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ABSTRACTS

CANNABINOL AS A GENERAL ANAESTHETIC IN DOGS. By Narinder Singh Faculty of Agriculture, R.S.N. Degree College, Dhampur U.P.

In this present paper the work is recorded on the cannabinoil, isolated in the alkali-insoluble fraction vide method by Mukhopadya *et al* (1943) in new colorimetric test; which is based on the hypothesis that all the pharmacologically active constituents are alkali-soluble phenols and that cannabinoil, one of the important members of this group is alkali insoluble in dilute alkalies.

10 Gm. of the isolated cannabinoil of the alkali-insoluble fraction of the *Cannabis Indica* resin, was dissolved in 90% alcohol 190 cc to obtain the dilution 1 in 20. To this was added equal amount of pyrogen free distilled water at the time of use to have the final dilution 1 in 40.

30 dogs (males & females) weighing from 10 lbs to 20 lbs. were selected and were kept under observation for twenty-four hours. Each dog was fasted overnight before that would go under the anaesthetic effect. The dog was held lying and the final dilution 1 in 40 was injected into the left recurrent tarsal vein, at the rate of 1.5 to 2 ml per minute to produce the deep anaesthesia (The interval between the disappearance and reappearance of the Pedal reflex). The opposite hind limb was selected to test the pedal reflex. As soon as the neck and body relaxed a little, the muzzle was removed and the jaws kept open. The tongue was pulled out and kept extended to one side to ensure an unobstructed breathing. No intra-tracheal intubation was adopted for this purpose.

It was observed that 20 mgs of the drug per lbs of body weight was found sufficient to produce the deep anaesthesia from 132 to 216 mts. with down time 256 to 362 mts. and return to normal time 646 to 828 mts., when its final dilution 1 in 40 was injected at the rate of 1.5 to 2 ml per mt. At the same time Minimal Lethal Dose is double the anaesthetic dose. As an isolated Cannabinoil of the alkali-insoluble fraction has shown the same anaesthetic effect as the resin of *Cannabis Indica* in my previous experiment, so it is clear that Cannabinoil is an active principle of *Cannabis Indica*.

It was observed that the drug was well tolerated even by the emaciated dogs suffering from hepatitis. Though the effect shown by them was more which might have been due to the delayed excretion of the drug.

* *Duration of Anaesthesia*—The interval between the disappearance and reappearance of Pedal Reflex.
Down Time—From onset of Anaesthesia until dog stood.
Return to normal time—From onset of anaesthesia until the dog could climb stairs without ataxia.

The skeletal muscle tone rapidly disappeared leaving the experimental animal completely flaccid. The other reflexes (palpebral and corneal) along with pedal reflex were also found completely depressed.

Out of the thirty cases only dog one died, as he was suffering from pyelonephritis which was confirmed on post mortem.

The respiration rate was found much decreased, though it was quite deep and regular. No salivation and vomiting was observed. Moreover it was also observed that the control group animals receiving the same strength of alcoholic solution alone I/v, did not show any anaesthetic effect, instead there was imbalance and ataxia.

PSYCHOACTIVE AGENTS AND HANDWRITING By **B.N. Dhawan, S.K. Bapat and V.C. Saxena.** *Department of Pharmacology, M.L.N. Medical College, Allahabad*

Handwriting is a reflex acquired fairly early in life and having a cortical integration. Four psychoactive agents—caffeine (300 mg), chlorpromazine (50 mg), methamphetamine (5 mg) and phenobarbitone (60 mg)—were investigated for effects on handwriting in medical students. Glucose was used as placebo. The students copied a paragraph containing certain key words—immediately before and after 30 and 60 minutes medication. The parameters employed included (i) number of words in the first two lines (N), (ii) average length of 5 key words (L), (iii) average breadth of 5 key words (X), (iv) the average upward projection of letters in key words (U), (v) the maximum upward projection of letters in these words (Max. U), (vi) average downward projection of letters in these words (D) and (vii) time taken to write the passage (T). T progressively decreased in the placebo group. The decrease was significantly more after methamphetamine treatment. Other agents produced insignificant effects. Chlorpromazine increased U. and Max U. Phenobarbitone increased L and to a lesser degree U. Methamphetamine decreased Max. U, while caffeine had no effect on any of the parameters.

As is evident, although several agents produced effects, it is not possible to differentiate various groups of drugs on the basis of their selective effect on certain parameters of handwriting. Only gross effects like central stimulation or depression can be detected on the basis of these changes. Legge *et al* (1964) using similar criteria found significant changes with non-anaesthetic doses of nitrous oxide particularly on X. None of the drugs tested in the present investigation had any effect on X.

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ANTICONVULSANT ACTIVITY OF ANTI-HISTAMINIC DRUGS. By **V.C. Saxena, S.K. Bapat and B.N. Dhawan*** *Department of Pharmacology, M.L.N. Medical College, Allahabad*

The most common side effect of antihistaminic drugs is sedation. Since many sedatives have anticonvulsant activity, 21 antihistaminic drugs were screened for anticonvulsant activity in albino rats. The drugs were tested by the supramaximal electroshock seizure pattern test (SMES, 150 ma for 0.4 sec., corneal electrodes) and the metrazol seizure threshold test (MST 80 mg/kg). The agents found effective were submitted to neuro-toxicity tests to determine the protective index (P.I.), and compared with phenobarbitone and diphenylhydantoin. None of the antihistaminic drugs were effective in MST and a few of them increased metrazol toxicity. 16 of the drugs tested were active in SMES. 6 of these (triprolidine, buclizine, meclozine, promethazine, hydroxyzine and cyproheptadine in decreasing order of potency) had a higher protective index than the standard drugs. Two of these (meclozine and cyproheptadine), however, increased metrazol toxicity. These effects of the drug could not be correlated with their antihistaminic potency.

In general the ethanolamines are more active than the alkylamines. In the piperazines, substitution at the terminal methyl group increases the activity. Furthermore, compounds having nitrogen in a closed ring structure are more active than those having it in an open chain.

The P.I. of triprolidine, the most active agent was 22.07 (cf. diphenylhydantoin 6.69 and phenobarbitone 4.45 respectively). It had a slower onset of action than diphenylhydantoin but the duration of action and the time of peak effect were almost the same. A clinical trial of this drug in grand mal epilepsy is warranted on the basis of the results obtained in the present investigation.

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SINGLE PENTYLENETETRAZOL TEST FOR RAPID SCREENING OF ANTIEPILEPTIC AGENTS*. By **A. Ahmad and B.N. Dhawan.** *Division of Pharmacology, Central Drug Research Institute, Lucknow*

A large number of tests are available today for screening of potential anticonvulsant drugs. All of these tests, however, pick up either compounds with diphenylhydantoin type of activity or those with trimethadione type of activity. It would be ideal to have a single but simple test whereby both these types of activities could be detected, particularly for a routine screening of large number of compounds.

It is well known that when gradually increasing doses of pentylenetetrazol are given to mice, clonic convulsions appear followed by terminal tonic convulsions (including tonic extension of the hind limbs) and death. As reported earlier (1) pentylenetetrazol produces all the three phases of seizures in mice in a dose of 100 mg/kg. s.c. The effects of diphenylhydantoin, phenobarbitone and trimethadione on various components of pentylenetetrazol-induced seizures have been studied and compared to their effects with SMES and MST tests. Diphenylhydantoin

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was capable of blocking only the tonic extension (ED 50 12.0 mg/kg, oral) and had no effect on the clonic phase or lethality even in a dose of 100 mg/kg, oral. Phenobarbitone as well as trimethadione could block all the phases of pentylenetetrazol induced seizures. The oral ED 50 to block clonic, tonic and lethal seizures were calculated to be 569.8, 498.9 and 439.4 mg/kg, respectively, for trimethadione and 38.4, 20.7 and 26.8 mg/kg respectively for phenobarbitone.

A perusal of these data clearly indicate that it is possible to pick up both types of compounds with this single pentylenetetrazol test. A compound blocking only the tonic extensor component will have diphenylhydantion type of activity while a compound blocking all the phases may have a phenobarbitone or trimethadione type of activity. It has been possible in this laboratory to pick up a potential anticonvulsant (4-(m-trifluoro-methyl phenyl)-1-(3-amino-4-pyridyl) piperazine) with diphenylhydantion type of activity using this test (1).

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EFFECT OF A DIBENZOTHIAZEPINE NEUROLEPTIC ON SOMATIC REFLEXES*. By J.N. Sharma and R.C. Srimal. *Division of Pharmacology, Central Drug Research Institute, Lucknow.*

Effect of 2-chloro-11-(4'-methyl) piperazino-dibenzo (b, f) (1,4) thiazepine was studied on (a) the monosynaptic patellar reflex (PR) and its inhibition due to ipsilateral sciatic nerve stimulation. (b) on the polysynaptic facilitation and inhibition of PR by contralateral sciatic nerve stimulation and by the electrical stimulation of the facilitatory and inhibitory areas of the reticular formation and (c) the flexor reflexes: linguomandibular reflex and the tibialis anterior flexor reflex. The compound inhibited polysynaptic reflexes more than the monosynaptic. The facilitation as well as inhibition of the PR due to stimulation of brain stem reticular formation and contralateral sciatic stimulation was blocked by 1.0 mg/kg i.e. dose of the compound. This dose also caused 50% inhibition of the linguomandibular reflex but the tibialis anterior flexor reflex remained unaffected. Ipsilateral inhibition of PR was potentiated. The compound was found to have a preferential action at the brainstem reticular formation rather than on spinalcord

PHARMACOLOGICAL ACTIVITIES OF 3-AMINO-6-7-BENZQUINAZOLE-4-ONE: A NEW SYNTHETIC BENZQUINAZOLONE COMPOUND**. By J.N. Sharma and C.P. Prasad. *Division of Pharmacology, Central Drug Research Institute, Lucknow.*

During the screening of a series of benzquinazolone compounds prepared by the substitution of 6-7-benzquinazol-4-one, 3-amino-6-7-benzquinazol-4-one was found to possess significant central nervous system depressant activity. The LD50 in mice was 160 mg/kg intraperitoneally and 525 mg/kg orally. Progressively increasing doses produced loss of spontaneous motor

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activity (15 mg/kg), catatonia (40 mg/kg) and loss of righting reflex (140 mg/kg). IDPN induced abnormal behaviour was antagonized at 10 mg/kg dose and pentobarbitone induced narcosis was prolonged significantly at 15 mg/kg. 40 mg/kg of the drug produced 50% protection in the maximal electroshock seizure and metrazol seizure threshold tests. In rats trained for avoidance behaviour 20 mg/kg i.p. blocked and secondary conditioned response only. The effect of the compound was also investigated on spinal reflexes in cats and 1-3 mg/kg produced 80 to 100% blockade of crossed extensor reflex while 4 to 10 mg/kg produced 20-80% blockade of lingomandibular reflex. The compound produced a transient fall of blood pressure in cats and dogs. It resembles chlordazepoxide in its profile of activity and also in intensity and duration of various effects.

ANTI-INFLAMMATORY ACTIVITY OF AN AMINOPYRIDINE DERIVATIVE*. By R.C. Srimal and J.N. Sharma. *Division of Pharmacology, Central Drug Research Institute, Lucknow.*

Interesting central nervous system depressant properties were found in the preliminary pharmacological screening of a series of non- and disubstituted aminopyridines. One of the disubstituted aminopyridines, (compound No 64-92) was found to possess anti-pyretic and anti-inflammatory activities. It was, therefore, taken up for detailed investigations. The compound was administered orally (p.o.) or intraperitoneally (i.p.). The LD₅₀ of the compound in mice was 948.8 mg/kg p.o. and 228.8 mg/kg i.p. It inhibited the formaline induced arthritis by 41% at a dose of 30.0 mg/kg p.o. Carrageenin induced oedema was also inhibited significantly (p—0.01) at the dose of 45.0 mg/kg p.o. The compound was effective in inhibiting the formation of granulation tissue. Granuloma formation tested by the granuloma pouch method was inhibited (44%) by 60.0 mg/kg p.o. of the compound. Significant inhibition of the granuloma formation due to cotton pellet implantation was obtained by 30.0 mg/kg p.o. dose of the compound. It was also effective in antagonising the writhing syndrome in mice and its ED₅₀ was 40.0 mg/kg i.p. compared to 169.5 mg/kg i.p. of sapirin. The compound had no significant effect on the blood pressure level of anaesthetised cat upto a dose of 5.0 mg/kg i.v. The subacute toxicity study in rats for 3 months did not show any toxic effect.

RESPIRATORY STIMULANT ACTION OF PHENAQUINE**. By G.K. Patnaik, R.C. Srimal and B.N. Dhawan. *Division of Pharmacology, Central Drug Research Institute, Lucknow.*

In a study of the pharmacological actions of a series of N-substituted 2,3-polymethylenequinolines, one of the compound designated as Phenazine was found to produce marked respiratory stimulation.

