerve from which the responses were recorded were tied. The parameters

of stimulation which usually elicited indirect response (H) did not elicit a motor response (M). Sometimes both 'M' response and 'H' response could be recorded.

The 'H' response usually had a latent period varying from 4-5 msec; its amplitude increased to some extent on increasing the strength of stimulation but later decreased while the amplitude of 'M' response increased. This response was very much reduced on increasing the frequency of stimulation.

It was observed that stimulation in the region of fastigial nucleus of cerebellum led to increase in amplitude of response while stimulation in the pontomedullary regions, in the vicinity of vestibular nuclei, led to a marked inhibition of response.

On the other hand, stimulation (with the same parameters) of certain parts of the head of caudate nucleus, putamen and subthalamic neclei did not produce any change in the monosynaptic reflex response.

SOME OBSERVATIONS ON METHYLPHENIDATE INDUCED GNAWING IN GUINEA-PIG*. **By R.C. Srimal and B.N. Dhawan.** *Pharmacology Division, Central Drug Research Institute, Lucknow.*

Gnawing is a compulsive behaviour in rodents. In the rat gnawing can be induced by apomorphine, amphetamine group of compounds and DOPA. Ernst (*Psychopharmacologia*, 10, 316, 1967) has shown that agents with phenylethylamine configuration having OH-groups at para and meta-positions of the phenyl ring can induce gnawing directly whereas dexamphetamine type of compounds have an indirect action, probably due to a release of endogenous dopamine.

The present study was undertaken to discover drugs capable of inducing gnawing and to see if they possessed the configuration suggested by Ernst (1967). Nineteen compounds belonging to various groups having an action on CNS were tested for their ability to induce gnawing in guinea-pigs. Methylphenidate induced vigorous gnawing like apomorphine and amphetamine. Ephedrine, caffeine, mescaline, LSD 25, yohimbine, cocaine and nalorphine did not induce gnawing. Antidepressants belonging to imipramine group as well as MAO inhibitors failed to induce gnawing. DOPA alone or combined with MAO or COMT inhibitor or both was ineffective in inducing gnawing behaviour in guinea-pig in contrast to the finding reported in rat (Ernst, 1967). Since methylphenidate lacks the phenylethylamine configuration an attempt was made to find whether it acted directly like apomorphine or indirectly like dexamphetamine. It was found that methylphenidate induced gnawing was not blocked by reserpine or *o*(-methyltyrosine) but was effectively blocked by *o*(-methyldopa) and morphine, whereas apomorphine induced gnawing was not blocked by *o*(-methyldopa) or morphine. Chlorpromazine could antagonise apomorphine induced gnawing but was ineffective in blocking methylphenidate gnawing. It thus appears that methylphenidate induced gnawing is different from apomorphine induced gnawing and dopamine may not be the endogenous substance responsible for inducing gnawing by all indirectly acting drugs.

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EFFECTS OF LSD ON OPEN FIELD PERFORMANCE IN RATS. *By* **P.C. Dandiya, M.L. Gupta, S.K. Patni and B.D. Gupta.** *Department of Physiology and Pharmacology, S.M.S. Medical College, Jaipur.*

LSD has been shown to cause different and sometimes opposite type of action on locomotor activity and exploratory activity in rats. In the present study LSD in doses ranging from 2 to 500 $\mu g/kg$ produced varying effects on different components of "Open Field" behaviour. The ambulation score (locomotor activity) indicated a linear increase with increasing log doses which rose rather steeply with the highest dose. However, the rearing (standing upon hind legs) and preening (scratching the face with forearms) scores exhibited in inverted U-type of dose response relationship; the inverstion of the cure taking place after injecting the dose beyond $8\mu g/kg$. Assuming that the results obtained are the specific effects of LSD produced determinants of stereotype, it can be suggested that LSD in normal (human) doses brings about increased stereotyped activity in increasing doses but in higher doses only that stereotyped activity increased which is simple in performance and for which no serious effort is required on the part of the subject; thus simple horizontal stereotyped activity increasing at the cost of vertical stereotype. Thus, LSD increases stereotyped activity with increasing dose, normal doses increasing both the horizontal and vertical type, while higher doses only the horizontal stereotyped response.

A PRELIMINARY REPORT ON THE PHARMACOLOGICAL ACTIVITY OF A NEW PROPIOPHENONE ANTIDEPRESSANT (COMPOUND 67/14)*. *By* **C.R. Prasad, J.N. Sharma and B.N. Dhawan.** *Pharmacology Division, Central Drug Research Institute, Lucknow.*

While screening a series of new propiophenone derivatives, compound 67/14 was found to have stimulant effects at lower doses and depressant activity at higher doses. The compound has therefore been tested as a potential antidepressant agent and results are briefly reported here. The LD_{50} of the compound was 270 *mg/kg* (i.p.) in mice and that of imipramine 125 *mg/kg* (i.p.).

The compound 67/14 in smaller doses (5-10 *mg/kg*, i.p.) counteracted reserpine induced depression (sedation, crouching, ptosis) and potentiated amphetamine induced activity (hyperactivity, pyrexia) in mice and rats. Medium doses (20-40 *mg/kg*, i.p.) potentiated amphetamine toxicity in aggregated mice. In higher doses (100 *mg/kg*, i.p. and over) the drug counteracted amphetamine induced hyperactivity as well as amphetamine toxicity in aggregated mice. It was an effective antagonist of reserpine induced emesis in pigeons. It inhibited polysynaptic reflexes (linguomandibular, contralateral sciatic facilitation) in cats and had an antinicotinic and antitremorine effect in mice.

The compound (1-5 *mg/kg*, i.v.) had no significant effect on the blood pressure of anaesthetised cats, except in large doses (5-10 *mg/kg*, i.v.) where it produced hypotension. Smaller doses, however, potentiated the pressor responses to epinephrine (E) and norepinephrine

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(NE) whereas larger doses produced reversa' of response to A and a reduction in response to NA.

The drug showed an imipramine-like activity but had a higher therapeutic ratio

LOCAL ANAESTHETIC ACTIVITY OF A NEW QUINOLINE DERIVATIVE*. *By* **G.K. Patnaik and B.N. Dhawan.** *Pharmacology Division, Central Drug Research Institute, Lucknow.*

While studying the pharmacological activities of a series of 4 N-substituted polymethylene-quinolines, the compound 65-124 showed marked local anaesthetic activity. It was therefore studied in greater detail and was compared with lignocaine.

Surface anaesthesia was tested by the rabbit cornea method. Infiltration anaesthesia was tested by the guinea-pig intradermal wheal method. For conduction anaesthesia the concentration required to block the pressor response to sciatic nerve stimulation following local application of the agent was determined. A 0.2% solution of 65-124 produced complete surface anaesthesia for 15 min, while a 0·0125% solution of the compound could produce complete infiltration anaesthesia lasting 25 min. Comparable degree of topical and infiltration anaesthesia were obtained with 1% and 0.1% solutions, respectively of lignocaine. 0.1 *ml* of 0.2% of the compound when injected into the sciatic sheath, reduced the reflex pressor response by 70%. A similar effect was also obtained by 1% solution of lignocaine. Thus it appears that the compound 65-124 is more potent local anaesthetic than lignocaine.

Unlike lignocaine 65-124 produced CNS stimulation in mice. In anaesthetized cats 2.5 *mg/kg* (i.v.) of the compound produced a substantial rise in blood pressure and completely abolished the depressor effect of histamine. The depressor response to acetylcholine (Ach) was unaltered while the pressor response to adrenaline (A) was potentiated. The compound also had a selective antihistamine action on the isolated guinea-pig ileum. At a concentration of $3x10^{-7}$ *g/ml* it completely abolished the effect of histamine while the responses to Ach, nicotine and serotonin were unaffected. In the anaesthetized cats lignocaine at a dose of 10 *mg/kg* (i.v.) had a weak hypotensive effect, decreased the ventilation but had no effect on the responses to histamine, Ach and A. Neither 65-124 (2.5 *mg/kg*, i.v.) nor lignocaine (10 *mg/kg*, i.v.) had any effect on the ganglionic and neuromuscular transmission in anaesthetised cats. Like lignocaine (100 μg), 65-124 (20 μg) had a negative inotropic effect on the isolated guinea-pig heart.

EFFECT OF MEDIAN EMINENCE LESIONS ON MAMMARY LOBULO-ALVEOLAR DEVELOPMENT IN HYPOPHYSECTOMIZED RATS BEARING ONE PITUITARY TRANSPLANT. *By* **S.C. Sud**, James A. Clemens and Joseph Meites.** *Department of Physiology and Dairy Science, Michigan State University, East Lansing, Michigan, U.S.A.*

Mature female virgin hypophysectomized rats were fed *ad libitum* with rat pellet foods supplemented with sugar cubes, oranges and carrots and housed in a constant temperature room (76±1°F) with automatic controlled lighting (14 hours light daily). Ten days post-hypophysectomy, each rat was transplanted with one rat anterior pituitary under the kidney

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**Department of Physiology and Pharmacology, College of Veterinary Medicine, U.P. Agricultural University, Pantnagar.

capsule. Approximately two weeks later, each rat was injected with 50 IU Pregnant Mare Serum and 60 hours later with 25 IU Human Chorionic Gonadotropin.

A week later, one group of rats was given bilateral median eminence lesions and the other group was sham-operated. All rats were sacrificed after a week. The lesioned rats showed significantly better mammary development and increased ovarian weight due mainly to the presence of large corpora lutea. It was concluded that in the lesioned rats, the Prolactin-Inhibiting-Factor was decreased or abolished and this resulted in lesser inhibition of prolactin release from the transplanted pituitary.

DISTRIBUTION AND FATE OF Mn^{54} IN THE RAT WITH SPECIAL REFERENCE TO THE CNS. *By* **Darab K. Dastur, Daya K. Manghani, V. Raghavendran and K.N. Jeejeebhoy**. *Neuropathology Unit, J.J. Group of Hospitals and The Radiation Medicine Centre, Tata Memorial Hospital, Bombay.*

In view of the still prevalent problems in certain mining communities, of chronic manganese toxicity affecting the CNS and the paucity of experimental data explaining the mechanism of this, the distribution and the fate of radioactive manganese in the rat, over a prolonged period was undertaken.

A dose of 20 μc (carrier-free) $Mn^{54}Cl_2$, in maleate buffer at *p*H 7-8, was injected intraperitoneally in 80 rats. The distribution and retention of Mn^{54} maleate in different organs and tissues and in the whole body was studied over a period ranging from 15 minutes to 34 days.

From the data obtained, the following parameters were calculated:

(*a*) Specific activity expressed as counts per minute (cpm) per gram of tissue; (plotted logarithmically).

(*b*) Retained radioactivity in the whole body; (plotted linearly).

(*c*) Exponential analysis of radioactivity in the whole body and in selected tissues; (plotted logarithmically).

(*d*) The "Relative retention" of radioactivity expressed as a ratio of cpm per gram of tissue/cpm per gram of whole body after washing out blood.