The actions of Phenazine have been studied in greater detail in mice, cats, dogs and rabbits. It produced a marked stimulation of respiration in anaesthetized, decerebrate and normal animal when given in amounts much below the convulsant dose. This effect was generally accompanied by a rise of blood pressure and it was absent in deafferented animals. The res-

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piratory stimulation was also obtained by close intra-arterial injections of minute amounts (50-100 μg) to the carotid body. Intra-cerebroventricular administration had no effect. The respiratory stimulation is produced by an action on the carotid body chemoreceptors. The activity starts immediately and lasts for about two hours. Phenacaine could antagonise the respiratory depression produced by various barbiturates, morphine and chloralose. It also antagonized the pentobarbitone sleeping time in mice. It had no effect on the isolated guinea pig ileum and the phrenic nerve-diaphragm preparation of rat. The drug was also without any effect on the body temperature.

The LD 50 of nikethamide (275 mg/kg i.p.) and Phenacaine (275 mg/kg i.p. 375 mg/kg p.o.) in mice are about the same. Phenacaine, is, however, about ten times more potent than nikethamide as a respiratory stimulant and has approximately double the duration of action.

CENTRAL VASOMOTOR EFFECTS OF (—)N-(1-PHENYLETHYL) GUANIDINE*. By **S.K. Bapat, R.C. Srimal and B.N. Dhawan**. *Department of Pharmacology, M.L.N. Medical College, Allahabad and Central Drug Research Institute, Lucknow.*

(—) -N-(1-phenylethyl) guanidine, a new adrenergic neuron blocking agent, has been investigated for its effects on the reflex as well as direct excitability of the central vasomotor loci. Intracerebroventricular injection of 5 to 10 $\mu\text{g}/\text{kg}$ of this compound in dogs and cats produced no significant effect on the blood pressure level but it potentiated the carotid occlusion pressor response and response to anoxia. There was no change in the peripheral norepinephrine response or contraction of the nictitating membrane obtained by electrical stimulation of the preganglionic fibres. Intravenous injection of this dose of the compound had no effect on any of the responses. Similarly, intrathecal injection of the compound (10 $\mu\text{g}/\text{ml}$) potentiated the spinal compressional vasomotor responses. Injection of the compound (100 μg) into the subclavian artery also resulted in potentiation of the carotid occlusion response. The pressor to direct electrical stimulation of the medullary vasomotor centre was potentiated when it was applied either directly to the floor of the fourth ventricle (0.4 ml of 0.3% solution) or injected intracerebroventricularly (100-200 μg) in cat. All these effects were obtained within 15 minutes and they lasted 60 to 80 minutes. It is suggested that this adrenergic neuron blocking agent has a stimulant effect on the vasomotor centre in low doses, in addition to the peripheral blocking action on the adrenergic neurons.

FURTHER STUDIES OF THE MECHANISM OF VENTRICULAR FIBRILLATION UNDER HYPOTHERMIA. By **P.S. Sinha**. *Department of Pharmacology, Kasturba Medical College, Mangalore.*

The extensive study of the literature on hypothermia reveals that ventricular myocardial cells are not able to utilise the oxygen present efficiently under hypothermic critical temperature and thus suffers from tissue anoxia. And under anaerobic condition the heart utilises glycogen as energy for its activity and lack of energy increases myocardial irritability and favours ventri-

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cular fibrillation. Minz (1955) has shown that besides neurohumoral function, acetylcholine protects the cardiac tissue against anoxemia. In our earlier studies we have reported that eserine afforded complete protection against ventricular fibrillation under hypothermia in dogs.

In the present study an attempt has been made to find out the effects of hypothermia on the glycogen content, acetylcholine content of frog's heart and liver and on the blood glucose level.

The glycogen content of auricles and ventricle and liver at 30 C. were 3.21 *mcg/gm.* 2.16; 5.12 *mcg/gm.* 4.250 and 6.62 *mcg/gm.* 5.8 Lowering the body temperature to 20 C did not affect the glycogen content of auricles but the glycogen level was found to be reduced by 16.8% in ventricle and by 50% in liver.

The acetylcholine contents of frogs auricles, ventricle and liver estimated at 30 C were 3.33 *mcg/gm.* 0.51; 2.32 *mcg/gm.* 0.61 and 3.38 *mcg/gm.* 0.72. Under hypothermia (at 20 C) the acetylcholine content of the auricle and liver was not found to be altered. Whereas the acetylcholine content of the ventricle was found to be reduced from 2.32 *mcg/gm.* to 2.0 *mcg/gm.* The blood glucose level of frog was also determined at 30 C. and was found to be 25 *mg/100 ml.* On lowering the body temperature to 20 C. it was increased to 45 *mg/100 ml.*

The results of our studies on frogs demonstrate that :—

1. The incidence of ventricular fibrillation in the frogs heart was only 20 per cent.
2. The glycogen level was found to be reduced in the ventricles and in the liver under hypothermia. However no change in the glycogen content of the auricles could be detected under hypothermia.
3. The blood glucose level was found markedly increased in peripheral circulation under hypothermia.
4. However, hypothermia caused only insignificant lowering of acetyl choline content of ventricles.
5. The acetylcholine content of the auricles and liver were not affected under hypothermia.

INCORPORATION OF GLUCOSE 14-C INTO LIPID, RNA AND PROTEIN OF THE RAT UTERUS IN THE PRESENCE OF INTRAUTERINE FOREIGN BODY. By H.S. Yadav and K.R. Laumas. *Reproductive Biology Research Unit, All-India Institute of Medical Sciences, New Delhi.*

The effect of intrauterine foreign body (IUFB) on the bio-chemical response of the rat uterus to exogenous estrogen was investigated. Rats were inserted with a silk suture in one horn and bilaterally ovariectomised at the same time. Three weeks after insertion of silk suture and ovariectomy, a group of animals was given a 5 ug injection of estradiol-17B and

another groups was used as a control. In vitro incorporation of glucose-C14 into uterine lipids, RNA and protein was investigated. The results showed that there was an increased incorporation of glucose in the IUFB treated horn in the untreated group. In response to estrogen the IUFB treated horn showed a much higher incorporation compared to the control estrogenised uterus. The sensitivity of the rat uterus to exogenous estrogen in relation to the mode of action of IUFB would be discussed.

ROLE OF DEHYDROISOANDROSTERONE SULPHATE AND 16 α -HYDROXY DEHYDROISOANDROSTERONE IN THE BIOSYNTHESIS OF ESTROGENS IN PLACENTA. By **G.S. Koshti, P.K. Malkani and K.R. Laumas.** *Reproductive Biology Research Unit and the Department of Obst. and Gynaecology, All-India Institute of Medical Sciences, New Delhi.*

Previous investigations (presented at the 12th Annual Conference, Patna, Dec., 1966) from this laboratory have shown that 19-hydroxyandrost-4-ene-3,17-dione acts as an efficient precursor for the biosynthesis of estrogens in placenta. Furthermore, it was found that the rate of biosynthesis of estrogens from this precursor are decreased in cases of placenta from placenta insufficiency. It was further considered that investigations may be made to find out whether conjugated androgenic steroids and hydroxylated androgens would also act as efficient precursors for estrogens biosynthesis. Therefore, in vitro incubation with placental microsomes were carried out with 16 α -hydroxy dehydroisoandrosterone and dehydroisoandrosterone sulphate. The results showed that sulpho-conjugated DHIA was also an efficient precursor for estrogens biosynthesis in placenta. The investigations are being further extended to various other cellular fractions in placenta to test their suitability for carrying out aromatization reaction in placenta.

FERTILITY CONTROL IN THE MALE WITH A SILASTIC BLOCK OF VAS DEFERENS. By **J.P. Uniyal and K.R. Laumas.** *Reproductive Biology Research Unit, All-India Institute of Medical Sciences, New Delhi.*

Reversible blocking of vas deferens in rats was achieved with the help of a silicon polymer which was injected into the vas deferens. Silastic - a silicon polymer is liquid at room temperature and on injection into the vas deferens the silicon polymer produced a block. It was found that the sperms above the silastic block in the vas deferens were either absent or dead. On removal of the silastic, the block was removed and sperm passage could be restored. The silastic was thus found to be an effective blocking agent in experiments where it was inserted in both the vas deferens.

In experiments in which silastic was put in one vas deferens, the left testis, the vas deferens of which contained silastic block, was found to have atrophied with failure of spermatogenesis. On the other hand the right testis with no block in the vas deferens, had hypertrophied and the spermatogenesis in this testis appeared normal. The hypertrophy of the right testis was further confirmed by measurement of the seminiferous tubal diameter and the radius of intratubular cellular elements. These were found to be higher in the hypertrophied testis compared to normal testis and this was statistically significant.

The silastic provides a useful method for fertility control in the male and the method is reversible.

COMPARISON BETWEEN CERTAIN ANTITUSSIVE DRUGS WHEN INVESTIGATED IN THE CONSCIOUS RABBIT. By E.C. Savini. *Department of Pharmacology, Faculty of Medicine, Paris, France.*

In order to avoid any interference between the possible joined effects of antitussives and general anesthetics on the cough center, the assays should be always made on conscious animals. The animal of choice is the rabbit and the screening is concerned with the activity of antitussives on (I) respiratory centre, (II) cough center and (III) bronchial motility.

I—*The action on the respiratory center* has been registered by using a pneumograph consisting of a float-recorder, an electric air-valve and a transistor unit operated by the spontaneous respiration of the animal. A volumetric registration of the expiratory air at each cycle is possible and in addition the respiratory frequency may be integrated by using an electronic or an electro-mechanical rate-meter (1). The minute volume is diminished by morphine (reference substance), dimethoxanate, codeine and ethylmorphine injected I.V. Noscapine, pentoxyverine, dextromethorphan, sodium dibunate and pholcodine rather stimulate respiration, given by the same route.

II—*The inhibition of cough center* has been studied after inhalation by the animal of formaldehyde aerosol (2). The sensitivity of the rabbit to the irritant vapours is good, the animal constantly coughs during an experimental period of 6 to 8 weeks. The morphine was the most active substance followed in decreasing order by the other respiratory depressants (codeine, dimethoxanate and ethylmorphine). Less active were the antitussives which stimulate the respiratory center, i.e. pholcodine, pentoxyverine, dextromethorphan, noscapine and sodium dibunate, when injected S.C.

III—*The effect on bronchial motility* was tested by using the method of Konzett and Roessler modified by us in order to make it suitable for experiments in conscious animals. Indeed, two main conflicting requirements have to be taken into account : the animal has not to be anesthetized but it must be kept immobile during the experiment. In order to comply with these conditions, the animal has been injected I.V. a long with lasting motor end-plate blocking drug. As histamine discharge could produce bronchoconstriction, gallamine triiodide appeared to be the drug of choice. The already known bronchoconstrictor effects of morphine and codeine have been registered and their intensity and duration could be measured. Ethylmorphine produced bronchoconstriction as well at dosage-levels higher than those producing cough depression. The other antitussives did not produce any significant alteration in the bronchial tree volume. All these results have been compared to the effects produced by the two most important bronchoconstrictor biogenic amines : acetylcholine and histamine.

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FURTHER OBSERVATIONS ON THE ANTI-DIABETIC EFFECTS OF *TINOSPORA CARDIFOLIA*. By **S.S. Gupta**.
Department of Pharmacology, Gandhi Medical College, Bhopal.

The bitter principle isolated from *Tinospora cardifolia* in 50—100mg/kg I.M. doses was found to inhibit the hyperglycaemic response of 10 mg/kg doses of corticotrophin and somatotrophin in rabbits and rats. Inhibition of epinephrine induced hyperglycaemia in Belgian rabbits injected with the drug was also observed and confirmed in a cross over tests. Further, inhibitory effect of the drug on epinephrine induced glycogenolysis in liver slices incubated with the drug (5 10) in phosphate buffer was also observed in several sets of in-vitro experiments. Average percentage release of glucose per gramme of liver tissue after incubation with 4 ug/ml of epinephrine was 31.2, but this release was completely inhibited from the tissues which were preincubated with 4 mg/ml concentration of the bitter principle of *S. Cardiolia*. This inhibitory effect was more marked than that observed to occur with 0.4 unit/ml concentration of insulin. The glucose release was only 1.23 mg/Gm as compared to 1.54 mg/Gm with insulin whereas the control with adrenaline gave output of 1.82 mg./Gm. In another set of experiment in which glucose 4 mg/ml was added to the phosphate buffer, the glucose concentration was found to decrease ven below the original level in flasks containing the drug, indicating some uptake by the tissue in response to the drug. This was confirmed in another set of experiments on rat diaphragm preparation, but the glucose uptake was significantly less than that caused by 0.02 unit/ml of Insulin. Detailed studies on the effect of bitter principle on carbohydrate metabolism are in progress.

RELEASE OF ACETYLCHOLINE FROM PERFUSED CEREBROV L VENTRICLES IN CONSCIOUS DOGS. By **P.S.R.K. Haranath and H. Venkatakrisna Bhatt**. *Department of Pharmacology, Kurnool Medical College, Kurnool (A.P.).*

Cerebral ventricles were perfused in conscious dogs from lateral ventricle to a cannula placed high in the cervical sub-arachnoid space according to the method described by Haranath (1968 *ibid* P. . .). Artificial cerebrospinal fluid was perfused at the rate of 0.1 ml/min and the half hourly effluent was assayed for acetylcholine-like activity on eserized frog rectus muscle. The samples showed in many instances acetylcholine-like activity and the output of acetylcholine ranged up to to 20 ng/min and usually about 10 ng/min.

AN INDIGENOUS DRUG WHICH PROMOTES CLOTTING. By **P.S.R.K. Haranath, M.K. Ramakrishna Rao and K. Sunanda Bai**. *Department of Pharmacology, Kurnool Medical College, Kurnool (A.P.).*

Powdered leaf of indigenous drugs *Actinopteris fanis* and *Allamania nodiflora* were given orally in doses of 300-600 mg/day to dogs. They were shown to antagonize the anti-coagulant action induced by Tromexan 150 mg/day given orally as determined by the prothrombin time.

A METHOD FOR PERFUSION OF CEREBRAL REUNATES By **P.S.R.K. Haranath**, *Department of Pharmacology, Kurnool Medical College, Kurnool (A.P.)*.

The lateral ventricle is cannulated in dogs under aseptic conditions under pentobarbitone anaesthesia according to the method described by Feldberg and Sherwood (1953). At the same time the laminae of either lower cervical or upper lumbar vertebrae were removed and a polythene tube is pushed high into the cervical sub-arachnoid space. After recovery the ventricles can be perfused from the lateral ventricle and the outflow can be collected from the cervical sub-arachnoid cannula.

EFFECTS OF PROCAINE PERFUSED INTO CEREBRAL VENTRICLES IN CONSCIOUS DOGS* By **P.S.R.K. Haranath and H. Venkatakrishna Bhatt**, *Department of Pharmacology, Kurnool Medical College, Kurnool (A.P.)*.

The cerebral ventricles were perfused in conscious dogs according to the method described by Haranath (1968 *ibid* P.....).

When procaine 1% was perfused for one hour at a rate 0.12 ml/min into cerebral ventricles and led out of the cervical subarachnoid space, it produced slowing and increase in amplitude of respirations, loss of consciousness, paresis, defaecation, nystagmus and vomiting.

When 2% was perfused, it also produced slowing and increase in the amplitude of respirations and loss of consciousness, paralysis and defaecation.

In dogs under chloralose anaesthesia, the cranial subarachnoid space around the medulla was perfused with procaine. Its entry into the 4th ventricle was prevented by a counter-perfusion with artificial cerebrospinal fluid from lateral ventricle. Under these conditions only respiratory depression was evident. Therefore the site of action for increase in amplitude of respiration is in the 4th ventricle.

ACTIONS OF CINCHOCAINE AND LIDOCAINE INJECTED INTO CEREBRAL VENTRICLES. By **P.S.R.K. Haranath and H. Venkatakrishna Bhatt**, *Department of Pharmacology, Kurnool Medical College, Kurnool (A.P.)*.

Cinchocaine 0.5 to 2 m and lidocaine 10 to 40 mg were injected into the lateral cerebral ventricles of conscious dogs. They produced paresis of limbs, nystagmus, retching, vomiting, defaecation and increase in depth of respirations. The blood pressure was recorded according to the method described by Haranath, *et al* (1967) and it rose after the injection of the drug. Lidocaine produced unconsciousness.

When perfused into the cerebral ventricles according to the method described by Bhattacharya and Feldberg (1958) in dogs under chloralose anaesthesia, cinchocaine 1:1500 or 1:200 produced slow and deep respirations and a rise of blood pressure. Later the respirations were

*The work was carried out with a grant-in-aid from ICMR, New Delhi.

depressed and finally stopped. Lidocaine O. 5 to 2% produced rise of blood pressure and increase in the rate and amplitude of respirations. Later the respiratory amplitude is depressed.

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EOSINOPHIL RHYTHM IN SOME NORMAL MEDICAL STUDENTS By S. Parvathi Devi and P. Advaitam
Department of Physiology, Madurai Medical College, Madurai.

Changes in haematological components have been reported as varying during the 24 hours' day—night cycles. A circadian periodicity in adrenocortical activity seems to have been established. A diurnal rhythm in the excretion of urinary ketosteroids in young men has been observed. Social habit has been considered as important in determining the timing of the eosinophil rhythm since in groups of individuals long habituated to early rising, the fall of eosinophil count starts somewhat earlier in the morning than in those accustomed to rising later. This investigation focusses on study of eosinophilic rhythm in some of our otherwise normal medical students, bearing in mind that these findings have to be correlated against the background of adrenocortical activity in the subject.

Twenty students conforming to certain desired standards were chosen—ten being drawn from among hostel residents and 10 from day students. Five were men and five were women in each group. Eosinophil counts were made twice daily at 8-00 A.M. and 4-00 P.M. respectively. Dunger's fluid was used for dilution and Fuchs—Rosenthal chamber for counting. Counts were made for 15 days on each individual. The values have been tabulated, analysed and discussed. A general feature was that in both groups of men students—hostel residents and day students—the eosinophil counts are conspicuously reduced relatively in the evenings—(the 4 P.M. values being lower than the 8 P.M. ones). It is needless to point out that all the counts fall more or less within the normal range of absolute eosinophil count values (70—450 cells c.mm.). This relative reduction in absolute eosinophil values in the evenings is significantly greater in the hostellers than in the day scholars. Amongst women students, the hostel students depict a relative and significant reduction in eosinophil values in the evenings, while the day students are a contrast in depicting a distinct increase in their eosinophil values in the evenings.

In students, adrenocortical activity is modulated through the day as a possible result of varying inputs into the hypothalamus—such inputs being derived from variable stressors drawn from environmental factors. Lower evening values in both groups of men students can possibly be due to the stress axis mediation at a juncture nearer University examinations and the associated fears. Even so, day-scholars seem not apparently “stressed” to the same extent as evidenced from their higher evening eosinophil values as compared with their Hostel friends.

Between the two groups of women students, the day-scholars have distinctly elevated eosinophil values. This observation may be explained on the fact that day scholars in their environment perhaps preserve a more confident attitude towards examinations and consequently stressor effects may be relatively less.

THE EFFECT OF CIBA GO *1002 ON CATECHOLAMINE STORES. By C.L. Kaul and R.S. Grewal. CIBA Research Centre, Goregaon East, Bombay.

An investigation has been made of the effect of Go. 1002 on the catecholamine stores in rat heart, brain, adrenals and cat heart. Three hours after treatment with Go. 1002(2.5 and 5mg/kg i. p.) a highly significant fall in catecholamine content of the heart was observed (40% and 70% respectively). The effect was more pronounced at six hours (81%) after the higher dose. Normal values were obtained by 12 hours. Comparison of the effect of Go. 1002 with Guanethidine (5mg/kg i. p.) at 6 hours showed that Guanethidine was slightly less potent as a catecholamine depleter in the rat than Go. 1002.

A significant lowering of brain catecholamine was observed (75%) in rats pretreated with Go. 1002 (10mg/kg i. p.). In the case of adrenals however, a higher dose of 30 mg/kg was necessary to produce significant reduction in the catecholamine content.

In cats treated with 5, 10 and 20 mg/kg of Go. 1002, a significant effect was observed only with 10 and 20 mg/kg. Guanethidine was very effective in lowering the catecholamine content of the cat heart. Thus, with 5mg/kg there was depletion of 60 to 80 from 3 to 12 hours Reserpine was even more potent in cats where 1mg/kg, 16 hours after treatment, resulted in 97% depletion of catecholamine of the cat heart. Go. 1002 therefore seems to be less potent in cats than reserpine or Guanethidine. Further there seems to be some difference in the action of Go. 1002 as a catecholamine depleter between the two species studied.

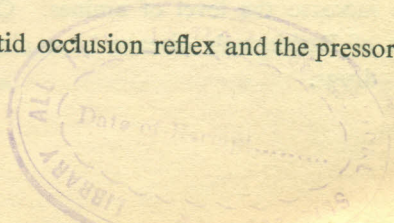
Go. 1002 was shown to interfere with uptake of infused noradrenaline in the rat heart.

PHARMACOLOGICAL PROPERTIES OF CIBA GO .1002. By R.S. Grewal, C.L. Kaul and J. David. CIBA Research Centre Goregaon East, Bombay.

Go. 1002 is a potent orally active hypotensive compound. It produces a prolonged fall of blood pressure in anaesthetised dogs and cats at doses of 0.25 mg/kg I.V. It produces adrenaline reversal without markedly affecting noradrenaline responses. It blocks the pressor effects of amphetamine and tyramine. It produces diminution of peripheral resistance by causing vasodilatation. Its vasodilator action is seen in coronary vessels as well.

This compound produces marked antihypertensive effect in renal hypertensive rats at doses of 5-10 mg/kg P.O. twice a day.

It blocks centrally mediated reflexes like carotid occlusion reflex and the pressor response seen after stimulation of central end of vagus.



The vasopressor response elicited by stimulation of posterior hypothalamus and reticular formation is markedly reduced by this compound.

Go. 1002 produces depletion of catecholamines from the heart, brain and adrenals.

Go. 1002 has central sedative tranquilising properties and shows potent anti-aggressive activity in rhesus monkeys.

EFFECT OF SOME CENTRAL STIMULANTS IN MICE TREATED WITH P-CHLOROPHENYLALANINE. By **J.S. Bapna, P.C. Dandiya and S.C. Chaturvedi.** *Department of Pharmacology, S.M.S. Medical College, Jaipur.*

LSD 25 is well known for its antagonism of 5-Hydroxytryptamine (5-HT) on peripheral organs. Its capacity to reverse the reserpine or 5-HT induced sedation has led many investigators to think that its central action might also be dependent on its antiserotonin effect. To investigate this possibility p-chlorophenylalanine, which selectively blocks the synthesis of 5-HT at tryptophanhydroxylase step has been employed. The dosage schedule which is known to deplete brain 5HT by more than 90% could not modify its effect. The findings of this experiment do not support the possibility that action of LSD 25 in brain is due to the antagonism of serotonin. For comparison, mescaline and d-amphetamine which are well known for their central stimulant action have also been employed. The significance of these findings have been discussed.

THE ANTIPARKINSONIAN ACTIVITY OF MONOAMINE OXIDES INHIBITORS AND OTHER AGENTS IN RATS AND MICE. By **P.C. Dandiya, L.P. Bhargava and J.S. Bapna.** *Department of Pharmacology, S.M.S. Medical College, Jaipur.*

Parkinson's syndrome is believed to be due to the disorder of basal ganglia of the brain. The exact nature of biochemical lesion responsible for the development of this syndrome is far from fully understood. The challenging concept of Barbeau (1962), that there exists an equilibrium in the brain between dopamine and acetylcholine; and serotonin and histamine, the disturbance of which may cause symptoms of extrapyramidal syndrome has initiated a considerable study in this direction. Monoamine oxidase inhibitors are well known for their ability to increase the level of brain amines like serotonin, noradrenaline and dopamine. In this study the monoamine oxidase inhibitor offered protection against drug induced parkinson like syndrome, suggesting the possibility that the action of these drugs is dependent upon their ability to increase the level of amines. Other agents which are commonly employed for the treatment of Parkinson's disease have also been screened for comparison, besides some unclassified drugs.

PHARMACOLOGICAL EVALUATION OF A GLUCOSIDE OBTAINED FROM THE PLANT VITIS QUADRANGULAR.
By V.S. Subbu. Department of Pharmacology, Medical College, Guntur.