While the curve for the whole body and for most organs could be resolved roughly into two exponential components, the slow and fast, of varying half times for different organs, the slower component was not present for the CNS.

The very low concentration, most of the time, of Mn^{54} in the blood, which was obviously the medium of transport from the peritoneum to the organs, could only be due to the rapid uptake from it by the organs. Thus, blood acted as a transport medium receiving and discharging the Mn^{54} rapidly.

While most organs showed a gradual decline with time in the cpm per gram of tissue and in the retained dose, the brain and the spinal cord exhibited a steady rise from the beginning toend. The suprarenal, pituitary heart and bone also evidenced this to some extent. This

greater capacity for retention of a small dose of manganese by the CNS, might be responsible for its selective vulnerability in chronic manganese toxicity in man.

A recent identical experiment on monkeys has shown comparable results during the period of observation of 6 hours to 225 days.

TSH ACTIVITY IN HYPOTHALAMUS. *By* **Dr. C.M. Francis.** *Department of Physiology, Medical College, Calicut.*

Hypothalamus, which plays an important role in the release of TSH, was investigated for TSH activity. Bovine hypothalami were divided by coronal cuts into anterior, middle and posterior portions and the respective portions pooled together. They were homogenized in the cold, extracted with acidified saline and adjusted to *p*H 6.8 with NaOH. A diluted fraction of the homogenate was assayed for TSH by the modified method of Kirkham. Thyrotropin was found to be present in all the three portions of the bovine hypothalamus.

In order to characterize the TSH better, a lyophilized extract of rat hypothalamus prepared with Kreb's Ringer-bicarbonate solution was filtered through a Sephadex G-25 column, using 0.9% saline at *p*H 5.8 as eluent. Fractions were collected at 15 min intervals. All fractions showing absorption at 280 $m\mu$ were assayed for TSH activity. Two peaks of activity, close to one another, were seen within the first 15 *ml* of eluate. There was some TSH activity in the eluates between 40 and 50 *ml*, though much less than in the first few fractions.

TSH activity had been observed in hypothalamic extracts but had been considered to be confined to the median eminence only and probably due to reflux from the pituitary. The present finding of TSH activity in all three fractions would indicate that the hypothalamus itself shows the activity. This is further borne out by the finding of thyrotrophs in sections of hypothalamus stained by the aldehyde-thionin method.

A NEW METHOD OF BIOLOGICAL EVALUATION OF ANABOLIC ACTIVITY OF TESTOSTERONE. *By* **S.L. Sarkar.** *Department of Pharmacology, M.G.M. Medical College, Jamshedpur.*

Castrated male rats were treated with 2.5, 5.0, 10.0, 25.0 and 65 micrograms of testosterone propionate and wet weight and dry ani of levator weight muscle and concentration of total protein of levator ani muscle were determined. Neither wet weight nor dry weight of the levator ani muscle was significantly increased but the concentration of total protein was remarkably increased and the increase was statistically significant. On 2.5, 5.0 and 10 micrograms dosage levels increase in total protein maintained a definite dose response relationship but on higher dosage, the increase in the concentration of total protein was not proportionate to the dosage. It is therefore suggested that estimation of total protein is more sensitive method of evaluation of anabolic activity of steroid hormone and this method may be employed for bioassay of the anabolic activity of steroid hormone.

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THYMUS AND MAST CELLS. *By* **L. Kameswaran and M. Madhavan**. *Department of Pharmacology, Madurai Medical College, Madurai.*

Ginsburg and other workers have reported that thymus plays a dominant role in the genesis of mast cell precursors. Hence an attempt has been made to study the effect of removal of the thymus on tissue mast cells and also the effect of direct stimulation of thymus with an antigen in adult albino rats. Observations were made on mast cells in dorsal skin, abdominal skin, mesentery, liver, spleen and kidney, blood leucocytes, tissue histamine content and tissue and plasma histaminase levels at regular intervals for about six weeks.

Thymectomy was done following the method of Farris and Griffith (1949). Histaminase level was estimated following the volumetric method of Kapeller-Adler (1956). Tissue mast cells were stained with toludine blue, as adapted by Gupta and Skelton (1968). Extraction of tissue histamine was done as described by Parratt and West (1957). For thymic stimulation, antigen (egg albumin diluted with normal saline) was injected into the thymus modifying the method followed by Radwon and West (1967).

Thymectomy reveals a sudden and transient rise in mast cell population and parallel rise in histamine content in abdominal skin during the immediate post-thymectomy period. Then the levels come down to near normal values. Total leucocyte count and absolute lymphocyte count fall in the immediate post-thymectomy period, but gradually ascend to even higher than normal values during the second week and return to normal thereafter. There is no appreciable change in tissue histamine and tissue histaminase level following thymectomy.

Plasma histaminase level goes up transiently in the first three days after thymectomy which may be due to the effect of injury as reported by Kameswaran and coworkers (1968).

While several workers have reported a fall in histamine level and mast cell count after tissue injury, thymectomy is followed by a parallel rise in mast cell population and histamine content even though there is associated tissue injury. This definitely implies a thymic role in regulation of mast cell population along with lymphocytes.

After antigenic stimulation of the thymus, a persistent rise in the total leucocyte count, differential and absolute lymphocyte count is observed. This can be correlated with the effect of thymic stimulation which, being an essential lymphoid organ, is likely to reflect its stimulant effect on the lymphocyte count.

There is no appreciable change in tissue mast cell counts, histaminase level following antigenic stimulation of the thymus.

FURTHER STUDIES ON PLASMA HISTAMINASE LEVELS AND CLOTTING TIME IN POST-OPERATIVE PATIENTS. *By* **L. Kameswaran, K. Kanakambal and V. Vijayasekaran**. *Department of Pharmacology, Madurai Medical College, Madurai.*

In continuation of our study on the role of mast cells in wound healing, estimations of plasma histaminase level and clotting time were made in post-operative patients from the first

day consecutively for twelve days. Male patients who underwent elective gastrojejunostomy only were used. Plasma histaminase levels were estimated by Kapeller-Adler's method and the clotting time by capillary tube technique. The results obtained are in agreement with our previous observation in rats on plasma histaminase levels, i.e. there was a sudden rise in plasma histaminase level in the immediate post-operative period and then a gradual fall to a low level on the fourth day. Following this the level slightly rose during the rest of the period. Unlike in rats there was no significant change in blood clotting time. Patients received streptopenicillin injections in the post-operative period. To eliminate the effect of streptopenicillin on the changes noted during the post-operative period, the effect of the drug was tested in normal individuals before and after giving an injection of streptopenicillin. There is no apparent significant influence. Hence the increase in plasma histaminase activity observed may be related to tissue injury and wound healing as envisaged.

MANNICH BASES OF ACETOPHENONE AS HISTAMINE LIBERATORS. *By* **C.B. Seth, R. Vijayvargiya and V.S. Murthy**. *Department of Pharmacology, M.G.M. Medical College, Indore.*

A few Mannich bases of acetophenone and its derivatives were synthesized in our laboratory and screened for pharmacological actions. Of these compounds, the Mannich base of *p*-aminoacetophenone was found to produce a delayed depressor response on the carotid B.P. of dog in the dose range of 100 to 200 *mcg/kg*. This hypotensive response was not blocked by atropine, but was modified by mepyramine maleate. Further this delayed depressor response showed tachyphylaxis. In view of these, the effect of the compound was studied on the tissue histamine levels. The compound was found to cause about 33% reduction in the histamine content of rat abdominal skin and 45% reduction in the histamine level of rat lungs when given in dose of 2.5 *mg/kg* intraperitoneally. On comparison the compound was found to be equipotent with polymyxin B on rat lungs but was less potent on abdominal skin for this histamine release from the tissues.

Further it was also observed that the compound caused degranulation of mast cells of rat mesentery *in vitro* to the extent of 46% in the dose of 0·8 *mcg/ml*. This property was found to be about 50% of the effect of compound 48 80 under similar experimental conditions.

The findings are suggestive of histamine liberating property of the compound.

STUDIES ON THE CARBOHYDRATE METABOLISM OF THE MYOCARDIUM IN THE PRESENCE OF EMETINE AND DEHYDROEMETINE USING THE ISOLATED PERFUSED RAT HEART. *By* **P.M. Stephen and Ranita Aiman**. *Department of Pharmacology, Christian Medical College, Vellore.*

The cardiovascular toxicities on the junctional tissue and cardiac conductivity of Emetine hydrochloride, a potent amoebicidal agent, and the relative lower toxicity of its more recent synthetic congener, Dehydroemetine, have been reported by other workers. Since no reports have been made so far on the effect of these agents on the metabolic profiles engendered by the action of these drugs on the heart, this study was undertaken.

Studies were made using the isolated perfused rat heart by the continuous perfusion techniques established by earlier workers and simplified to some degree by us, to maintain the lowest effective re-circulating volume possible, under a constant pressure-head using a small volume perfusion pump (AMINCO). The isolated hearts were perfused with Krebs-bicarbonate buffer, stabilized by liberal aeration with carbogen (95% oxygen-5% carbon dioxide mixture) and enriched with 8.5 mM glucose, at 37°C, and 55-60 *mm* Hg constant pressure, adjustable by the pump, for 75 minutes. Glucose uptake from the perfusate, glycogen content of heart muscle at the end of perfusion, lactate output into perfusate and lactate content of heart muscle after perfusion were estimated as parameters to study glycogenesis and anaerobic glycolysis.

Both emetine and dehydroemetine increase the glucose uptake, but depress glycogenesis, as compared to the controls. Dehydroemetine 2 $\mu g/ml$ shows a greater increase of glucose uptake and a lesser decrease of glycogenesis, the latter not statistically significant ($P>0.05$). Emetine 2 $\mu g/ml$ produces a less marked increase of glucose uptake than 1 $\mu g/ml$, while the decrease of glycogenesis is markedly lower. Lactate output in the perfusate and lactate content in the heart muscle are significantly increased above the control ($P<0.025$) with both Emetine and Dehydroemetine, and significantly more so with Emetine 2 $\mu g/ml$ ($P<0.025$). When acetoacetate was substituted for glucose as a nutrient substrate in concentrations of 0.4 mM, the functional ability of the heart remained normal, and the glycogen content of the heart remained constant even in the presence of Emetine or Dehydroemetine. The heart appeared to readily utilise the acetoacetate, an intermediary product of carbohydrate metabolism, which directly enters the aerobic glycolytic cycle of Krebs.

It would appear therefore that the Myocardial contractility in the presence of Emetine, demands greater glycogen breakdown than Dehydroemetine, thus depleting this ready source of energy to a greater degree. Since acetoacetate is so readily utilised with a sparing of glycogen, anaerobiosis is the more probable pathway of this glycogenolysis resulting in the greater lactate formation in the perfusate and lactate content in the muscle which may simulate conditions of earlier "muscular fatigue" which may, in some measure contribute to the greater toxicity of Emetine as compared to Dehydroemetine.

POTENTIATION OF HYPNOTIC ACTION OF BARBITURATES BY CHLORAMPHENICOL AND ITS ANALOGS*.