The plant *Vitis Quadrangularis* (VQ) grows in a wild state in many parts of Southern India. The juice obtained from the succulent stem of VQ is used as a medicament in Ayurvedic practice. An active principle in the form of a glucoside was isolated from the dried stem of VQ. The glucoside(G) is freely soluble in water and when applied over the skin, mucous membrane or the cornea did not produce any local effects in a concentration of upto 5%. Oral administration of G in doses of 1 mg/kg body weight daily to mice, rats and guinea pigs, for a period of 10 days did not elicit any toxic effects when observed over a period of six weeks. When G was administered intravenously the animals developed convulsions and died in five minutes. The MLD works out to 15.5 mg/kg body weight, in guinea pigs. G when administered intravenously to anaesthetised cats and dogs produced a proportionate fall in blood pressure depending on the dose. With a dose of 30 mg/kg. body weight the blood pressure dropped to zero. Respiration was not markedly affected and the slight change was due to the fall in blood pressure. The animal could be revived with supportive measures like artificial respiration and external cardiac massage, if intituted within one or two minutes. In a few cases (2% of the animals) there was spontaneous recovery of blood pressure to original level. The fall in blood pressure was observed in vagotomised, atropinised and spinal animals. Perfusion of G in a dilution of 1 mg/ml. through the femoral artery with the outflow recorded from the femoral vein, did not reveal any change in the peripheral vascular system. With a dose of 600 mg/ml. G produced arrest of the isolated right atrial preparation. The drug is surface acting since the effect could be washed even after exposing the atrial tissue for three hours. The negative chronotropic effect produced by G was specific since the atrial tissue responded to small doses of isoprenaline and histamine during the negative chronotropic phase.

The negative chronotropic effect produced by G could be surmounted with 7.5 M of Calcium in a 50 ml both. G produces a fall in blood pressure by its negative chronotropic effect on the myocardium. It acts on the cell membrane by preventing the permeability of calcium ions into the cell substance.

SOME INTERSTING OBSERVATIONS OF THE EFFECTS OF ATROPINE ON ISOLATED TISSUE PREPARATION.
By G.K. Narayanan and D.K. Basu. Department of Commerce and Pharmacy, I.T.I. Pusa Campus New Delhi.

The muscarnic effects of acetylcholine are blocked by atropine is an accepted fact. However in the isolated guinea pig ileum, Hazard Savini and Renier (1959) have reported that atropine in very low concentrations of the order of 10-20 to 10-16 potentiates the effect of acetylcholine. Cuthberth (1963) has also observed that the electrical and mechanical stimulations of the chick amnion muscle are potentiated by atropine, hyoscine, homatropine, propantheline and their methyl derivatives.

The present investigation has been undertaken with a view to study the mechanism of this atropine induced potentiation of acetylcholine.

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The probable mechanism for this potentiating effect might be : weak ganglion stimulating property of atropine or weak anticholinesterase activity of atropine, or weak acetylcholine like activity of atropine. The ganglion stimulating effect is ruled out as atropine augments the effect of acetylcholine in the chick amnion muscle preparation which is a nerve and ganglion free tissue.

Hence the frog rectus abdominis muscle was selected, for if atropine has got any anticholinesterase activity. In any other tissue this is not possible as the doses of atropine used to establish its anticholinesterase effect will block the acetylcholine receptors thereby masking any anticholinesterase activity of atropine. It was observed that low concentrations of atropine of the order of (10-16) potentiated the acetylcholine action in the rectus abdominis preparations. This also confirmed that the potentiating action of atropine has nothing to do with ganglion stimulation.

A series of experiments were conducted to study the anticholinesterase activity of atropine on the frog rectus muscle. After incubation of serum cholinesterase with atropine for 15 mins. at room temp, acetylcholine was added and incubated for a further 15 minutes. This incubated acetylcholine had no acetylcholine activity, thereby indicating atropine has no anticholinesterase activity. If atropine had any, it would have given protection to acetylcholine. This was confirmed by paper chromatographic experiments. Acetylcholine alone had an Rf value of 0.59 by the ascending chromatography with a solvent system of Butanol, acetic acid water. When the incubate of a mixture of atropine, serum cholinesterase, and acetylcholine were subjected to chromatography, there was no development of any spot indicating the destruction of acetylcholine.

The fact that atropine by itself in small doses did not produce any stimulating effect of various tissue preparation, shows that atropine has no acetylcholine like activity. It is therefore suggested that atropine does something to do with the lowering of the threshold of the various tissue preparations to the acetylcholine induced contractions.

PHARMACOLOGICAL STUDIES ON SODIUM LAURYL SULPHATE. By **B.G. Vad, V.K. Deshmukh and R.M. Jalit.** *Research Laboratory Hindustan Antibiotics Ltd., Pimpri, Poona.*

Sodium Lauryl Sulphate, a surface active agent is employed as emulsifying, detergent and wetting agent in ointments and various pharmaceutical preparations. Pharmacological studies were undertaken in view of the utility of this agent. When used as 1% vehicle Sodium Lauryl Sulphate facilitates the oral absorption of Chlortetracycline, Neomycin and Tolbutamide in animals. On chronic oral administration (100mg/kg) it prolongs the duration of pentobarbitone sleeping time in rats. It possesses local anesthetic activity on intradermal infiltration followed by necrosis at the site of injection.

KEROSENE SMOKE AFFECTING LUNGS. By **B.P. Sinha, and Taru Lata Ghosh** *Department of Physiology, Maulana Azad Medical College, New Delhi*

Kerosene (paraffin oil) contains hydrocarbons, monocyclic and dicyclic naphthenes, aromatic naphthenes in C12 -C15, unsaturated cyclic compounds with boiling point of 175 -275 (George 1960). Accidental poisoning on ingestion occurs in children (Ghosh, 1963, Dechmann *et al*, 1944). Commonest entry is ingestion, but as an enema as amoebicidal agent in a child of 4 years is reported (Collins 1954). Irrespective to the portals of entry the demagging effect in order of preference falls on lung, brain, stomach intestine, liver, kidney, spleen and heart.

Unlike ingestion in an accidental poisoning, the presenting series entails subjection to daily kerosene smoke exposure, to four healthy rabbits, for fifteen minutes, in a chamber 106 by 90X60 cubic centimetres filled a minute earlier, by placing an ignited smoking burner; and continued for 8-20 weeks, along with a control of four rabbits of similar weight having standard meal and being kept at 13 C 0.5 C. No abnormal changes were discernible Mn them rather a gain in weight by 25—100 gms.

Autopsy :—absence of fluid Mn chest cavity, congested lung bases, emphysematous bullae, in upper lobes were found. Moist cut surfaces did not yield fluid on pressure and floated in water. Other viscera and haematological observations are excluded from the presenting topic.

Microscopic lung findings :—Interstitial patchy congestion, emphysema, atelectasis, thickening and denudation of alveolar linings, with spetal cells debris and erythrocytes and pinkish transudate in alveoli were seen. Extreme thickening of media. intimal swelling with ray floret appearance of cells almost obliterating the lumen of the pulmonary artery and some having pinkish transudate simulating oedematous fluid had been the characteristic features. The accompanying pulmonary veins were dilated with intimal swelling and nuclear disruptions.

The vascular changes seen in the rabbit's lung were different from that of the canine group. The latter had extreme degree of congestion of pulmonary vessels, extravasation in lung parenchyma, atelectasis, emphysema, pulmonary oedema, with hyaline membrane formations, and extensive hyperplasia of septal cells without leucocytic infiltration. There had been no accumulation of carbon particles, but black spots simulating foreign substances at lower magnification were seen which on higher magnification (1000 X), their true characters as piling of erythrocytes were revealed.

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EFFECT OF HIGH FAT DIETS ON THE LIPOPROTEIN LIPASE AND FREE FATTY ACIDS OF BLOOD IN RABBITS. By **I.D. Saxena**, *Department of Physiology, College of Medical Sciences, B.H.U., Varanasi.*

In rabbits, the diets rich in saturated fats give rise to hyperlipidemia and atherosclerotic lesions, even though the blood cholesterol levels are not raised as much as on feeding cholesterol. On the other hand, on feeding the diets containing polyunsaturated fats to the rabbits, the blood lipid levels are not affected, though fibrous type of lesion might be produced in the aorta. Whether these different effects of the saturated and polyunsaturated dietary fats have any relation with the lipoprotein lipase activity of the plasma was the question investigated in the present study.

The rabbits were fed ad lib. on the diets containing 20% coconut oil and 20% saffola (safflower oil). The control rabbits were given Anidiet-B. On 60th, 90th and 120th day of the feeding, blood was collected from the marginal ear vein, ten minutes after I.V. administration of heparin (5 mg/Kg.). In the post heparin plasma lipoprotein lipase activity and free fatty acids were estimated according to Korn and Dolf, respectively. The atherogenic effect of the diets was assessed by measuring serum total cholesterol of the rabbits.

The lipoprotein lipase activity was found to increase, as compared to controls, in both the fat fed groups at 90th and 120th day of feeding. The free fatty acids increased on feeding the fatty diets significantly. The differences between the coconut oil and saffola groups were not significant at any period of the study. No simple correlation could be found between the plasma cholesterol and the lipoprotein lipase activity and between the plasma cholesterol and the free fatty acids. On the basis of these results, it is suggested that the dietary fats stimulate primarily the lipolytic activities of the tissues and the post heparin lipoprotein lipase activity is merely a reflection of the tissue enzyme content and does not have much physiological significance in rabbits.

INFLUENCE OF INTERVAL TRAINING ON BLOOD SUGAR LEVEL. By **D.N. Mathur and K. Venkateswaralu**. *National Institute of Sports, Patiala.*

Interval training is a form of training featuring formal fast-slow running which involves repeatedly running a specific distance at a predetermined speed, resting a specific period of time, following each fast run. It has been believed that this training serves as a stimulus to muscle groups and also as a stimulant for concentration of energy delivering substances in the muscles.

Thirty healthy males ranging in age from 15 to 21 years were selected for the study.

Two groups, control and experimental, consisting of 15 subjects each, were formed. Both the groups participated in usual physical training programmes, but the experimental group was, in addition, given interval training for a period of 12 weeks.

Weight and dietary intake of both the groups remained fairly constant throughout the period of investigation. Blood sugar levels were estimated once in three weeks, in both the groups, under fasting and identical conditions. The data, thus collected on both the groups, showed a greater decrease in blood sugar level of the experimental group, from a group average of 98.73 \pm 6.78 to 79.00 \pm 3.14 mg%, that is, a decrease of 19.73 mg%, as a result of interval training. The statistical comparison of the two means of the initial and final tests of the experimental group showed $t = 7.36$, which was found to be significant with 14 degrees of freedom, even with P approaching 0.01. But in the control group the blood sugar level decreased from a group average of 99.47 \pm 8.33 to 96.00 \pm .15mg%, that is, 3.47mg%. The statistical comparison of the two means of the initial and final tests of the control group showed $t = 73$, which was found to be insignificant.

The progressive decline in blood sugar level of the experimental group may be attributed to increased conversion of blood glucose into glycogen in muscles. This also explains that the interval training serves as a stimulant for the concentration of energy delivering substances in the muscles.

THE ANTAGONISTIC ACTION OF BERBERINE HYDROCHLORIDE AGAINST CERTAIN BIOGENIC SUBSTANCES. By **M.B. Bhide and N.K. Dutta**. *Haffkine Institute, Bombay.*

Berberine hydrochloride is introduced in the therapy of gastro-intestinal disturbances. To elucidate the mechanism of action; the dose ratios for berberine hydrochloride and acetylcholine, histamine, 5-hydroxytryptamine, syntocinon, adrenaline and barium chloride were determined from the dose response curves of the agonists elicited before and after berberine hydrochloride in the isolated tissues superfused by the method described by Gaddum. For results see Table No. I.

TABLE I
Dose-ratio for berberine hydrochloride
(Numbers in the brackets show the number of experiments)

Sr. No.	Concentration of berberine in <i>mcg/ml</i>	Agntaonist	Dose-ratio	Test organ
1.	0.4	Histamine (4)	11.33 0.27	G.P. Ileum;
2.	Do.	Bradykinin (4)	4.49 0.38	Rat Uterus,
3.;	1	5 HT. (4);	153 39.7	Do.
4.	Do.	Acetylcholine (4)	46.26 38.6	Do.
5.	Do.	Barium chloride	20.05 15.3	Do.
6.	Do.	Syntocinon (3)	5.91 1.78	Do.
7.	Do.	Adrenaline (3)	4.41 2.79	Rabbits' duodenum

Berberine has much more depressant effect on the responses induced by histamine and bradykinin as no dose-response curve could be plotted after 1 mcg/ml of berberine. Though the dose ratio for histamine was more than that of bradykinin, the two results were not comparable as the tissues and the species used were different. From the point of specificity it could be seen that the dose-ratio for 5-hydroxytryptamine was significantly more than that of acetylcholine, while that of acetylcholine was not significantly different from barium chloride which in turn was not different from syntocinon.

In the series tested histamine, bradykinin and 5-hydroxytryptamine are the agents which increase the capillary permeability. The effects of all these agents are reduced by berberine. So it may be possible that berberine may be acting in severe diarrhoeas and cholera by reducing the increased capillary permeability.

STUDIES ON PHYSIOLOGICAL PROBLEMS OF MAN IN SPACE. By J.K. Sengupta-Physiology and Biochemistry Laboratory, J.J.M. Medical College, Davangere (Mysore).

Complete conformity in the space-craft for duplicating earth conditions is never possible and so there exist some physiological problems which are peculiar to space flight. One of the most interesting of the residual problems is that posed by the fact that after cessation of power thrust, when the space craft is coasting the orbit, the craft and the pilot are for all intents and purpose in free fall and there are no gravitational force (zero 'G' state) at all acting on the pilot. Naturally this creates a completely different homeostatic situation.

There have been three changes noticed which may pose problems. They are as follows -

1. Degeneration of the ability of the circulatory system to respond to change in body position.
2. Decrease in the ability to perform work (Physical work capacity).
3. Increase in urinary elimination of calcium, which was been associated with dissociation of the bone materials.

Physiological studies are worked out on the above problems include the possible toxic effect of ultraviolet rays and ionising radiation and effects of extreme heats and colds encountered in space.

Another interesting facet of space flight is the analysis of man-machine relations the bulk of such researches has fallen to the physiological psychologist. His work has used extensively the concepts of cybernetics (controlling system), where man is often considered as a part of a system, with a transfer function relating his response to stimulus situations and he is to these researches, essentially a cybernetic component.

The development of circulatory intolerance is apparently associated with inactivity as is the decrease in physical work capacity. Having the individual assume an erect position for a part of each day prevents the circulatory degeneration and a small amount of exercise each day prevents the decrease in physical work capacity. Persons continuously resting in bed

did not have their urinary calcium excretion reduced by such procedures. Just how serious this problem may be is not yet known ; but it is conceivable that in space flights in cramped quarters with the flights lasting months or even years, skeletal degeneration would prove very serious. Indications are that the forces produced in the skeleton by gravitational pull are necessary for bone maintenance.

As we have said, the solutions to all these problems are provided at once in the development of adequate supportive equipment, designed to produce earth conditions as far as possible. The artificial environment is a closed ecology and must contain all factors necessary for normal life.

“PRELIMINARY PHARMACOLOGICAL STUDIES WITH THE AQUEOUS SOLUBLE FRACTION OF ACETONE EXTRACT OF MORINDA CITRIFOLIA LINN.” By **K.K. Agarwal**. *Department of Pharmacology Lady Hardinge Medical College, New Delhi.*

The roots of 'Morinda Citrifolia Linn', a shrub of Rubiaceae family, known in Hindi as 'Ach' have been used as a source of dye. The total root extract was reported to possess hypotensive activity clinically and antispasmodic action on isolated uterus. The acetone and alcoholic extract was found to exert an vaso depressor response in anaesthetised dogs. The water soluble fraction of acetone extract contains the glycosidic components. Pharmacological studies were conducted with this fraction because being water soluble, it neither lowered the blood pressure nor altered the normal bracket responses to acetylcholine, adrenaline, nor-adrenaline carotid occlusion and vagus stimulation. The fraction showed marked antispasmodic effect when tested against various agonist i.e. acetylcholine, Histamine, Barium chloride and Nicotine on isolated smooth muscle preparations. The inhibitory action was of non-specific nature. On isolated frog's heart the test material produced inhibitory effect which was dose dependent. While on mammalian heart the action was opposite and the coronary flow was enhanced. The properties of the fraction so far studied appears to resemble that of papaverine like compound.

FURTHER PHARMACOLOGICAL STUDIES OF CROTALABURNINE. By **S. Snehalata and M.N. Ghosh**. *Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry-6.*

Crotalaburnine (CL), an alkaloid from the dried seeds of *Crotalaria luburnifolia* Linn, had been reported earlier to have intestinal antispasmodic, local anaesthetic and slight hypotensive actions (*Ind. J. Physiol. Pharmacol.* 10, 8, 1966).

When compared with papaverine on the isolated guinea pig ileum against acetylcholine and barium-induced contractions, CL was found to be almost as effective as papaverine against acetylcholine but about 5 times less potent against barium. On isolated trachea of guinea pig, CL was almost as effective as papaverine in reversing the spasm induced by acetylcholine, while on that induced by histamine it was ineffective. When bronchoconstriction was recorded in anaesthetised guinea-pig, CL was again found effective in antagonising acetylcholine-induced

bronchospasm but not that induced by histamine. CL 50 mg/kg i.p. protected unanaesthetised guinea-pig from experimental asthma induced by acetylcholine aerosol but not from that induced by histamine aerosol. Acute toxicity test in mice revealed the intravenous LD50 value of 83 mg/kg.

SOME ANTI-INFLAMMATORY STUDIES OF CROTALABURNINE. By **Hardyal Singh and M.N. Ghosh.** *Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry-6.*

Emanuel and Ghosh (*Ind. J. Pharma.*, 26, 322, 1964) reported the isolation of the alkaloid (subsequently named Crotalaburnine) (CL) in pure crystalline form from the seeds of *Crotalaria laburnifolia* Linn and its antagonistic activity against acetylcholine, 5HT, histamine, nicotine and barium induced contractions of guinea-pig ileum. Histamine and 5HT being the important mediators in the process of inflammation their antagonism by CL led us to screen CL for any anti-inflammatory activity. Three different types of inflammation were employed for the purpose.

(1) Formaldehyde-induced arthritis was produced in albino rats (100-200 gm.) by the method as described by Brownlee (1950). Hydrocortisone (Standard) was administered 40 mg/kg. s.c. daily for 10 days and CL 40 mg/kg. s.c. on alternate days (this dose and interval was arrived at after preliminary trials). (2) Carrageenin-induced rat hind paw oedema was produced after the technique of Winter et al. (1962) except that for the measurement of foot volume a modified plethysmometer developed in our laboratory was utilised. Both CL and hydrocortisone were administered s.c. in a single dose of 10 mg/kg. (3) The cotton-pellet granuloma was produced by the technique as described by Winter and Porter (1957) and CL 20 mg/kg. and hydrocortisone 40 mg/kg. injected daily s.c. for 6 days. For all the three methods, a group without CL or hydrocortisone served as control.

The results suggest that CL has significant anti-inflammatory activity against Carrageenin-induced oedema producing 69% inhibition and also against cotton-pellet granuloma producing 58% inhibition. The formaldehyde-arthritis however, was inhibited by CL only for the first 3 days of the experiment.

A STUDY OF ANTIBIOTIC SENSITIVITY OF COMMONLY OCCURRING PATHOGENIC BACTERIA ISOLATED AT MADURAI. By **L. Kameswaran, K. Kanakambal and V. Vijayasekaran.** *Department of Pharmacology, Madurai Medical College, Madurai.*

The sensitivity pattern of commonly occurring bacteria isolated from suspected pathological specimens sent for culture and sensitivity reports from the local hospitals and tested in the department of Bacteriology, Madurai Medical College, Madurai has been studied. A comparison has also been made with some of the previous similar studies at different places and at different times.

We have also tested the sensitivity of the same organisms to four different tetracyclines to see if there is any difference.

The study reports includes that from 1964-1967 March. The standard disc method was used for testing the sensitivity of bacteria.

Both gram positive and gram negative bacteria are highly sensitive to chloramphenicol. In the case of gram positive organisms penicillin ranks lower than chloramphenicol. Streptomycin continues to be very effective against gram negative organisms with chloramphenicol closely following it in its range of activity. The coccal organisms tested are also highly sensitive except *Strep. faecalis*. Penicillin as expected is insensitive to all gram negative bacilli, sensitivity of *Staph. pyogenes* is very low while the streptococci are retaining their sensitivity to a great extent. Tetracyclines are poorly active against most gram-negative bacteria and only haemolytic and non-haemolytic streptococci and *H. influenzae* are fairly sensitive.

On comparison with previous reports the sensitivity of the organisms tested has not undergone any significant change even the techniques used were not the same always. However in the case of many gram positive and gram negative organisms there has been a steady reduction in the number of sensitive strains to tetracyclines and penicillin during the course of the last 15 years. This difference in the sensitivity is all the more significant because much higher concentrations of antibiotics were used in the *in vitro* tests here.

The sensitivity response to tetracycline, chlortetracycline, oxytetracycline and demethyl chlortetracycline is similar in the duplicate plates used for each strain in all the cases tested. The sensitivity response to all the tetracyclines tested is similar i.e., an organism is sensitive to all the four tetracyclines or not sensitive to any.

In brief the spectrum of activity of chloramphenicol and streptomycin are the same as before and are effective against many number of strains and species of bacteria whereas the of tetracycline and penicillin have been narrowed.

STUDY OF SKIN HISTAMINE AND PLASMA HISTAMINASE LEVELS IN WOUND HEALING, By L. Kameswaran, K. Kanakambal and V. Vijayasekaran. Department of Pharmacology, Madurai Medical College, Madurai.

Kameswaran and West found in their study of regeneration of liver after partial hepatectomy that for 24 hours after operation the operated rat excretes enormous amount of histamine in urine which they have suggested may be due to rupture of mast cells in the area of injury. They have also reported that chronic treatment with histamine liberators delays wound healing but prior treatment for a short duration before wounding with polymyxin B a histamine liberator augments healing. Recent work of Rilet (1962) WEST (1962) and Sanyal (1968) indicate a relation between wound healing, inflammation and repair on one hand and the mast cells and its constituents on the other hand.

An attempt was made to study the probable role of mast cells in wound healing rate by noting changes related to the release of its constituents. Under ether anaesthesia, clean incised wounds of uniform length were made under aseptic conditions on the dorsal skin of Wistar

rats of either sex weighing 110-190 gms, closed with 4 sutures and studied for 7 days. Histamine content of the skin in the region of the wound the plasma histaminase activity, clotting time and eosinophil count were estimated. [There is a fall in skin histamine content in injured area immediately after injury and this is associated with an increase in plasma histaminase activity.] Change in plasma histaminase activity has no correlation with changes in absolute eosinophil count. Clotting time was found to be prolonged throughout the week.

The results suggest that the release of histamine after injury probably activates plasma histaminase activity, and releases heparin from the injured area.

A STUDY OF CERTAIN PHYSIOLOGICAL CHANGES OCCURRING DURING PREGNANCY IN ALBINO RATS.
By **J.I.V. Jeyapaul and L. Kamewaran.** *Department of Pharmacology, Madurai Medical College, Madurai.*

Certain changes occurring during pregnancy in the albino rats were correlated with simultaneously occurring biochemical changes and changes in the endocrine glands, organs of reproduction and other viscera.

Healthy female virgin rats weighing 120 Gm were selected and allowed to mate and the probable date of mating was noted by the presence of copulation plug.

Changes in body weight in general and changes in the weight of the mother in relation to number and size of the embryos and the stage of pregnancy were also studied. Interesting patterns of implantation were noted.

We observed certain findings which differed from hitherto reported results. (1) The copulation plug forms early and disappears within 12 hours after mating. (2) In virgin mated rats, the number of foetuses in the right uterine horn is always greater than in the left. (3) Some times, certain organs like liver and kidney show very gross enlargement in otherwise healthy rats, which is not always constant in all rats.

All the endocrine glands show an increase in absolute weight during pregnancy. However when their weights were calculated in mg 100 Gm body weight, the ovaries, adrenals, and thyroids show increase in their proportionate weights in that order throughout pregnancy. Pituitary shows an increase in weight in early pregnancy, but at term it falls down, which is true for thymus also.

All the viscera show a increase in absolute weight throughout pregnancy. When the weight of viscera was calculated in mg 100 Gm. body weight, the maximum increase in weight is shown by uterus. Liver increases in proportionate weight throughout pregnancy. Pancreas shows an increase which has a maximum at the second week and falls down in the final week of pregnancy. In spleen the increase stops at the end of second week and decreases to a lower level in the final week. Kidney shows a steady decrease in its proportionate weight throughout the gestation period. Increase, in weight of heart is seen till second week which decreases later. Brain shows a decrease in proportionate weight from mid-pregnancy onwards.

The blood level of Glucose remains fairly constant throughout pregnancy and reaches the maximum just before parturition, as has been reported in human pregnancy. This may be due to the stress the animal experiences then. Total cholesterol increases steadily as pregnancy advances. Non-protein nitrogen level increases in the final week of pregnancy which is said to decrease in human pregnancy. Creatinine decreases slightly whereas serum bilirubin increases steadily as gestation proceeds.

ROLE OF CHOLINERGIC AND ADRENERGIC FACTORS IN PRODUCTION AND MAINTENANCE OF AURICULAR ARRHYTHMIAS INDUCED BY ACONITINE. By Alice Kuruvilla, P.M. Stephen and Ranita Aiman, *Department of Pharmacology, Christian Medical College, Vellore.*

Atrial flutter and fibrillation induced by aconitine in experimental animals are said to be of focal origin, initiated by rapid impulse formation from a single ectopic focus. Influence of cholinergic drugs on these arrhythmias has been stressed by several workers. The present study was undertaken with the view of understanding the role of cholinergic factors on the impulse production and to study the role of catecholamines on maintenance of atrial arrhythmias.