By **Balwant N. Dixit and I. Glenn Sipes.** *Department of Pharmacology, University of Pittsburgh, Pittsburgh, Pennsylvania* 15213, *U.S.A.*

D-Threo-chloramphenicol, the first broad-spectrum antibiotic to be introduced into therapeutics, is of unique interest for a variety of reasons. It inhibits protein synthesis in bacterial cells and cell-free systems, and this action may be responsible for its observed bacteriostatic action. It is shown here that chloramphenicol and its analogs potentiate the action of hexobarbital, pentobarbital, and amobarbital.

The duration of action of hexobarbital, pentobarbital, and amobarbital was measured in male Wistar rats or male Swiss-Webster mice by measuring the "sleeping time". The

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TABLE 1

Animal Species	*Drug, Dose mg/kg, i.p.*	*Pretreatment (i.p.)*	*Duration of Response (per cent of control)*
Rat (male)	Hexobarbital Na. 100 *mg/kg*	D-threo-chloramphenicol succinate (60 min.) prior) *mg/kg*	
		100	900
		45	330
		Actinomycin-D, 0.5 *mg/kg* (60 min. prior)	105
		Actinomycin-D, 0.05 *mg/kg* (every 60 min. for 240 min.)	98
Mouse (male)	Hexobarbital Na. 90 *mg/kg*	D-threo-chloramphenicol succinate, 50 *mg/kg* (60 min. prior)	520
		L-threo-chloramphenicol, 50 *mg/kg* (60 min. prior)	680
		D-threo-thiocymetin, 50 *mg/kg* (60 min. prior)	400
		L-threo-thiocymetin, 50 *mg/kg* (60 min. prior)	320
	Pentobarbital Na. 45 *mg/kg*	D-threo-chloramphenicol, *mg/kg* (60 min. prior)	
		100	2200
	Amobarbital Na. 98 *mg/kg*	100	500
	Barbital Na. 300 *mg/kg*	100	95
Cat	Pentobarbital Na. 35 *mg/kg*	D-threo-chloramphenicol succinate, 25 *mg/kg* (15 min. prior)	400

results (Table 1) show that chloramphenicol is quite effective in potentiating the duration of action of hexobartital, pentobarbital, and amobarbital. There is no significant effect on the action of barbital. As hexobarbital, pentobarbital, and amobarbital are metabolized by rat and mouse liver-microsomal enzymes while barbital is excreted unchanged, it seems quite likely that chloramphenicol exerts its effect by inhibiting the liver-microsomal enzyme system(s). The action of chloramphenicol is manifest practically immediately after its administration and so it is unlikely that the effect is produced by inhibiting the *de novo* synthesis of microsomal enzyme protein. This is further supported by the observation that pretreatment with actinomycin-D was without any significant effect on the action of hexobarbital.

Chloramphenicol is metabolized mainly by glucuronoid conjugation. It has been reported that glucuronoid conjugation is at a very low level during neonatal and infant life, and that chloramphenicol freely equiliberates with fetal blood. It is also known that in very early life the mammalian liver microsomal drug metabolizing enzymes are poorly developed. These observations indicate that this effect of chloramphenicol on the barbiturates is of particular significance during neonatal and infant life. It may also be of importance in persons who have a

poor capacity for glucuronoid conjugation, e.g. diabetics, persons with Gilbert's disease, congenital jaundice, and neonatal jaundice.

Similar action of chloramphenicol has been observed in dogs and cats in this laboratory. Cats were found to be very susceptible to the action of chloramphenicol. It is known that cats have a poor capacity to form glucuronoides of many drugs and so one would expect that the chloramphenicol would remain in the body for a very long time, thus producing a prolonged effect.

Fasting also reduces the capacity of the animal to form glucuronoides. In the present experiments it was found that in rats 18 hr fasting potentiated the effect of chloramphenicol on hexobarbital "sleeping time".

It was also shown that D-threo- and L-threo-isomers of chloramphenicol and D-threo- and L-threo-isomers of thiocymetin were equally active in prolonging the action of hexobarbital, thus indicating that stereo-specificity is not required for the inhibitory effect.

EFFECT OF COLD ENVIRONMENT ON CITRATE METABOLISM. *By* **M.L. Gupta and S.D. Bhardwaj**. *Department of Physiology and Biochemistry, S.M.S. Medical College, Jaipur.*

Studies were made on 60 albino rats weighing from 80 to 100 *gms*. The animals were divided into four groups : Group I served as normal while groups II, III and IV were exposed for two hours to 0°C, −5°C and −10°C respectively. After exposure the animals were sacrificed. Blood was collected and analysed for citric acid. Liver slices were incubated with sodium pyruvate (5 mM) or citric acid (1.5 mM) in Kreb's ringer bicarbonate medium for the study of biosynthesis and oxidation of citric acid. After incubation, the tissue was analysed for citric acid and alpha ketoglutaric acid.

The results of these experiments showed that exposure to cold caused significant elevation of blood citrate level as compared to the controls (26°C=1.4±0.25; 0°C=1.8±0.12;−5°C =2.1±0.11;−10°C=2.4±0.34). The results also showed that there was no significant difference between the amount of citrate synthesized from pyruvate by liver slices of animals exposed to room temperature (26°C) and to cold environment (0°C,−5°C and−10°C.). The oxidation of citrate was significantly decreased in cold (26° C=13·5±0·81 ; 0°C=11·5±0·1 ; −5°C=10.4 ±0.31;−10°C=8.5±0.90 μmoles/hr/100 *mgm*). The changes were proportional to the fall in environmental temperature.

EFFECT OF LOW BAROMETRIC PRESSURE ON CITRATE METABOLISM. *By* **M.L. Gupta and S.D. Bhardwaj**. *Department of Physiology and Biochemistry, S.M.S. Medical College, Jaipur.*

Sixty albino rats were divided into four groups : Group I served as control while groups II, III and IV were exposed to simulated altitudes equivalent to 1420, 7200, 14000 and 18000 ft respectively. After exposure, blood was collected and analysed for citrate. The liver slices were prepared free-hand. Biosynthesis of citric acid was studied by incubating liver slices with sodium pyruvate (5 mM) in Kreb's bicarbonate buffer, while oxidation of citrate was studied with the mixture of citric acid and Kreb's bicarbonate buffer. Sodium arsenite was

used to inhbit alpha ketoglutarate dehydrogenase in order to provide the maximum accumulation of alpha ketoglutarate.

The observations showed that exposure to simulated increased altitude caused highly significant rise in blood citrate level (1420 ft.=1.4±0.25; 1000 ft.=1.6±0.30; 14000 ft.=1.9±0.30; 18000 ft.=2.1±0.40) and decrease in oxidation of citrate (1420 ft.=13.5±0.81; 7200 ft.=12.10±0.70; 14000 ft.=11.05±0.81; 18000 ft.=9.85±0.35). There was no significant effect on biosynthesis of citrate.

EFFECT OF ZINC SULFATE ON CARBON TETRACHLORIDE HEPATOTOXICITY IN ALBINO RATS. *By* **S. Srinivasan and J.H. Balwani**. *Department of Pharmacology, B.J. Medical College, Poona.*

Pretreatment of rats with zinc sulfate ($ZnSO_4$, 7 H_2O) in the dose of 2 $\mu g/g$ body wt. reduced the extent of liver damage produced by carbon tetrachloride (2.5 *ml/kg* body wt. administered after 5 hours) as studied by bromsulfthalein excretion and succinic dehydrogense activity of the liver *in vitro*. Hexobarbitone sleeping time and histological appearance of the liver were not affected significantly.

OBSERVATIONS ON CHRONIC ORAL ADMINISTRATION OF SOME ANTIFUNGAL ANTIBIOTICS TO RATS. *By* **B.G. Vad, R.N. Jalit and V.K. Deshmukh**. *Research Laboratories, Hindustan Antibiotics Ltd., Pimpri, Poona.*

Various methods, such as duration of action of hexobarbitone and zoxazolamine, plasma levels of phenylbutazone in dogs, measurement of urinary excretion of 6 hydroxycortisol, ascorbic acid and D-glutaric acid in rats, have been employed for studying action of drugs on the microsomal enzyme systems of liver. Urinary ascorbic acid excretion was studied in rats before and after chronic oral treatment with griseofulvin, nystatin, hamycin and carboxymethylcellulose (CMC), with the rats treated with CMC acting as controls. It was observed that urinary excretion of ascorbic acid was reduced in groups of rats receiving griseofulvin, nystatin and hamycin with maximum reduction in the hamycin treated group.

It thus appears that hamycin, griseofulvin and nystatin exert an inhibitory effect on the drug metabolizing microsomal enzyme systems of liver.

EFFECT OF NEGATIVE PRESSURE RESPIRATION ON URINE FLOW IN RATS. *By* **S.N. Ghosh and R.R. Chaudhury**. *Department of Pharmacology, Post Graduate Institute of Medical Education and Research, Chandigarh.*

An experimental model of negative pressure respiration-induced diuresis in the rat was produced by means of a water suction pump in a glass chamber provided with some adjustable leaks to maintain the pressure at 8 *cm*. An increased urine flow (average 42.8%) was obtained during the negative pressure respiration. Antidiuretic hormone (ADH) and angiotensin both caused antidiuresis during negative pressure respiration. The intensity of antidiuresis was similar to that produced by comparable concentrations of these substances before negative

pressure respiration was begun. The results indicated that the negative pressure induced diuresis was probably of central origin and ADH estimations of plasma during negative pressure respiration are being undertaken.

EFFECT OF TEMPERATURE, WIND VELOCITY AND DURATION OF EXPOSURE ON THE SEVERITY OF COLD INJURY IN THE RAT. *By* **R.K. Srivastava, H. Faruqi and P.R. Pabrai**. *Department of Defence Research Laboratory (Materials), Gwalior.*

A technique has been developed to produce controlled degree of cold injury in small laboratory animals. A blast of air from an air compressor is dried by passing through suitable desiccants. The dried air is then led through a series of glass coils placed in a cooling chamber wherefrom the air enters a small receptacle in which the rat paw is exposed but the body of the animal is protected from the cold wind by keeping it in a small wooden rat holder. The three parameters which are independently as well as simultaneously controlled and measured include wind velocity, temperature of the air blast and duration of exposure.

Lightly anaesthetised (morphine+phenobarbitone) unfasted male albino rats weighing 200 to 250 *g*, are used in the study. The limb of the animal to be exposed is moistened with water and 0.2 *ml* water for injection is injected subcutaneously on the dorsoplantar region just before exposure. Five animals have been found adequate for each set of observations.

The extent of tissue loss. viz. autoamputation of phalanges (first degree), autoamputation upto plantar region (second degree) and autoamputation upto knee joint (third degree frostbite) can be caused by appropriate combination of duration of exposures, temperature of air and the velocity of air blast. Thus, first degree of cold injury is produced if the rat paw is exposed for 15 minutes to the blast of air at $-10°C$ with a velocity of 60 meters/minute. Exposure of rat paw to the same duration and wind velocity but to a blast of air at $-15°$ C, produced second degree of cold injury but if the temperature of the wind is lowered to $-25°$ C exposure for 15 minutes to a wind velocity of 60 meters per minute results in cold injury of third degree. Experiments have been done with isoxsuprine hydrochloride and the results obtained are in conformity with those obtained by Talwar *et al.* (*Angiology*, **18**:242, 1967) using rabbits as experimental animals.

The results obtained by the technique developed in this laboratory are reproducible and provide a quick and economical screening procedure for assessing antifrostbite activity of drugs.

EFFECTS OF HIGH SPEED ON HUMAN BODY. *By* **Dr J.K. Sengupta.** *Department of Physiology, J.J.M. Medical College, Devangere.*

Most of the Physiological effects of high speed flight arise not from the velocity, but from the peculiar circumstances in which the speed is achieved and maintained.

Two major problems are independent of the imperfections of the atmosphere. The first arise because the time required to perceive, recognize and react to a stimulus does not diminish

as the speed of flight increases. The second results form the inconvenience of travelling in a straight line at a constant velocity.

In a situation where the observer is moving, and particularly when he has control of the vehicle, it is more pertinent to think of reaction distance than reaction of time. In the simplest case this amounts to approximately one foot for each mile per hour; a car moving at 50 miles per hour will travel about 50 feet before its driver can respond to a sudden signal by placing his foot on the brake.

The effect of centrifugal acceleration during turns and aerobatics was studied in the human beings in human centrifuge. It was observed that increased weight of the limbs impaired motor activity, it was just possible to rise from a seat at 2*g*; at 3*g* the legs become almost too heavy to lift; at 6*g* the arms could not be raised above the head. Fine movements of the fingers and hand could still be made, but only if the rest of the arm was well supported. The Physiological mechanism that maintained the circulation despite the earth's gravity became less and less adequate as the weight of the body increased.

Of greater consequence are the effects of accelerative stress upon the cardiovascular system. The physiological mechanisms that maintain the circulation despite the earth's gravity become less and less adequate as the weight of the blood increases.

The arterial blood pressure at head level falls, and the dependent parts of the body suffer congestion as blood pools in them. The venous return is diminished, and the output of the heart declines, adding to the difficulty of supplying a reasonable flow to the cerebral vessels. Compensatory reflexes—tachycardia and vasoconstriction—help to restore the blood pressure but they do not become fully effective for several seconds, and may be too late to save the situation.

VARIATION OF RESPONSE TO PAIN DUE TO GENETIC CONTROL AS SEEN FROM THE COLOUR OF IRIS. *By* **D.S. Salunkhe and J.H. Balwani.** *Department of Pharmacology, B.J. Medical College, Poona.*

The colour of the iris was noted and the pain threshold was determined in 124 male and 60 female healthy medical students. 5.99% of the students had grey blue irises. The mean pain threshold in the light brown iris group was 48.8 sec. In the brown iris group, it was 46.9 sec., in the dark brown iris group it was 41.2 sec., and in the grey blue iris group, it was 26.6 sec. There was no statistically significant variation of the pain threshold between males and females within the same colour of iris group, as well as light brown, brown and dark brown iris groups. However, there was statistically significant variation of the pain threshold between shades of brown iris group and the grey blue iris group. Grey blue pigmented iris represents a distinct genotype.

HUMAN CYTOGENETICS. *By* **Dr F.V. Bapana.** *Department of Physiology, J.N. Medical College, Belgaum.*

A newly developed science of finding the genetic sex of an individual by examining nuclei and perinuclear mass of tissue cells. This can be done by examining the cells of skin, buccal mucosa, Amniotic fluid, as well as the blood neutrophils.

The sex chromatin mass of tissue cells other than blood neutrophils is a fixed entity from which we can determine the female genetic sex of the individual. This chromatin mass does not get affected by a change in hormonal level of the body; but the percentage of nucleolar appendages of blood neutrophils, changes according to sex hormone level in the blood.

This fact has been taken advantage of by the author in the Prediction of Fetal Sex by examining the maternal blood, in which the change is reflected by a decrease or an increase in the nuclear appendages if the fetus is a male or a female respectively. Good results (99%) are obtained by the author for the cases referred to for Prediction of Fetal Sex.

Divergence of Phenotype from the Genotype may be due to omission or addition to the normal 'XY' or 'XX' pattern. Thus abnormalities like Super female (XXX); Klinefelters Syndrome (XXY), Turner's Syndrome (XO) or Super male (XYY) can be diagnosed by Sex-chromatin study; further supported by chromosome study by Karyotyping according to Denver system. Here cells are cultured and cell division is arrested at metaphase by colchicine; and then staining after squashing. This technique is at present envisaged by the author in the particular study of the Super male (XYY) syndrome, in which these tall males are basically inclined to acts of arson, rape, violence, etc. These unfortunate criminals after they are properly diagnosed may be segregated from those other criminals in the same category, who may be considered for reform. Those belonging to 'YY' syndrome may be considered amenable to hormone treatment on the basis of possible over-action of their male hormones by undertaking the investigation of Blood hormone level or by estimating the urinary 17-Ketosteroids.

Karyotyping will also help in the diagnosis of diseases like Down's syndrome due to deletion, translocation etc., of the autosomes or the finding of the Philadelphia chromosome in cases of Leukemia.

COLOURBLINDS AND ABO BLOOD GROUPS. *By* **J.K. Patel, R.M. Bhatty and H.G. Desai.** *Department of Ophthalmacology, S.S.G. Hospital, Baroda.*

A survey of colourblindness was carried out totally in 3149 students of both sexes (2334 males and 845 females) of M.S. University, Baroda, with the help of Ishihara Charts (1964). It was found that colourblindness was more common among the male population (3.7%) than among the female population (0.12%). The overall incidence was 2.81%. Considering the subgroups among the colourblinds, anomalous trichromatism was found in 0.26% and dichromatism was found in 2.38% subjects. No monochromat was found and 0.17% remained unclassified other than red-green blind. Results were compared with the data obtained by other workers.

ABO blood group typing was carried out in all 89 colourblind subjects, and control subjects. ABO blood groups distribution among colourblinds, strong deutans, controls and blood donors was found to be different. Totally 13000 blood donors' ABO blood group distribution was available from the Blood Bank, Medical College, Baroda.

In comparing the results of ABO distribution, apparently 'O' group subjects were maximum (53.8%) in strong deutans. In colourblinds 'O' group was in 84.4% subjects. Among the controls and blood donors, 'O' group subjects were 42.1 and 31.9 per cent respectively.

Gene frequencies were calculated to confirm this. There was an increase in the proportions of 'O' blood group subjects, as shown by gene frequencies, calculated according to Bernstein over control, as well as colourblind subjects, especially over deutronopes. These results suggested the predilection of colourblindness to 'O' group.

But when tested statistically ABO distribution in the colourblinds and strong deutans in comparison with control subjects was found to be not significant. Chi-square values obtained were 3.1 and 5.54 giving significance levels less than 0.3 and 0.1 respectively.

But when ABO distribution in colourblinds was compared with those of blood donors, the difference was statistically significant (x^2 11.39, and $P < .01$) and the significance increased when strong deutans were compared with blood donors (x 15.9, and $P < .01$). However, the observed predilection could not be considered significant unless more data are avaiable, particularly because this study is the first of its kind and merits further investigation.

A STUDY OF SERUM CAROTENE AND VITAMIN A LEVELS IN CLINICAL CASES OF DEFICIENCY. *By* **L. Kameswaran, M. Sukumar and S. Subramaniam**. *Department of Pharmacology, Madurai Medical College, Madurai.*

Serum carotene and vitamin A levels were estimated in normal individuals and persons exhibiting ocular symptoms of avitaminosis A.

An attempt has been made to find out correlation, if any, between carotene and vitamin A levels and also between serum vitamin A levels and age, food habits, social habitat and severity of ocular deficiency symptoms.

Venous blood was drawn four hours after breakfast. Serum carotene and vitamin A levels were estimated by the method of Kimble (1939) and Kaser and Stekol (1943), using Carr-Price reaction.

Electrophoretic patterns of the serum proteins were also studied with special focus on albumin fraction.

Few of the cases were given 100,000 units of vitamin A acetate in oil daily, for ten consecutive days and then all the above mentioned estimations were repeated.

IN NORMAL INDIVIDUALS

In all the four age groups 1-5 yrs, 6-10 yrs, 11-20 yrs, and 20-40 yrs, the mean serum carotene levels were found to be below the previously reported normal levels (100 μg/100 *ml.* serum).

Mean serum vitamin A levels were above the critical lower limit for the appearance of ocular deficiency symptoms as suggested by Maclaren (1944; 20 μg./100 *ml.* serum).

There is no correlation between the serum carotene and vitamin A levels of the corresponding age groups.

IN DEFICIENT INDIVIDUALS

In all the four age groups, the mean serum carotene values were lower than the normal levels, the level in the children below 5 years being the lowest. So also the mean serum vitamin A levels were below the critical lower limit in the first three age groups, the level in the first group being the lowest.

There is no correlation between the serum carotene and vitamin A levels of the corresponding groups.

Mean serum carotene and vitamin A levels were found to be higher in the patients from urban areas. In the case of vegetarians from both urban and rural areas, the carotene level is higher than in non-vegetarian counterparts.

Mean serum vitamin A level is higher in non-vegetarians from both urban and rural areas than in vegetarians.

No correlation was found to exist between the serum vitamin A levels and severity of ocular deficiency symptoms.

After treatment with oily injections, the rise in serum vitamin A levels was not consistent.

Study of electrophoretic patterns of serum proteins revealed slight reduction in the albumin fraction which failed to improve after the treatment with oily injections

DEGRANULATION OF BETA CELLS OF THE ISLETS OF LANGERHANS FOLLOWING INTRAGASTRIC ADMINISTRATION OF MAGNESIUM CHLORIDE. *By* **Madad Ali, R.K. Mishra, and K. Anand**. *Department of Biophysics, All India Institute of Medical Sciences, New Delhi.*

Studies by Paavo Suomalainen on hibernation demonstrated increased magnesium concentration in blood (1). In his experiments this was associated with shift in the α/β ratio in the islets of Langerhans along with necrosis of the β cells in several species like hedgehog, mouse and some but not all strains of rats; the guinea-pig was resistent. In previous experiments by one of us (RKM) the necrosis of the β cells was not observed consistently in the rabbit but a degranulation of these cells was always noted. In the present studies magnesium chloride $6H_2O$, 182.25 *mg/kg* body weight was injected intragastrically in 2 *ml* distilled water to Sprague-Dawley albino rats (60) of 122 ± 6 *gm* average body weight. The vehicle-controls (29) of same average body weight were administered 2 *ml* of distilled water by the same route and the absolute controls (10 rats) were administered nothing. The pancreases were taken out at 5, 10, 15, 20 and 30 minutes, and processed for staining by *dl*-pseudoisocynine hydrochloride, a metachromatic stain specific for insulin. All the animals in experimental groups (100% incidence) showed reversible degranulation of β cells, which reached maximum around 10-15 minutes and the reaction was recovered at about 30 minutes. The controls being all negative the result are highly significant statistically. These findings will be discussed in the light of several theories

of insulin secretion (2-5) as well as magnesium-dependent steps in carbohydrate metabolism and the possible role in insulin biosynthesis.