In anaesthetised dogs, topical application of aconitine over the auricular appendage preceded by an intravenous administration of atropine 0.2 mg/kg, produced only a slow grade flutter, of 32-40 minutes duration, whereas atropine when administered in the same dose to dogs after an aconitine-induced auricular fibrillation, reversed the auricular rhythm to regular activity. The role of adrenergic factors was studied by increasing the adrenergic influence through exogenous application of adrenaline locally at the ectopic focus and also by depleting cardiac stores of catecholamines by pretreatment of animals with reserpine. In contrast to aconitine-induced arrhythmias, which lasted for 55-68 minutes in untreated animals, the arrhythmia-induced in reserpinised animals was short lived with a duration of 16-22 minutes. Adrenaline supplemented with aconitine in these reserpinised animals, prolonged the duration of arrhythmia to 38-41 minutes. Cardiac stores of catecholamines seem to play a role in the maintenance of arrhythmia for long periods. Adrenaline supplemented to aconitine exogenously at the ectopic focus exerted a facilitatory influence on arrhythmia by prolonging its duration and increasing the rate of the auricles. Supplementation of Noradrenaline or Isoprenaline to the aconitine had similar augmentatory influence on these arrhythmias. The effect of was more pronounced and prolonged than the other two catechol amines in that, they were more persistent with more marked irregularity in rhythm.

EFFECTS OF NATURAL AND SEMISYNTHETIC ADRENAL CORTICAL HORMONES ON THE GONADS OF ADULT FEMALE ALBINORATE By S.L. SARKAR. *Department of Pharmacology, M.G.M. Medical College, Jamshedpur.*

Effect of four corticosteroids, namely prednisolone, triamcinolone, dexamethasone, and hydrocortisone were studied in adult female albino rats. Parameters of study were uterine and ovarian weight, alkaline phosphatase activity of ovary and histology of ovary. In both bio-

chemical and morphological studies an inhibitory effect of all corticosteroids were noted although no detectable change in the histology of ovary was noticed. Out of four corticosteroids used in this study hydrocortisone produced most prominent inhibitory effect and least adverse effect was produced by dexamethasone.

POTENTIATION OF ANALGESIC DRUGS BY SOME TRANQUILIZERS. By **S.L. Sarkar and P.P. Chawla.** *Department of Pharmacology, M.G.M. Medical College, Jamshedpur.*

Hydroxyzine (Vistaril), prochlorperazine (Stemetil) and trifluoperazine (Eskazine) were found to have no analgesic action as such up to a period of one hour after administration but they profoundly potentiated the analgesia produced by sodium noramidopyrine methanesulphonate (Novalgin). None of these drugs were found to potentiate the analgesic effect of pethidine except 1/2 hours and 2 hours after administration of hydroxyzine, a statistically significant potentiation of analgesic effect of pethidine was obtained.

EFFECT OF NATURAL AND SEMISYNTHETIC ADRENAL CORTICAL HORMONES ON WEIGHT AND CHOLESTEROL CONTENT OF ADRENALS OF SEX HORMONES TREATED MALE AND FEMALE ALBINO RATS. By **S.L. Sarkar** *M.G.M. Medical College, Jamshedpur.*

Four adrenocortical hormones viz prednisolone, triamcinolone, dexamethasone and hydrocortisone were injected intramuscularly to intact male rats, testosterone treated castrated male rats, intact female rats and oestradiol treated ovariectomized female rats.

Adrenal weight and adrenal cholesterol concentration were parameters of study. Maximum reduction of adrenal weight was noted in intact male rats. In testosterone treated castrated male rats loss of adrenal weight was prevented by testosterone. However, corticosterones produced inhibition of adrenal cholesterol in both intact and testosterone treated castrated rats. Corticosterones failed to produce any alteration of adrenal weight either in intact or in oestradiol treated ovariectomized rats. In the former group, adrenal cholesterol concentration was reduced while in later group oestradiol prevented any alteration of adrenal cholesterol concentration.

PERIPHERAL BASIS OF CARDIAC ACCELERATOR MECHANISMS OF ANGIOTENSIN. By **S.D. Nishith J.P. Saxena and M.G. Amin.** *Department of Physiology, Medical College, Baroda.*

Angiotensin showed a cardioaccelerator effect which is partially masked by sinoaortic reflexes in the intact animal. This effect is present after the vagotomy but is reduced after transverse section of the spinal cord and after bilateral sympathectomy through T1-T6 showing that a component of the cardiac accelerator action of angiotensin is, via cardiac accelerator centre and via sympathetic fibres to the heart.

The accelerator effect which is present after transverse section of the spinal cord and after sympathectomy is due to peripheral action of angiotensin on heart.

This peripheral action could be either due to stimulation of post ganglionic sympathetic nerve endings to the heart or because of the direct stimulation of sinoatrial node of the heart. The possibility of stimulation of adrenal medulla by angiotensin is also there, which could increase the heart rate.

It has been observed that adrenals do not play any role in this mechanism.

STUDIES ON ADVERSE REACTIONS TO DRUGS IN CLINICAL PRACTICE By **S.N. Dutta, P. Sen and R.K. Sanyal.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

Cases of adverse reactions to drugs in common use were studied. The offending drugs were thiacetazone, chloramphenicol, chlorpromazine, vitamin B. complex, penicillin, prednisolone, and chloroform. Thiacetazone mainly produced skin lesions; severe liver damage resulted in death in one case. Chloramphenicol mainly produced blood dyscrasias. Allergic reactions were noted with penicillin and vitamin B. complex. Prolonged use of chlorpromazine produced pigmentation of skin and retina. Prednisolone produced haemorrhagic disorders and chloroform produced hepatotoxicity.

STUDIES ON THE ACTION OF ACETYLCHOLINE ON THE SINO-AURICULAR NODE. By **O.N. Tripathi, S.N. Dutta and R.K. Sanyal.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi, and Central Drug Research Institute Lucknow.*

It was seen that acetylcholine injected directly into the artery supplying the sino-auricular node produced positive chronotropic response. The pattern and duration of response closely resembled that produced by adrenaline and noradrenaline. The response was potentiated by cocaine and abolished by DCI. A negative chronotropic action was seen when acetylcholine was similarly injected in reserpinized dogs. Intrarterial infusion of adrenaline or noradrenaline temporarily restored the positive chronotropic effect of acetylcholine in reserpinized animals.

ANTIACETYLCHOLINE ACTION OF IMIPRAMINE. By **P.K. Lahiri and S. Arora.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

Imipramine, an antidepressive compound was found to block the muscarinic action of acetylcholine at the postganglionic parasympathetic nerve endings in several species. It also blocked certain nicotinic actions particularly associated with neuromuscular junctions. Preliminary studies indicate a competitive type of antagonism.

NEWER CORTICOSTEROIDS IN ANAPHYLACTIC SHOCK. By **A.R. Laddu and R.K. Sanyal.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

The effect of certain newer synthetic corticosteroids were investigated on anaphylactic shock in the rat and the mouse. Betamethasone and dexamethasone were effective in the rat, but

not in the mouse. Triamcinolone was effective only in the latter species. Dexamethasone was effective in both species. The protective action was not due to specific inhibition of the steps of anaphylactic reaction but probably related to a nonspecific tolerance to shock like state.

CHLOROFORM AND ISOLATED HEART. By **S. Arora and S.N. Dutta.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

Continuous perfusion with Ringer Locke solution saturated with chloroform produced diastolic arrest of the isolated rabbit heart. Presence of 5-HT prolonged the period required to produce arrest and also hastened recovery following cessation of chloroform perfusion. 5-HT is known to produce coronary vasodilatation. Other drugs producing similar vasodilation such as a new norcamphane derivative (L-64) also had a similar action. However, the degree of coronary vasodilatation and the amount of chloroform required to produce cardiac arrest could not be correlated.

RABBIT HEART IN ANAPHYLAXIS. By **H.L. Dhar, P. Sen and R.K. Sanyal.** *Department of Pharmacology, Maulana Azad Medical College, New Delhi.*

The electrocardiographic changes in the rabbit heart during anaphylaxis are indicative of coronary spasm and thrombosis. Pretreatment with heparin prevents anaphylactic death, and also abolishes the electrocardiographic changes associated with myocardial infarction. It is concluded that coronary thrombosis is a contributing factor of anaphylactic death in this species.

EFFECT OF GUANETHIDINE ON SURVIVAL TIME OF DOGS SUBJECTED TO HAEMORRHAGIC SHOCK. By **P.K. Pispati and B.B. Gaitonde.** *Department of Pharmacology, Grant Medical College, Bombay.*

Eleven dogs were subjected to haemorrhagic shock in two bouts of bleeding at an interval of four hours. Another group of nine dogs were pre-treated with guanethidine sulphate in the dose of 10 mg/kg for 48 and 24 hours before they were subjected to haemorrhagic shock induced in an identical manner. The results indicated a significant prolongation of survival time (p. .01). Initial values of blood pressure in these animals were lower than those in control dogs (p .01), and the animals showed better percentage recovery of blood pressure after the first bout of bleeding (p .02). The significance of these findings is discussed.

VISUAL PROJECTION TO THE SUPERIOR COLLICULUS OF THE ALBINO RAT. By **S.K. Lal.** *Department of Physiology, Jawaharlal Institute of Post-Graduate Medical Education and Research, Pondicherry.*

The primary problem in visual physiology is the identification of the visual pathways, their precise localization boundaries and extent of terminal areas of the pathways. Secondly, to determine whether the original spatial and dimensional relationship in the visual space and retinal representation are preserved in the pathways, and the centres. And if they are how and where the various areas of the retina are represented at various levels of the visual pathways.

The projection of the rat's retina upon the superior colliculus was plotted by micro-electrode recording, while stimulating the retina by a Neon-flash subtending 0.5 in visual field. The rats were lightly anaesthetised and mounted in a holder which permitted 180 access retinal stimulation ; and the eye was sutured to a ring to prevent movement.

A precise retinotopic arrangement evoked by stimulation of the contralateral visual field, was plotted across the surface of the superior colliculus. An ipsilateral projection appeared to be absent. There is little evidence of any macular area in the rat retina and no magnification appears on the map. There is, however, evidence that in the colliculus the information is more generously displayed around the horizontal than around the vertical plane through the optic axis.

Few units were studied and typical "on " and "off" units were detected.

ULCER INDEX IN THE SHAY RAT AND ITS RELATION TO BLOOD SUGAR LEVEL. By **A.K. Ganguly, S.K. Lal, S.D. Nishith and S.K. Sreepathi Rao.** *Department of Physiology, Jawaharlal Institute of Post-Graduate Medical Education and Research, Pondicherry.*

Ulcers have been produced by Shay's operation technique in albino rats and the stomachs have been studied for assessment of ulceration. Ulcer index has been prepared on the basis of the ratio between the area of ulceration and the area of the stomach.

83.3% ulcer incidence in Shay-rats under normoglycemic condition has gone upto hundred per cent under hypoglycemia induced by insulin whereas alloxan-hyperglycemia has reduced it to 61.5%.

Quantitative study shows mean ulcer-index values of 0.44, 0.65 and 0.1 under normo-, hypo,- and hyperglycemic conditions respectively.

Ucer-index in relation to volume and acidity of the gastric content under different glyceimic conditions has been compared, which shows an increase in the volume of gastric content, rise in total acidity and ulcer index under hypoglycemic condition whereas with higher levels of blood glucose these parometers slow a fall.

It would thus appear that an inverse relationship can be established between the blood sugar levels on the one hand and volume of gastric contents, acidity and ulcer index on the other.

AN INVESTIGATION OF THE BAINBRIDGE REFLEX. By **B.R. Goyle and S.K. Lal.** *Department of Physiology, Jawaharlal Nehru Institute of Post-Graduate Medical Education and Research, Pondicherry.*

Ten anaesthetized dogs were infused I.V. with normal saline for 4 minutes at an average rate of 90-100 ml/mt through a polythelene catheter introduced in the femoral vein with it's tip positioned in the inferior vena cava just above the diaphragm. The alternations in the heart rate so induced were determined.

The Bairenbridgreflex was elicited effectively in all the animals where the initial heart rate was slowed positively by increasing the vagal restraint by pre-treatment with morphine sulphat 3 mg/kg subcutaneously one hour prior to the administration of chloralose 120 mg/kg I.V. for anaesthesia. If the intial heart rate was high, the infusion elicited a bradycardia. Bradycardia was also induced in five dogs chemically vagotomized with atropine and in another five after ganglionic blockade with pentolinium targate.