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EFFECT OF CARBACHOL ON TRANSMISSION IN VASOMOTOR CENTRE. *By* **Om Chandra, K.P. Gupta, K.C. Singhal, S.N. Chawla and P.N. Saxena**. *Pharmacology Department, J.N. Medical College, A.M.U., Aligarh.*

Cholinergic transmission has been shown to play an important role in the central vasomotor regulation (Sinha *et al.*, 1967). These workers have also reported that the reflex vasomotor response to carotid occlusion is blocked by hemicholinium given intracerebroventricularly (i.c.v.) and reappears on giving choline by the same route. In the present study we have tried to gain further insight into the role of cholinergic mediation in the central vasomotor regulation by studying the effect of carbachol on carotid occlusion response.

The experiments were performed on adult dogs of either sex anaesthetised with pentobarbitone sodium (30 *mg/kg* intravenously). Drugs were administered by i.c.v. route and their effect was seen on the reflex pressor response to carotid occlusion.

A marked and persistent rise in blood pressure was noted after 50μg. dose of carbachol i.c.v. The carotid occlusion pressor response was found to be markedly potentiated after 50 μg i.c.v. dose of carbachol. Atropine in a dose of 8 *mg* i.c.v. blocked the rise in blood pressure by carbachol and also the potentiation of carotid occlusion. This suggests a probable role of cholinergic mediation in the reflex central vasomotor response.

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PHARMACOLOGICAL STUDY OF A NEW AMINOPROPANOL ADRENERGIC NEURON BLOCKING AGENT (COMPOUND 66/12)*. *By* **K.C. Mukherjee, G.K. Patnaik, R.C. Srimal and B.N. Dhawan**. *Pharmacology Division, Central Drug Research Institute, Lucknow.*

During initial pharmacological screening of aminopropanol derivatives, a phenoxyethyl aminopropanol compound (66/12) was found to possess promising hypotensive activity and was, therefore, selected for detailed investigations. The LD_{50} of this compound in mice was 175 *mg/kg* (i.p.). In anaesthetised (pentobarbitone sodium) cats, 1.0 *mg/kg* (i.v.) of the compound lowered the blood pressure by 30% for 30 min. Higher doses produced more marked lowering of arterial pressure for longer duration. In spinal cats the hypotensive response was less marked and transient. The compound did not produce any hypotension when injected into a lateral cerebral ventricle of cat upto a dose of 200 μg.

1.0 *mg/kg* (i.v.) of the compound blocked the pressor response to tyramine and potentiated the pressor responses to adrenaline and noradrenaline. This dose also inhibited the transmission along the sympathetic nerves without inhibiting the autonomic ganglia as indicated by (*i*) almost equal block of contraction of the nictitating membrane following pre- as well as postganglionic nerve stimulation in cat, (*ii*) almost equal block of the increase in heart rate after stimulation of pre- and postganglionic sympathetic fibres to heart in dog, (*iii*) block of the decrease of bladder pressure due to stimulation of hypogastric nerve in cat, and (*iv*) block of the contraction of rabbit uterus induced by hypogastric nerve stimulation. In dog 3.0 *mg/kg* (i.v.) dose of compound 66/12 reduced the cardiac output by 12% when blood pressure decreased by 40% for more than 60 min. In dog heart-lung preparation this dose of the compound had no significant effect.

RELATION OF NORADRENALINE UPTAKE AND RETENTION TO EXTRACELLULAR IONS. *By* **Arun R. Wakade, S.M. Kirpekar and R.F. Furchgott**. *Department of Pharmacology, Medical College, Baroda, and State University of New York, New York.*

Effect of changes in ionic composition of the regular Krebs solution was investigated on the uptake and retention of radioactive noradrenalime (H^3-NA) by the isolated left atria of guinea-pig. One atrial half was kept in regular Krebs solution throughout, while the other half was washed with Krebs solution of modified ionic composition and remained in this medium for 10 to 30 min. Under their respective conditions, both halves were then exposed to 5 *ng/ml* of *dl* H^3-NA for 5 min, washed for 40 min and then analysed for H^3-NA as well as NA content of the tissue.

The absence of Ca^{++} ions from the Krebs solution had no effect on the uptake-retention of H^3-NA. Complete removal of K^+ ions reduced the amount of H^3-NA taken up and retained by 20-50%. Removal of Na^+ ions (sodium salts of regular Krebs solution were completely replaced by equimolar choline chloride or iso-osmolar sucrose) caused 80-90% reduction in H^3-NA uptake-retention, without affecting the endogenous NA content of the atria. Lithium was totally ineffective as a substitute for sodium to maintain the normal uptake mechanism. Ouabain (10^{-5} M) and tetracaine (0.33-0.66 M) markedly inhibited H^3-NA uptake-retention

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y about 66 and 70%, respectively. It appears that presence of external sodium is an absolute equirement for the transport of noradrenaline into the sympathetic nerve terminals.

N EXPERIMENTAL STUDY ON PROARRHYTHMIC AND ANTIARRHYTHMIC EFFECTS OF RESERPINE. *By* **R.B. Arora, N. Bagchi and M. Singh**. *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

Recent interest on the effect of reserpine and beta-adrenergic blocking agent, propranolol, on digitalis toxicity has resulted in a number of provocative hypotheses on their mechanism of action. In the present study an attempt was made to study the mechanism of action of reserpine on ouabain induced cardiac arrhythmias.

In guinea-pigs, ouabain was infused at a constant rate till there was evidence of digitalis toxicity in the form of extrasystoles, ventricular tachycardia, ventricular fibrillation or cardiac standstill. It was observed that reserpine manifests both proarrhythmic and antiarrhythmic property depending on the experimental situation.

In one group of animals, reserpine was administered intravenously after the animals received an infusion of a subtoxic dose (40% of the lethal dose) of ouabain. In this situation, reserpine acted as a proarrhythmic agent by precipitating the onset of arrhythmias. This proarrhythmic effect was probably due to increased automaticity as a result of release of catecholamines since this effect was not manifested in animals which had received pretreatment with reserpine 24 hours before.

An antiarrhythmic effect was manifested by reserpine in animals, which were treated with a catecholamine depleting dose of reserpine 24 hours before the experiment. Reserpine was found to increase both the arrhythmic and lethal doses of ouabain. Pretreatment with a low dose of reserpine, hot-sufficient to cause complete depletion of cardiac catecholamines, failed to afford significant protection against ouabain toxicity.

Another experimental situation was created in which the animals, already pretreated with adequate doses of reserpine 24 hours before, were subjected to ouabain infusion till the appearance of ventricular tachycardia. Once ventricular tachycardia was established, reserpine was administered intravenously. It was observed that reserpine casued a change from ventricular tachycardia to complete heart block or nodal rhythm. From all these observations, the following conclusions can be made:—

(*i*) Reserpine has no antiarrhythmic activity in animals with normal cardiac catecholamine levels. In such animals, sudden injection of reserpine may even precipitate the arrhythmias as susceptibility of the hearts to arrhythmias has already been intensified by a subtoxic dose of reserpine. This experimental observation also serves as caution against administration of reserpine in patient receiving full doses of digitalis.

(*ii*) The protection afforded by reserpine to ouabain toxicity in the form of increases of toxic or lethal doses is manifested only after severe catecholamine depletion.

(*iii*) The *per se* antiarrhythmic effect is normally not observed because of its antagonism by catecholamine release. But once catecholamines have been sufficiently depleted by prior pretreatment, the catecholamine release action is not manifested and we observe its power to antagonise the established arrhythmias. This is probably due to its direct action which is manifested only in catecholamine depleted heart. This hypothesis receives support from earlier work of Innes *et al.* (1958) who observed direct action of reserpine in the form of negative inotropic effect and bradycardia in catecholamine depleted animals.

STUDIES ON THE ANGIOTENSIN LIKE ACTIVITY IN THE RAT UTERUS HOMOGENATE. *By* **H.B. Walia and R.R. Chaudhury**. *Department of Pharmacology, Postgraduate Institute of Medical Education and Research, Chandigarh.*

Angiotensin, vasoconstrictor polypeptide, is released by the action of an enzyme, renin, on the α_2-globulin present in blood. It has recently been reported that the renin content is increased in the plasma of pregnant women (Brown, Davies, Doak, Lever, Robertson ; 1966). Gross, Ziegler and Berger (1964) have shown that a renin like substance is present in the placenta and uterus of the rabbit. Studies on uterine renin content by Gordon, Ferris and Mulrow (1966) have shown that the pregnant rabbit uterus has a higher concentration than non-pregnant uterus. No studies have been conducted studying angiotensin levels in the rat uterus. This has been done in the present investigation. The uterine homogenates of oestrus and dioestrus rats were assayed for angiotensin like activity on the isolated rat colon (Regoli and Vane 1964). It is seen that the rat uterine homogenate contains a substance both at oestrus and dioestrus—which contracts the isolated rat colon. The concentration of this substance appears to be higher at dioestrus but it is not significant statistically ($P>0.05$). Cinnarizine at a dose of 50 microgram left in the bath for 30 minutes did not block the effect of the homogenate although it did block the effect of angiotensin. The activity is present more in the supernatant than the residue ($P<0.01$). The type of contraction produced by the homogenate is similar to that produced by the angiotensin but is not similar to that produced by 5-hydroxy-tryptamine. UML-491 (Sandoz) at a dose of 50 μg left in bath for 30 minutes reduced the effect of 5-hydroxy-tryptamine while the effect of angiotensin and the homogenate was unchanged. The results indicate that the rat uterus homogenate contains a smooth muscle stimulating substance similar to angiotensin.

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BIOASSAY OF ADRENALINE ON FROG INTESTINE. *By* **C.B. Seth, V.S. Murthy and S.K. Tongia.** *Department of Pharmacology, M.G.M. Medical College, Indore.*

The isolated intestine (duodenum) of frog was used as a preparation for the bioassay of adrenaline. The preparation was found to be sensitive to adrenaline in as low a concentration

as 10 nanograms per ml. of bath fluid. The preparation showed a stable sensitivity for several hours. The responses in different doses were repeatable and gave steep dose response curves, in the range of 20 to 50 *ng/ml.* On comparison with other known techniques the frog's intestine was thus found to be a fairly sensitivie preparation for bioassay of adrenaline.

Other significant observations have been that the tissue maintained its sensitivity to adrenaline in frog's Ringer saline at room temperature, irrespective of seasonal variations. Further, the biological variation in the sensitivity of the pieces of intestine obtained from different frogs was insignificant. Rhythmic movements were minimal in comparison to Rabbit's intestine.

The findings are indicative of a useful experimental tool, in the frog's intestine (duodenum) for bioassay of adrenaline.

EFFECT OF ASCORBIC ACID ON SMOOTH MUSCLE. *By* **J.N. Bhatnagar, V.S. Murthy and C.B. Seth.** *Department of Pharmacology, M.G.M. Medical College, Indore.*

Effect of ascorbic acid on the spasmogenic action of acetylcholine and histamine on guinea-pig intestine has been reported in the past. In our laboratory effect of ascorbic acid on smooth muscles of rat and rabbit was studied.

In our experiments, ascorbic acid was found to produce inhibition of acetylcholine, serotonin and barium chloride induced contractions of rat intestine and rat uterus in doses of 0.1 and 1 *mg/ml.* of bath fluid. Further when effect of ascorbic acid was studied on the duodenum of rabbit, it produced relaxation of the duodenum without affecting the motility in doses of 1 *mg*, 2 *mg*, and 4 *mg/ml* of bath fluid.

On isolated frog heart, it produced a negative *inotropic* effect which was not antagonised by atropine showing thereby that this was also a direct action.

In none of the tissues studied, we could find a potentiation as has been reported on guinea-pig ileum. This is probably due to species difference. In view of the above observations it can be concluded that ascorbic acid has a direct depressant action on the smooth muscles of rat and rabbit.

FURTHER STUDIES ON THE EFFECT OF 1,4-BENZODIAZEPINE DERIVATIVES ON GUINEA-PIG ILEUM AND RABBIT INTESTINE. *By* **B.P. Mukherjee and S.R. Dasgupta.** *Department of Pharmacology, Institute of Basic Medical Sciences, University College of Medicine, Calcutta University. Calcutta.*

In an earlier communication we had reported the antagonistic activities of three 1,4-benzodiazepine derivatives, namely, chlordiazepoxide, diazepam and nitrazepam against spasmogens such as acetylcholine, carbachol and histamine on isolated guinea-pig ileum and rabbit intestine preparations (1). Present investigation was carried out to study the influence of benzodiazepine derivatives on the action of barium chloride, a directly acting musculotropic agent, on guinea-pig leium and rabbit intestine. In the isolated guinea-pig ileum diazepam, nirazepam and chlordiazepoxide antagonized barium chloride-induced spasm in decreasing order of potency. Similar findings were obtained on the isolated rabbit intestine prepara-

tions. Thus, besides the anti-ACH, and anti-histamine activities, these compounds are found to possess, in addition, a musculotropic activity.

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UPTAKE OF NORETHYNODREL-H^3 AFTER CONSTANT INFUSION IN FEMALE RATS. *By* **Vimla Laumas, P.K. Malkani and K.R. Laumas**. *Reproductive Biology Research Unit and Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi.*

Adult female rats were primed with radio-inert norethynodrel for a week and then constantly infused with tritium labelled norethynodrel for a period of 4 hr. After the termination of the infusion, the animals were killed by cervical dislocation and muscle, ovary, uterus, vagina, liver intestine, pancreas, lung, kidney, adrenal thymus, thyroid, eye, hypothalamus (anterior, middle and posterior), cingulum, corpus callosum, hippocampus, caudate nucleus, thalamus, midbrain, pons, cerebellum, medulla-oblongata, frontal cortex and parietal cortex were removed. The radioactivity in the tissues was determined after solubilization of tissues in hyamine hydroxide and counting in a liquid scintillation counter. Each sample was corrected for quenching. There was a high uptake of norethynodrel-H^3 in the liver, kidney and adrenal. This could be ascribed to the metabolic function of these organs. Amongst the reproductive tissues a high uptake was found in the ovary which supports the previous hypothesis of the authors that norethynodrel may be acting through the ovary and this may constitute an additional point of action besides the suppression of gonadotrophins. None of the brain areas showed any high activity.

A MODEL FOR THE MECHANISM OF ACTION OF INTRA-UTERINE CONTRACEPTIVE DEVICE (IUCD) IN THE RAT. *By* **K.R. Laumas and H.S. Yadava**. *Reproductive Biology Research Unit, All India Institute of Medical Sciences, New Delhi.*

Experimental studies on glucose-U-C^{14} metabolism in ovariectomised oestrogen and progesterone treated rats and rats on fifth day of pregnancy were carried out. All these animals had IUCD in one horn and the other acted as control. There was an increased incorporation of glucose-U-C^{14} into lipid, RNA and proteins in the IUCD horn compared with the control horn in ovariectomised and oestrogen treated animals. This indicated an oestrogen like effect by the IUCD. Progesterone produced an enhanced effect in the IUCD horn compared to the control horn. These experiments indicated an increased sensitivity of the rat uterus to progesterone. On fifth day of pregnancy when increased level of progesterone is available in the uterus, there was a decreased metabolism of glucose in the IUCD horn compared with the control horn. Previous studies from this laboratory showed that the IUCD did not alter the uptake and disappearance of radioactive progesterone from the rat uterus. The results suggested that although the uptake of progesterone was not altered in the presence of IUCD, the response of the rat uterus to it was considerably altered. A working model for the mode of action of IUCD based upon the increased sensitivity of oestrogen and progesterone in the presence of IUCD is proposed.

THE INFLUENCE OF THE INTRA-UTERINE DEVICE ON THE MAST CELL POPULATION OF HUMAN UTERUS. *By* **G. Choudhury, S. Arora, S. Bhagat and A. Dass**. *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

Strips were obtained from human uterus removed at hysterectomy for conditions like prolapse, fibroid or dysfunctional uterine bleeding. The strips were examined for mast cell population. In some cases an intra-uterine device (IUD) was inserted 7-28 days before operation. The mast cell count was found to be lower in uteri with IUD than in control uteri. The difference was statistically significant.

EFFECT OF ORALLY ADMINISTERED AZASTEROIDS ON IMPLANTATION IN RATS. *By* **S.K. Saksena and R.P. Chaudhury**. *Department of Pharmacology, Postgraduate Institute of Medical Education and Research, Chandigarh.*

Azasteroids are compounds in which nitrogen forms an integral part of steroid nucleus, without altering the shape and size of the ring and, therefore, also are known as nitrogen containing steroids. The introduction of trigonal nitrogen leads to marked alteration in the chemical and physiological properties. Aza-analogues of steroid hormones are interesting to pharmacologists today, since they may interact with the same enzyme systems as the natural hormones, and so may act as anti-hormones. Such antihormones could be of great value in prostate hypertrophy, as well as may have an important place in controlling fertility.

The present studies on nine azasteroids were carried out to elucidate their anti-implantation activity.

Colony bred adult female rats of known fertility (170-225 *gm*) were used for these studies. Azasteroids were tested by a method described by Khanna and Chaudhury (1968) which would detect antifertilization, antizygotic, blastocysto-toxic, anti-implantation and early abortifiend activity. The only modification used in this case was that the drugs were administered at the dose level of 10 *mg* per kilogram bodyweight, from day 1-4 of pregnancy in alcoholic solution instead of gum-accacia suspension, orally with a gastric catheter.

When the rats were treated with the compound 3-B-hydroxy-androst-5-one (16, 17-C)-5′-methyl-pyrazole, 11 out of 15 rats had no implantation sites. The other azasteroid 1,2,3,4-tetrahydro-N-tosyl-8-methoxy-4-oxo-benzo (b) quinoline inhibited implantation in 8 out of 15 rats.

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FREE AMINOACIDS OF HUMAN SEMEN BEFORE AND AFTER VASECTOMY. *By* **V.V. Subbarao and M.L. Gupta***. *Department of Physiology, Medical College, Ajmer.*

Studies on free aminoacids of human semen are not many. In the human semen free aminoacids are formed after ejaculation as a result of the action of endogenous proteolytic

*Department of Physiology and Biochemitsry, S.M.S. Medical College, Jaipur.

Though the weight of spleen increases till second week of pregnancy, it decreases during third week in normal and adrenalectomized rats. But in ovariectomized and thymectomized rats, the weight of spleen increases throughout pregnancy.

Though there is an enlargement of pancreas in all rats during pregnancy, it is very marked in thymectomized rats.

There is a gradual decrease in the proportionate weight of kidneys as pregnancy advances.

The enlargement of uterus is directly proportionate to the period of gestation and the number of foetuses.

The erythrocyte count increases in thymectomized and unilateral ovariectomized rats till term as in normals and only till mid-pregnancy in adrenalectomized rats.

The leucocyte count falls in thymectomized rats. Leucocytosis is marked in adrenalectomized rats which falls gradually as pregnancy advances and leucocytosis is progressive in ovariectomized rats.

ISOIMMUNIZATION OF FEMALE MICE WITH SPERM ANTIGENS. *By* **A. Farooq and P.C. Panda**. *Reproductive Biology Research Unit, All India Institute of Medical Sciences, New Delhi.*

The problem of fertility control in female mice after immunization with isologous sperm antigens was investigated. A relatively short immunization procedure was devised consisting of 6 weekly injections of the antigen along with complete Freund's adjuvant. The results indicated that agglutinating isoantibodies were produced in the immunized mice and the treatment caused the animals to become infertile in subsequent mating experiments. *In vitro* sperm immobilization and agglutination tests revealed that a specific immune agglutination of the spermatozoa in the female genital tract was the most likely cause of the induced infertility in the immunized mice.

EFFECT OF THE EXTRACTS OF SIX INDIGENOUS PLANTS ON EARLY PREGNANCY IN ALBINO RATS. *By* **S.K. Garg and S.B. Vohora***. *Department of Pharmacology, Postgraduate Institute of Medical Education and Research, Chandigarh.*

Six indigenous plants reputed to have antifertility activity, viz. *Abrus precatorius* Linn. (seeds), *Calotropis gigantea* Linn. (seeds and roots), *Randia dumetorum* Lam. (fruits), *Semecarpus anacardium* Linn. (seeds), *Taxus baccata* Linn. (leaves and stem) and *Uraria lagopoides* DC. (plant) have been tested.

All the extracts were prepared by successive extraction with petroleum ether (b.p. 60-80°C), 95% alcohol and distilled water. The dosage forms were prepared in a suspension of gum accacia. Pharmacological testing was done by a method, standardized in this laboratory. The method would detect any antifertility, antizygotic, blastocystotoxic, anti-implantation and early abortifacient activity. Female rats (150-225 *g*) of known fertility were mated with fertile males

*Present Address : Department of Pharmacology, Lady Hardinge Medical College, New Delhi.

at the proestrus phase of the oestrus cycle. The presence of vaginal plug and thick clumps of spermatozoa in the vaginal smear were taken as criteria for day 1 of pregnancy. The plant extracts, were fed to these rats at different doses by an intragastric catheter either for 1-4 or 1-7 days. The animals were laprotomised under light ether anaesthesia on day 10 and implantation sites were counted in the two horns of the uterus.

Aqueous extracts of *Taxus baccata* leaves and *Uraria lagopoides* plant showed encouraging anti-implantation activity as only 50% of the rats had implantation sites on the day 10 of pregnancy. The other four plant extracts did not show any anti-implantation activity.