EFFECT OF SOME ANTIEPILEPTIC DRUGS ON PHYSICAL TOLERANCE. *By P.N. Saxena. Department of Pharmacology, Jawaharlal Nehru Medical College, A.M.U., Aligarh.*

This report deals with the acute effect of some antiepileptic drugs on physical tolerance in normal and stressed mice. Phenobarbitone sodium, morphine hydrochloride and amphetamine sulphate were included for reference. They were injected intrapetitoneally; other drugs were fed orally.

Mice trained to run at a speed of 125 feet per hour on a treadwheel were divided in groups of six. Room temperature ranged between 23-25.C. The percent decrease in running time in the treated group from the control value in the same group is presented in column 3 of Table 1.

TABLE 1

Effect of Antiepileptic drugs on running time and swimming Trials of mice.

Drug	Dose Mg./Kg.	Running-time Percent Decrease	Swim-Trials	
			Over-all fatigue	Rate of Develop- ment of fatigue
Control	..	+ 4	11	43
Phenobarbitone	10	22	66	130
Dilantin	100	76	44	150
Tridione	100	40	-10	3
Zarontin	250	38	-14	-12
Milontin	100	8	8	126
Mysoliine	100	59	82	225
Phenurone	100	+24	15	40
Morphine	5	+ 9	-12	-33
Amphetamine:	5	+17	-23	-45

In another experiment, mice trained to swim 1.5 M in a water alley to an escape ramp were divided in groups of nine. Each mouse was forced to attempt 60 trials by placing it back from the ramp to the starting end of the alley. The swim time of each trial was recorded. The temperature of the water was maintained at 20-21 C.

The percent increase of the index, swim time/number of trials, in the medicated group over its control value is presented in column 4 of the table showing the over-all effect on fatigue. Column 5 of the Table presents the rate of development of fatigue calculated after Kiplinger et al. (Pharmacologist. 5, 171, 1964).

The antiepileptic drugs in general adversely affect physical tolerance : phenobarbitone, mysoline, dilantino, milontin and tridione-in that order. Phenurone improves physical performance but this effect disappears unddr stressful condition. On the other hand zorontin shows some improvement in physical tolerance in stressful condition only.The beneficial effect of 5 mg./kg. each of amphetamine and morphine is manifest under both conditions. It will be worthwhile to investigate whether such effect aggravates or disappears with prolonged use of these drugs.

PHARMACOLOGY OF THE ACTIVE PRINCIPLES OF LYCOPERSICON ESCULENTUM LEAVES A PRELIMINARY REPORT. By **Om Chandra, K.P. Gupta, S. Ajmal and P. N. Saxena.** *Pharmacology Department, J.L.N. Medical College, A.M.U., Aligarh.*

Leaves of *Lycopersicon esculentum* (tomato) have been shown to possess antihistaminic and atropine like activity. In a recent report aqueous extract of tomato leaves has been shown to produce lethal action when given intravenously in rabbits and guineapigs. It was also shown to intensify the tone and motility of isolated smooth muscle organs. These actions have been attributed mainly to an alkaloid tomatine. No attempt has so far been made to explore its pharmacological actions. It was therefore thought worthwhile to study its pharmacological actions with an attempt to identify the active principles present therein.

Studies were conducted with 100% W/V of the acetone extract of the leaves on the isolated frog's heart preparation, dogs heart lung preparation, dog's blood pressure, isolated guineapig ileum and isolated oestrogenized rat uterus. Descending paper chromatography was also done to isolate the active principles.

Effect on Isolated Frog's Heart:

In a concentration of 1:5000 the acetone extract produced stimulation which was not blocked by the dose of propranolol which completely blocked the stimulant action of the equipotent doses of adrenaline. In this concentration the extract also produced reversal of the depression induced by 10 $\mu\text{g/ml}$ pentobarbitone sodium.

Effect on Dog's heart lung preparation:

In dog's heart lung preparation cardiac output was increased. The extract produced complete reversal of the pentobarbitone induced cardiac failure. The heart rate was however not increased suggesting that the extract possesses cardiotonic activity.

Effect on dog's blood pressure:

In a dose of 0.1 ml/kg intravenously it produced a prolonged fall of blood pressure in dogs anaesthetized with 30 $\mu\text{g/kg}$ of pentobarbitone sodium. The fall in blood pressure was not blocked by atropine (1 mg/kg), mepyramine (10 mg/kg) or by nexamethonium (10 mg/kg).

Effect on isolated guineapig ileum and isolated rat uterus:

It produced stimulation of the isolated guineapig ileum and repeated doses of the extract produce tachyphylaxis. Similar findings were observed with isolated oestrogenized rat uterus.

It produced stimulation of the isolated guineapig lileum and repeated doses of the extract produce tachyphylaxis. Similar findings were observed with isolated oestrogenized rat urerus.

Results of descending paper chromatography:

Descending paper chromatography revealed seven distinct fractions. Effect of these fractions was seen on all the test preparations and activity was found to be present in the R6 fraction (RF 0.52) only. Other fraction did not reveal any activity.

It can therefore be concluded that the activity in the acetone extract of the tomato leaves is due to R6 fraction. These actions are probably not by virtue of the alkaloid tomatine which is present in tomato leaves as tomatine can neither be extracted in acetone nor it can be separated by descending paper chromatography.

FURTHER STUDIES ON THE MECHANISM OF RESERPINE EMESIS IN PIGEONS. By **R.C. Saxena, B.P. Jaju, K.N. Dhawan and G.P. Gupta.** *Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

We have reported that reserpine produces emesis in pigeons. In a previous communication we suggested the this emesis is mediated through catecholamines. The present work was undertaken to provide further evidence for this hypotehsis. It was found that in'ection of non-adrenaline as well as drugs which release catecholamines produced emesis in pigeons. Moreover, pretreatment of pigeons with the releasers of catecholoamines, considerably reduced the incidence of reserpine emesis sbut not that of nor-adrenaline emeis.s However the emesis induced by nor-adrenalne and reserpine could not be locked by (or B- adrenergic receptor blocking agents.

A SCREENING METHOD FOR ANTIDEPRESSANT ACTIVITY. By **G.P. Gupta, B.P. Jaju, R.C. Saxena and K.N. Dhawan** *Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

It has been reported earlier that anti depressant drugs like imipramine and monoamine oxidase (MAO) inhibitors antagonize the reserpine induced emesis in pigeons. The present work was undertaken to test the validity of the antagonism of reserpine-induced emesis in pigeons as a screening method for the antidepressant drugs. Clinically, electroconvulsive therapy (ECT) is still the most effective form of treatment for depressive psychoosis. Therefore, it was thought desirable to study the effect of electroconvulsions on reserpine emesis. In addition the effect of pentylenetetrazol induced convulsions and insulin shocks, which have also been employed for the treatment of depression, was studied on reserpine emesis. It was found that the emesis was blocked after electroshock and pentylenetetzoal convulsions. However insulin was ineffective probably because birds are makedly resistant to insulin. Reserpine emesis, therefore, seems to be a valid test for assessing the anti-depressant effect of drugs

EFFECT OF MAGNESIUM SULPHATE ON MELANOPHORES OF RANA TIGRINA. By **Meena S. Kelkar and J.H. Balwani.** *Department of Pharmacology, B.J. Med. College, Poona.*

The study of drugs on frogs melanophores is a fascinating subject. During the course of our routine experiments it was found that magnesium sulfate (20%) produces a colour change (from black to yellowish green) in *Rana tigrina*. It was found that this lightening is reversed by caffeine but not by calcium which counteracts the depressant effect of magnesium. The colour change was assessed according to Hogben's method. Caffeine-induced darkening is also reversed by magnesium sulfate. In order to elucidate the mechanism of action of magnesium sulfate on melanophores, frogs were pretreated with dibenzylamine and reserpine both of which blocked the action of magnesium sulfate. From these observations the conclusion reached is that magnesium sulfate acts through release of catecholamines from stores.

THE MECHANISM OF ANALGESIC EFFECT OF CODEINE AND ITS POTENTIATION BY AMPHETAMINE. By **Sunita D. Kulkarni and J.H. Balwani.** *Department of Pharmacology, B.J. Medical College, Poona.*

Analgesic response of various drugs was tested on rats by Haffner's tail clip method. Effect of codeine, 12.5 mg/kg injected intraperitoneally, was tested alone and in combination with amphetamine (1 mg/kg) in normal as well as reserpinised animals. (24 hrs. after in. of 2 mg/kg of reserpine) One week interval was kept between two drug-administration. Self control was kept throughout the experiment. It was found that amphetamine induces potentiation of codeine analgesia and this is lost totally after reserpine. Even codeine analgesia is significantly reduced after reserpine. It is suggested that codeine analgesia is through the release of catecholamine centrally.

The same animal when tested 8 weeks after reserpinisation, showed complete restoration of analgesic effect of codeine as well as potentiating effect of amphetamine. This restoration may be attributed to the repletion of catecholamine stores.

EFFECT OF LIV-52* ON THE GROWTH AND FOOD CONSUMPTION OF LABORATORY ANIMALS. By **S. Srinivasan and J.H. Balwani.** *Department of Pharmacology, B.J. Medical College, Poona.*

Liv-52, an indigenous proprietary medical preparation, was administered to freshly weaned rats, mice and guineapigs daily in the dose of 0.4 ml/100g body wt. by intragastric tube over a period of 9 weeks. The control group was given a corresponding amount of water. Both groups were fed ad lib with the same diet. Spontaneous food consumption (as wet food) was recorded daily and weight was recorded weekly.

It was observed that Liv-52 treated group showed a higher rate of growth after about the 4th week (P 0.05), consumed more food per 100g body wt. (P 0.05) and had improved efficiency of food utilisation as expressed by feed conversion ratio.

"FURTHER STUDIES ON THE EFFECT OF PHYSOSTIGMINE ON TISSUE GLUCOGEN." By **R. S. Rathor and P. K. Das**, *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi-5.*

In an earlier communication it has been reported that Physostigmine (PSM) salicylate (0.1 mg/kg., I. V.) induced glycogenolysis in dogs which was potentiated by pretreatment with atropine sulphate and blocked by pretreatment with pentolinium tartrate (Rathor and Das, 1967). Further studies were conducted to elucidate the mechanism of action of PSM on tissue glycogen. Acute bilateral adrenalectomy in dogs slightly raised tissue glycogen. PSM insignificantly raised the glycogen contents of heart and liver with no change in skeletal muscle glycogen in acute bilaterally adrenalectomised dogs. PSM (I. P.) in acute bilaterally adrenalectomised albino rats produced a generalised increase in the glycogen contents of all tissues, however, the increase was significant in heart only. PSM administration in DCI (20mg./kg. I. P.) pretreated albino rats produced significant rise in the glycogen contents of all the tissues. The glycogenetic action of PSM in DCI pretreated albino rats was blocked by atropine in the heart whereas it was not blocked in liver skeletal muscle.

"STUDIES ON THE ANTIHISTAMINIC ACTIVITY OF 14 QUINOLINE DERIVATIVES". By **M. K. Raina, P. K. Das and A. K. Sanyal**, *Department of Pharmacology, College of Medical Sciences, Banaras Hindu University, Varanasi*

In an earlier communication it has been reported that Quinoline derivatives with 0. CH₂ CH₂, NR attachment at position four have antihistaminic properties (Raina, Das and Sanyal, 1967). Further studies have been conducted on 14 such quinoline derivatives. A comparison of the *in vitro* spasmolytic ED₅₀ against equipasmodic concentrations of histamine dihydrochloride, acetylcholine bromide, barium chloride and 5-HT creatinine, sulphate and *in vitro* anti-anaphylactic activity showed that 8 compounds have potent and specific antihistaminic activity. Four of these compounds significantly dogs without affecting hypotension caused by acetylcholine and papaverine. The histamine inhibitions caused by the dimethyl and pyrrolidino derivatives were marked and prolonged. Pyrrolidino derivatives were marked and prolonged. Pyrrolidino derivative protected the guinea pigs against anaphylaxis *in vivo*.