UTERINE ACTIVITY OF A PURE PHENOLIC GLYCOSIDE FROM SARACA INDICA LINN. *By* **D.N. Prasad, C.V. Satyawati, S.P.Sen and P.K. Das**. *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

The bark of *Saraca indica* was found to contain a number of phenolic and non-phenolic glycosides. One of the phenolic glycosides (glycoside Q) was found to have most consistent and marked uterine activity. In extremely high dilution glycoside Q increased the tone and amplitude of contractions of uterus of albino rat *in vitro*, of guinea-pig *in vitro* and *in vivo*, of rabbit *in vitro*, of dog *in vivo* and of human *in vitro*. Pretreatment with oestrogen sensitized the rat uterus to the glycoside.

PLASMA HISTAMINE LEVELS IN CHEST DISEASES. *By* **K.C. Singhal, Om Chandra, M. Prasad, K.P. Gupta, A. Hasan and P.N. Saxena**. *Pharmacology Department, J.N. Medical College, A.M.U., Aligarh.*

Histamine is well known to play an important role in allergic disorders. Release of endogenous histamine in these conditions manifest as a rise in plasma histamine level. Increased plasma histamine levels have been reported by some workers in tropical pulmonary eosinophilia and bronchial asthma (Schultz *et al.*, 1959). The present study was, therefore, undertaken to find out the plasma histamine level in some of the common chest diseases. The blood samples were collected from the tuberculosis and chest diseases of out patient's department. The plasmas collected from these blood samples were tested for their histamine content on the isolated guinea-pig ileum perfused in tyrode solution containing 0.5 $\mu g/ml$ of BOL to prevent the action of plasma 5-hydroxytryptamine on the intestine. Plasma histamine levels were found to be increased in pulmonary tuberculosis, bronchial asthma and tropical pulmonary eosinophilia.

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ANTI-INFLAMMATORY EFFECT OF ALCOHOL SOLUBLE AND WATER SOLUBLE ALKALOIDS OF WITHANIA ASHWAGANDHA. *By* **C.L. Malhotra, V.L. Mehta and Y.K. Aggarwal**. *Department of Pharmacology and Therapeutics, Lady Hardinge Medical College, New Delhi.*

Alcoholic extract containing alkaloids and water soluble crude extract of Patiala variety of *Withania ashwagandha* was seen for anti-inflammatory activity by employing techniques

corresponding to both acute and chronic inflammations. Alcohol soluble alkaloidal fraction significantly inhibited inflammation produced by all the different techniques employed in this study. Water soluble extract significantly inhibited inflammation produced by carragennin induced arthritis and turpentine induced pleurisy which corresponds to acute inflammation. Though the water soluble extract slightly inhibited inflammation produced by techniques leading to chronic inflammation (cotton pellet method and formation induced arthritis), the results were statistically insignificant.

STUDIES ON THE CHROMATOGRAPHIC SEPARATION OF HUMAN GASTRIC MUCOPOLYSACCHARIDES. *By* **R. Ghai and M.L. Pai**. *Department of Biochemistry, Medical College, Baroda.*

An attempt was made to study the different types of mucopolysaccharides, and the carbohydrate composition thereof in the gastric juice of persons with no abnormality of the gastric mucosa.

Twenty-eight persons, mostly medical students of age 18 to 25 years, volunteered to undergo the fractional gastric analysis, which was done according to the standard procedure, using a 7% alcohol meal as a stimulant. The specimens collected were kept in the cold. An aliquot was removed from each specimen for routine analysis. The remaining gastric juice was pooled, frozen overnight, thawed, centrifuged for 30 minutes at 10,000 r.p.m. to remove solid particles and cell debris. The centrifugate was treated with diastase (175 *mg.* for 100 *ml.* of gastric juice) at 37°C for five hours followed by a reduction in volume to about 1/20th its original volume by incubating at 45° to 50°C for 4-8 days.

The above sample was then hydrolysed with $2N$-H_2SO_4 for two hours, the hydrolysate was neutralized with barium carbonate, contrifuged, the supernatant evaporated to dryness in vacuo and redissolved in the minimum quantity of water for chromatography. The carbohydrate components were identified by descending chromatography, using the solvent system, *n*-butanol-pyridine-water (6:4:3). Three runs each of 16 hours duration were done for each chromatogram. The sugars were detected by Partridges' method (1949) and Trevlyn and Proctoc's method (1950).

From the chromatograms galactose, glucose, mannose and fucose were identified. The identification was based on (*a*) the R_f values, and (*b*) on the fact that external addition of these sugars to the hydrolysate resulted in the intensification of the spots but not the appearance of further ones.

Our results do not support the common assumption that human gastric mucopolysaccharides contain uronic acid. The chromatograms of 28 samples showed no uronic acid but when uronic acid was added to the gastric secretion and hydrolysed, it did appear on the chromatogram. A 1% solution of chondroitin sulphate, hydrolysed as above, showed the presence of uronic acid, thereby proving that our method of hydrolysis sets the uronic acid free but does not destroy it.

A COMPARISON OF THE EMETIC EFFECTS OF PROTOVERATRINE A, PROTOVERATRINE B AND SOME SYNTHETIC PROTOVERINE ACETATES. *By* **P.K. Gujral**. *Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.*

A comparative study of the emetic effects of the acetate esters of protoverine and protoveratrines A and B was undertaken.

The drugs were injected intravenously into the axillary vein of albino pigeons of either sex weighing between 400 and 600 *g*. Emesis usually resulted within 2 to 5 minutes after the injection.

Protoveratrine A was about 2·3 times as potent as protoveratrine B with regard to the emetic effects. The data obtained were analysed according to the method of Litchfield and Wilcoxon (1949) and are summarized below :

The emetic action of Protoveratrine A and Protoveratrine B in the pigeon

Drug	*No. of Expts.*	ED_{50} *µg/kg*	*Slope*
Protoveratrine A	48	2.5 (1.66 to 6.8)*	1.3 (1.08 to 1.56)*
Protoveratrine B	40	5.75 (4.8 to 6.8)*	1.34 (1.30 to 2.35)*

Protoverine tri-, penta-, isopenta- and hexa-acetates and protoverine acetonide di- and triacetates did not induce emesis in doses upto 6*mg/kg* although retching, opening of the beak, flapping of the wings, unsteady gait, blinking, shivering, increased salivation were observed as seen with smaller subemetic doses of protoveratrines A or B.

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ANTHELMINTIC STUDIES ON ZANTHOXYLUM ALATUM ROXB. AGAINST ASCARIDS**. *By* **Narinder Singh**. *J.S.A. Pharmacology, Antibiotic Project Unit, Virbhadra (Rishikesh).*

In Ayurvedic Medicine, fruits of *Zanthoxylum alatum* Roxb. have been mentioned to possess wormicidal activity. However, no scientific screening work has been reported so far.

The present study was undertaken to screen (1) ether extract (EE) (thick greenish yellow saponifiable oil with disagreeable smell and slightly tingline taste), (2) hydrodistillate (HD) from uncrushed fruits of *Z. alatum* (unsaponifiable thin oil with strong aromatic agreeable odour

*Figures in parentheses refer to the 19/20 confidence limits.
**Work conducted under facilities available in the pharmacological lab. of Mathura Vetrenary. College.

and markedly tingline taste), (3) hydrodistillate (HD) prepared by passing steam through EE. Instillation of two drops of extracts into the rabbit conjuctival sac led to marked irritation in the case of HD but hardly any in the case of EE. Of 1 *ml* of emulsion of each of EE and HD with water (1:10 dilution) were sprayed on 2 separate batches of 20 earthworms each. EE reduced the motility of the worms within 5 to 9 *min.* and killed them within 1.5 to 2 hr, whereas HD produced the same effects in 1.5 to 2 *min.* and 3 to 5 *min.* respectively. Different concentrations of HD in normal saline *in vitro* had paralytic to fatal effect on motility of ascarids (*A. galli*). *In vivo* HD (0.1 *ml/kg*) had marked ascaricidal activity against *A. lumbericoides* (pig), *A. vitulorum* (buffalo and cow), *A. galli* (poultry), but did not show any ascarifugal activity. Its effect on eggs obtained from females passed out in faeces of treated and control animals, on culturing, indicated its not interfering with fertility of worms. Administration of 0.1 *ml/kg* (1:10 dilution) to anaesthetised dogs caused transient fall in blood pressure which was neither blocked by atropine nor by mepyramine. Transient hypotension observed may be due to the direct effects of HD on blood vessels as studied by microcirculation experiments. Therapeutic and maximally tolerated dose orally showed no toxic effect on cardiovascular and respiratory systems. HD had little effect on skeletal muscle but produced marked relaxation of smooth muscle. Its relaxing effect on isolated intestine was not blocked by tolazoline. The intestine could be restored to normal activity by washing. $BaCl_2$ effectively antagonised the relaxation. This indicated that there was no structural or functional damage to intestinal musculature. Finally, the therapeutic index of HD (1:10) suggested that the drug could be used with reasonable safety as an anthelmintic. Relaxing property of HD warrants the use of postpurgative to expel paralysed worms.

RELEASE OF ACTIVE SUBSTANCES BY CHOLERA TOXIN. *By* **M.B. Bhide, V.A. Aroskar and N.K. Dutta**. *Haffkine Institute, Bombay.*

The exact mechanism(s) responsible for the production of diarrhoea in cholera is ill-understood. One of the favoured views is that there is altered permeability in the vessels of the villi. Histamine, 5-hydroxytryptamine and bradykinin are some of the agents which alter permeability. Panse and Dutta had shown that histamine was released in blood in choleraic animals. The study was extended to study the roles of the remaining two.

Infant rabbits 10 days old were infected by the method of Dutta and Habbu, and 5HT in blood was estimated by the method of Weissback and bradykinin by the partial modification of the method of Ferdos and Miwa. Rats were injected intradermally with syncase cholera toxin and 5HT from the skin was estimated by method of Udenfriend.

From the table it will be seen that 5HT and bradykinin were released in the blood in choleraic animals. The two agents in addition to histamine may be responsible in increasing capillary permeability, and helping in formation of diarrhoeal fluid.

Concentration of 5HT and Bradykinin

S. No.	*Species*	*Tissues*	*Treatment*	*Value 5HT in mcg/ml. or g.*	*t found out, p=.05 t (from table =2.3)*
1	Rat (6)	Skin	Salire Toxin	3.09±0.05 4.12±0.1	4.3
2	Rabbit (6)	Blood	Normal Infected	3.4±0.22 6.9±0.69	23.46
				Bradykinin in *ng/ml*	
3	Rabbit (6)	Blood	Normal Infected	100±5.7 15±1.7	14.16

NEURO-MUSCULAR BLOCKADE WITH ADRENERGIC BLOCKING AGENTS. *By* **V.K. Patel, M.N. Jindal, V.V. Kelkar and R.B. Doctor.** *Department of Pharmacology, B.J. Medical College, Ahmedabad.*

Both alpha and beta adrenergic blocking drugs in comparatively moderate doses have shown curare-like activity in both *in vitro* and *in vivo* skeletal muscle nerve preparations. This conclusion is based on the observation that blockade is relatively prompt to appear and disappear, is dose dependent, antagonised by neostigmine and potassium and augmented by tubocurarine and calcium. The direct contraction of the muscle is not affected. Generally speaking the beta blockers were found to be more active than alpha blockers. However, both these were less potent than *d*-tubocurarine. The block produced by these agents does not appear to be due to the local anaesthetic activity possessed by some of these agents. The bock produced by alpha blockers was antagonised by beta blockers and vice versa. The most potent alpha and beta blocking agents (yohimbine and propranalol) were also the most potent neuro-muscular blocking agents in respective groups, but such a relationship could not be demonstrated for other agents.

EFFECTS OF SOME DRUGS ON ELECTRICALLY STIMULATED ISOLATED, INNERVATED PREPARATION OF URINARY BLADDER OF RAT. *By* **A.S. Dhattiwala, V.V. Kelkar and M.N. Jindal.** *Department of Pharmacology, B.J. Medical College, Ahmedabad.*

In the present work, the effect of agents known to reduce Ach output from pre-ganglionic fibres and skeletal muscle nerves was ascertained on rat isolated urinary bladder (1), stimulated indirectly through the periureteral nerves. Hemicholinium-3 (100-300 *mg/ml*) and WIN 4981 (100-200 *mg/ml*) produced a gradual blockade of indirectly induced contractions in 1 to 2 hrs. Methylpentynol (100-200 *mg/ml*), strychnine (60-90 *mg/ml*) and chloral hydrate (6-10 *mg/ml*) also produced a variable degree of blockade in about an hour which depended upon concentration. TEA (50-100 *mg/ml*) augmented the responses in the initial period, producing a minor blockade in the latter phase. Morphine (10-20 *mg/ml*) also produced a minor blockade of indirect contractions. Paraldehyde (0.002-0.004 *ml/ml*) produced a quick onset

of block; the blockade was considerable in higher concentrations. Effect of methylpentynol, strychnine and chloral hydrate was partly reversible on repeated washings while effect of HC-3 or WIN 4981 was not reversible on washing. Effect of paraldehyde, however, was transient.

Choline chloride partly reversed the effect of paraldehyde and HC-3. Effect of other agents was not affected by choline. In concentrations used, none of the agents significantly affected the dose-response curves for Ach when maximal blockade was established. It is concluded that the blocking effect of these agents is mainly, though not exclusively, exerted by a reduced Ach output/release.

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STERILITY AND INFERTILITY IN RELATION TO HISTAMINE RELEASE FROM ENDOMETRIUM. *By* **S.S. Gupta, B. Gulati and Nishat Alvi**. *Department of Pharmacology and Obstetrics and Gynaecology, Gandhi Medical College, Bhopal.*

Histamine content of the endometrium obtained after curettage from women manifesting primary sterility in comparison to normal women was determined after extraction with trichloroacetic acid as per method of Paratt and West (1957). The average histamine content in sterile women during proliferative and secretory phases respectively was found to be 2.57 and 2.48 as compared to 4.73 and 6.65 in normal women. Release of histamine from the endometrium of sterile and normal women was also investigated by incubating about 100 *mg.* of the chopped tissue in phosphate buffer together with histamine releasers like compound 48/80 and dextran for 40 min. at 30° in a thermostatic shaker as per technique of Mongar and Schild (1957). The average percentage release of histamine from endometrium of sterile women on incubation with compound 48/80 (0.2×10^{-3}) and dextran (0.2×10^{-4}) was 21.9 and 7.74 respectively as compared to 46.41 and 13.9 in normal women. The defective release of histamine from the endometrium of sterile women has been postulated to be responsible for ineffective implantation of the ovum or desidum formation.

EFFECT OF A PLANT SAPONIN ON HISTAMINE RELEASE IN RELATION TO THEIR ANTI-CHOLINESTERASE ACTIVITY. *By* **Paresh R. Modh and S.S. Gupta**. *Department of Pharmacology, Gandhi Medical College, Bhopal.*

Saponin of *Clerodendron serratum* inhibited the serum cholinesterase activity estimated as per method of Rappaport *et al.* (1959) which is based on the colorimetric measurement of decolourisation of *m*-nitrophenol by the acid liberated during the action of cholinesterase on acetylcholine. The average pseudo-cholinesterase activity of 45.25 ± 2.5 unit was found to decrease to about 50% after intraperitonial administration of 0.3 *mg/kg* of saponin of *C. serratum*. The effect was similar to that observed after 0.04*mg/kg* of physostigmine in rabbit. In *in vitro* studies, the saponin in graded concentrations inhibited the cholinesterase activity of rabbit

serum in proportion to the increasing concentrations, and the inhibition in cholinesterase activity to the extent of about 50% was observed after 2×10^{-5} and 10^{-6} concentrations of *C. serratum* and physostigmine respectively. The anti-cholinesterase activity of saponin was also confirmed on acetylcholine responses on guinea-pig tracheal chain preparation, rat isolated ileum and frog rectus muscle. Incubation of chopped guinea-pig lung tissues with 4×10^{-4} and 10^{-5} concentrations of *C. serratum* saponin in buffered Tyrode solutions at 3700°C. for 40 minutes, caused release of $21.20\pm9.5\%$ of histamine in comparison to $23.0\pm0.59\%$ release caused by 4×10^{-4} concentration of physostigmine. The disruption of mast cells in the rat mesentery was also observed in the above concentrations of *C. serratum* but the higher concentration 10^{-3} was found to inhibit the disruption of mast cells.

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EFFECT OF BRAIN LESIONS ON SEMEN IN MONKEYS. *By* **G.S. Chhina, H.K. Kang and B.K. Anand.** *Department of Physiology, A.I.I.M. Sciences, New Delhi.*

In Rhesus monkeys semen was obtained by Electro-ejaculation using mono-phasic AC current pulses at a frequency etween 10 and *b* 20 per second, duration of 25-50 milli-seconds and varying from 20 to 40 volts. The electrodes were directly applied on the surface of the organ. The ejaculate was studied for total sperm count, motility, coagulability, liquefaction and fructolysis in 10 animals, 2 to 3 times both before and after brain lesions. The ejaculates were obtained on different days and the magnitude of the stimulation required was noted in addition to the study of other characteristics of the semen. Lesions in these animals were located in anterior amygdala (3), Pre-motor cortex (1), Septum (2) and Cingulate (2). Two of the monkeys were not operated and were studied at about the same time as the operated animals.

The lesions of amygdala and Septum showed an increase in the threshold of stimulation for ejaculation and required higher voltages and longer stimulation time. The lesions of the cingulate produced a decrease in senstivity and thus required shorter duration of stimulation and lower voltage for eliciting ejaculatory response. The animals with lesions of Pre-motor cortex and unoperated controls showed no significant changes in the thresholds of stimulation for obtaining ejaculatory responses.

The lesions of the amygdala in addition showed reduced coagulability in 2 out of the 3 animals. In one of these there was complete absence of coagulation which occurred more or less immediately after ejaculation before the lesions. There was also increased fructolysis per million sperms per hour and drop in the total number of sperms per unit weight of the ejaculate. The lesions of septum and cingulate produced only minimal changes in the semen.

EFFECT OF PROTEIN MAL-NUTRITION ON EMG, EKG AND EEG. *By* **G.S. Chhina, G.J. Jha and M.G. Deo**. *Department of Physiology, A.I.I.M. Sciences, New Delhi.*

Rhesus monkeys were maintained on low (10 monkeys) as well as high (5 monkeys) protein diet by tube feeding with a diet mixture prepared in the Laboratory. Each monkey received 100 calories per day per *kg* body weight. EMG, EKG and EEG were recorded in each animal before putting them on the diet schedule and subsequently at intervals of 7 weeks. EMG was recorded with concentric needle electrodes from the calf and thigh muscles, EKG with three limb leads and EEG with Bipolar scalp electrodes. In 5 monkeys on low protein diet EMG showed reduction in voltage and absence of normal interference reaction. Two of these showed an increase in the insertion activity and fibrillation potentials after about 7 weeks' ingestion of low protein diet. These changes, however, gradually disappeared in 3 monkeys which were fed high protein diet after a period of 7 weeks on low protein. In one of these monkeys feeding of high protein diet was unable to reverse the changes.

The EKG changes consisted of a drop in the voltage of R-wave and prominent S-wave in three out of the 5 monkeys which had shown changes in EMG. These changes however could be reversed in one animal after feeding high protein diet. The other two showed only a tendency towards a very slow recovery.

In two monkeys showing changes in EMG after low protein diet a generalised slowing in EEG was noticed. In the rest of the monkeys on low protein diet there appeared to be an increase in the faster frequencies in the basal EEG records.

The monkeys on the high protein diet showed no changes in the EMG, EKG or EEG.

REVERSAL OF BETA ADRENERGIC RECEPTOR BLOCKADE AND ITS PROBABLE MECHANISM. *By* **M.V. Natu, Deepak Bose, I.S. Gandhi and C.B. Seth.** *Department of Pharmacology, M.G.M. Medical College, Indore.*

The beta adrenergic blockade induced by propranolol is known to be reversed by methylamphetamine. The possible mechanism of the reversal was studied on the carotid blood pressure of anaesthetised mongrel dogs. When the responses of isoprenaline were completely blocked by propranolol, D-INPEA or MJ 1999, they could be reproduced by methylamphetamine, but when the beta receptor blockade was produced only partially, methylamphetamine not only caused reversal of blockade, but the recovered isoprenaline responses were potentiated. Further methylamphetamine potentiated the responses of adrenaline, noradrenaline and isoprenaline while those of histamine and acetylcholine remained unaltered. Similarly other agents like cocaine, tranylcypromine which also potentiated the catecholamine responses were also found to cause the deblockade of β-receptor blockade. Another observation was that when β-receptor blockade was induced after prior potentiation of catecholamine responses, methylamphetamine could not reverse the blockade. The above findings are suggestive of a potentiation of isoprenaline responses by methylamphetamine, which may be the cause of reversal of beta adrenergic receptor blockade.

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AN IMPROVISED TECHNIQUE FOR THE MEASUREMENT OF INFLUENCE OF DRUGS ON THE SPONTANEOUS MOTILITY OF RATS. *By* **S.K. Sharma* and B.R. Madan****.

An improvised technique for the evaluation of the effect of drugs on the voluntary activity s described. The modification is of the technique of Vad *et al.* (1963) but with the additional advantage of imparting the quantitative idea of drug action which the former lacked.

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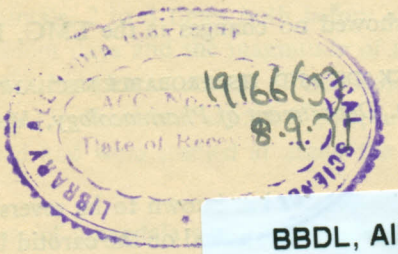

*Department of Pharmacology, Jawahar Lal Nehru Medical College, Ajmer.
**Department of Pharmacology, S.P. Medical College, Bikaner.