"ANTI-INFLAMMATORY ACTIVITY OF SEMECARPUS ANACARDIUM, LINN." By **G.V. Satyavati, D.N. Prasad, P.K. Das and H.D. Singh**, *Department of Pharmacology and Microbiology, College of Medical Sciences, Banaras Hindu University, Varanasi.*

Milk extract of nuts of *Semecarpus anacardium* (S.A.) was screened for anti-inflammatory activity against a variety of inflammatory reactions produced by immunological and non-immunological methods in albino rats. Drug was administered orally and equivalent quantity of milk was given to control animals. Betamethasone was used for comparison. S.A. was found to suppress the acute inflammations of hind paw induced by carragenin, 5-HT and formaldehyde. It, however, did not suppress granuloma formation induced by either corton oil or carragenin pellet implantation in adrenalectomised rats. S.A. was found to significantly

inhibit tuberculin sensitivity reaction in sensitised rats seen after 24 and 48 hours of intradermal injection of purified tuberculin. In mycobacterial adjuvant induced arthritis S.A. exhibited good anti-inflammatory activity on the primary phase of inflammation but had no effect on delayed secondary lesions which appeared after 8 to 10 days of injection of mycobacterial adjuvant. S.A. was, however, found to be toxic drug as 20% of the animals developed alopecia and gangrene of limbs, tail and ear. It was concluded that S.A. inhibited acute inflammations without having any effect against sub-acute and chronic inflammations.

The work was conducted with grants in aid from the Indian Council of Medical Research.

PHARMACOLOGICAL STUDY OF TERTIARY BASE FROM SEEDS OF DAUCUS CAROTA, LINN. By **S.S. Gambhir, S.P. Sen, A.K. Sanyal, M.K. Raina and P.K. Das.** *Department of Pharmacology and Medicinal Chemistry, Faculty of Medical Sciences, B.H.U., Varanasi.*

The pharmacological actions of water soluble fraction of alcoholic extract of seeds of *Daucus carota*, Linn and the actions of Quaternary base isolated from the above extract have been reported earlier (*Ind. Jour. Med. Res.*, **54**, 178, 1966 and **54**, 1053, 1966). Further phytochemical work has led to the isolation of a tertiary base from the same extract. On pharmacological study, the tertiary base has been found to possess relaxant action on isolated smooth muscles of ileum and uterus of different animals. It has nonspecific antispasmodic action against drug induced spasms in ileum, uterus and tracheal smooth muscle. The antispasmodic E.D. 50 of the base hydrochloride shows that the drug is approximately 10-15 times less potent than papaverine hydrochloride.

CENTRAL PROJECTIONS OF SUPERIOR LARYNGEAL NERVE-LOCALIZATION OF THE SWALLOWING CENTRE By **I.S. Aneja and S.K. Manchanda.** *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Manchanda (1966) reported widespread suprabulbar influences on the reflex swallowing as elicited by the stimulation of the superior laryngeal nerve (SLN). He suggested that the existing concept about the location of the swallowing centre in the medullary region subjacent to ala cinerea needed a revision in view of the recent researches.

Considering that the superior laryngeal nerve is the main afferent pathway for the reflex swallowing a study was planned to map out its central projections. In "encephale isole" cats medulla oblongata was explored for potentials evoked on stimulation of the central end of the cut superior laryngeal nerve. The evoked responses could be grouped under two main types:

TYPE I: These were double peaked responses of short latency (1 to 2 msec.), short duration (2 to 4 msec.) and small magnitude (50 to 90 μ V) and were not affected on increasing the frequency of SLN stimulation. Such responses were localised in tractus solitarius, dorsal motor nucleus of vagus, spinal tract and spinal motor nucleus of the Vth nerve, reticular formation 1 to 2mm ventral to tractus solitarius, medial lemniscus and medial longitudinal fasciculus. The characteristics of the type I potentials signified that there is direct projection of SLN to these regions.

TYPE II responses were of longer latency (8 to 40 msec.), longer duration (6 to 60 msec.) and higher amplitude (85 to 800 μ V) and were markedly affected by increasing the frequency of SLN stimulation from 1 per second to 20 per second. These responses were mostly localized in a large strip of ipsilateral reticular formation extending from 4mm. anterior to obex to about a mm posterior to obex. Dorso-ventrally the strip was localised at 1.5 to 2mm. ventral to dorsal motor nucleus of vagus and tractus solitarius and extended further ventrally for about another 3 to 4mm. These responses were also obtained from ipsilateral medial longitudinal fasciculus and contralateral reticular formation.

Obtaining of the type II responses signified summated activity of the interneurons located mainly in the reticular formation. It is suggested therefore that if the neuronal centre for any reflex activity is to be defined as that area which integrates the activity of sensory and motor nuclei concerned with that activity then in the case of swallowing this integrative function is subserved by an area of reticular formation as delineated in this study by the localisation of the type II responses. Further it is suggested that the region subjacent to the ala cinerea which has tractus solitarius in it is just a sensory receiving centre and therefore should not be considered the swallowing centre.

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A STUDY OF THE MECHANISM OF FATAL HYPERTERMIA INDUCED BY IMIPRAMINE IN MAO INHIBITORS TREATED RABBITS. By R.K. Srivastava, K.S. Dixit, J.N. Sinha, K.M. Dhasmana and K.P. Bhargava. *Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

Imipramine therapy in patients previously treated with monoamine oxidase inhibitors produces serious toxicity characterized by hyperthermia and hypertension. Intravenous administration of imipramine in rabbits pretreated with niamid produced fatal hyperthermia. In the present investigation an attempt was made to analyse the underlying mechanism in the production of such reaction in rabbits and to find out some agent which could prevent the above syndrome. Slow i.e. injection of imipramine (5 mg/kg) in rabbits pretreated with niamid (100 mg/kg I.P.) produced 100% hyperthermic response. Chlorpromazine 5 mg/kg i.p. was found to block the hyperthermic response. Pretreatment with either propranolol or INPEA did not block the hyperthermic response while dibenzylamine 10 mg/kg i.p. protected the animal from it. Prior reserpine administration of the animals (0.5 mg/kg i.p. for two days) also abolished the fatal hyperthermic response. It is concluded that the hyperthermic response is adrenergically mediated. This study also indicates that chlorpromazine and dibenzylamine may prove beneficial in the prevention of such a hyperthermic reaction.

EFFECT OF SOME PHENOTHIAZINE DERIVATIVES ON CORONARY FLOW *By M. A. Shamshi, V.K. Kulshrestha, K. N. Dhawan and K. P. Bhargava. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

The coronary dilator effect of thiopropazate, perphenazine, and promazine was studied on isolated rabbit's heart according to the Langendorff's technique in Anderson's Coronary perfusion apparatus. All the three phenothiazines produced positive inotropic and chronotropic effect with smaller doses, whereas higher doses produced negative inotropic and chronotropic effect. The doses of promazine, thiopropazate and perphenazine required to increase the coronary flow by 5%, as calculated by log dose response curves were 16 μ g, 30 μ g and 42 μ g respectively. Thus promazine was found to be most potent coronary dilator amongst the phenothiazines studied.

ANTI-INFLAMMATORY ACTIVITY OF BOERHAAVIA DIFFUSA *By T. N. Bhalla, M. B. Gupta P. K. Seth and K. P. Bhargava. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

Aqueous and acetone extracts of Boerhaavia diffusa (Punarnabea) and its active principle (Punarnavine) were tested for their anti-inflammatory activity on carrageenin induced oedema and formaldehyde induced arthritis in albino rats.

The study revealed that aqueous and acetone extracts of Boerhaavia diffusa as well as the punarnavine in dose of 4 mg/100 gm each showed significant anti-inflammatory activity on carrageenin induced oedema and formaldehyde induced arthritis.

Biochemical effects of these agents were studied on serum transaminases and liver ATP-ase activity in albino rats. They inhibited the serum transaminases (S-GOT and S-GPT) and increased the liver ATP-ase activity.

SOME CENTRAL EFFECTS OF APIUM GRAVEOLENS (LINN) II. *By V.K. Kulshrestha, R.C. Saxena and R.P. Kohli. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

Tranquillizing and anticonvulsant activities of an essential oil of Apium Graveolens have already been reported earlier from this laboratory. In the present study nitrogenous and non-nitrogenous portions of the oil were tested for central effects. Only the nitrogenous portion was found to possess CNS activity. It provided protection against supramaximal seizure threshold test but was not effective against convulsions induced by metrazol or strychnine. It also had tranquillizing activity as it potentiated pentobarbital sleeping time and produced loss of conditioned avoidance response. However, it had no effect on amphetamine toxicity in aggregated mice. The results were discussed.

A STUDY OF ANIT-ARRHYTHMIC ACTIVITY OF SOME C.N.S. ACTIVE DRUGS. By **V.K. Kulshrestha, K.N. Dhawan and K.P. Bhargava.** *Department of Pharmacology and Therapeutics, King Georges Medical College, Lucknow.*

In the present study ten drugs possessing C.N.S. activity were screened for their anti-arrhythmic activity. Quinidine sulphate was included in the study for comparison. In the preliminary screening the effect of these drugs was observed on the refractory period of isolated atria of rabbit using the Dawe's technique and on the conduction time in dogs. The drugs which were comparable with quinidine sulphate in prolonging the refractory period of isolated atria of rabbit were further studied for their anti-arrhythmic activity against atrial arrhythmia induced by sub-epicardial injection of aconitine solution (.5%) and ventricular arrhythmia following coronary artery ligation in dogs. E.C.G. records were taken by Grass Polygraph. The results of this study indicate that promethazine hydrochloride and hydroxyzine hydrochloride possess anti-arrhythmic activity comparable to quinidine sulphate and may prove to be more advantageous in the treatment of cardiac arrhythmias due to additional tranquillising activity.

PPb (N-O-TOLYL)—A NEW —ADRENERTIC BLOCKING AGENT. By **K.C. Singhal, V.K. Kulshrestha, K. Shankar, S.S. Parmar, R.P. Kohli and K.P. Bhargava.** *Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow.*

PPb (N-O-tolyl), a biguanide derivative of Piperazine, synthesised in this laboratory reversed the epinephrine pressor response in dose of 15 mg/kg (i.v.) in dogs and this effect lasted upto 12 hrs. It diminished contraction of cats nictitating membrane obtained by electrical stimulation of cervical sympathetic trunk and epinephrine induced contractions of vas-deferens. In 15 mg/kg dose it reversed cardiac arrhythmia induced by intra-cerebrventricular administration of aconitine (5 ug—10ug). The results show that PPb (N-O-tolyl) is a potent -adrenergic blocking agent. Acute and chronic toxicity studies show it to be a safe compound.

UNIT ACTIVITY OF HYPOTHALAMIC NEURONES SENSITIVE TO GLUCOPENIA. By **T. Desiraju, M.G. Banerjee, and B.K. Anand,** *Department of Physiology, All India Institute of Medical Sciences Ansari Nagar, New Delhi.*

The spontaneous unit activity of neurones ventromedial nucleus and of lateral area of hypothalamus was recorded in cats paralysed with gallamine. The firing rates of units of ventromedial nucleus were commonly between 1 and 6 and of lateral area between 2 and 10. After obtaining a stable unit 2-deoxy-d-glucose was administered by intracarotid infusion. It was observed that the discharges of the units of ventromedial nucleus were inhibited to 20% of normal in a 50 min. period, while the unit discharges of the lateral area were augmented to 160% of normal in the same period. Injections of saline did not cause such effects. Other units in anterior, middle or posterior hypothalamus did not show changes following injection of 2-deoxy-d-glucose. At the dose range of 100-200 mgm/kgm used in the study, 2-deoxy-d-glucose did not produce any generalized changes of blood sugar or its utilization. In view of the s

specific inhibitory response of the satiety centre to 2-deoxy-d-glucose, it is discussed that possibly the cells in this region are sensitive to glucose utilization and in turn may influence the activity of the neurones in the feeding centre.

NEURO-ENDOCRINAL PARTICIPATION IN THE REPRODUCTIVE ACTIVITIES. G. S. Chhina, K. Kaur, N. D. Bajjal, G. Chowdhury, Baldev Singh and B. K. Anand. *Department of Physiology. All India Institute of Medical Sciences, Ansari Nagar, New Delhi.*

The participation of Hypothalamus and some other regions of the brain in the regulation of reproductive activities in different animals is well known. However neither the exact part played by different areas in the regulation of gonadal activities nor the role of gonadal secretion in changing the responses of neural elements, is clear. Investigations therefore were undertaken, to study the changes in electrical activity of different parts of the brain produced by genital stimulation, in the presence of circulating gonadal hormones on the one hand and to note the changes in responses of genital regions as a result of nervous lesions on the other.

The EEG and unit activity recorded from antero-lateral regions of the hypothalamus, through stereotaxically implanted electrodes, showed changes in response to genital stimulation after gonadal hormone injections. The changes were localised in the hypothalamus to begin with, but spread to septal region, anterior cingulate gyrus and orbital surface of frontal lobes, if the hormone injection was continued for some more days.

Effect of injection of Oestrogens in female monkey on the urinary output of these hormones was also observed, in normal and operated animals with brain lesions. The injections seem to depress the normal urinary excretion of oestrogens, although they increase the tendency of cyclicity. On withdrawal of injections there was either menstrual bleeding or an increase in oestrogen excretion in urine. The injections of linstrol after lesions in the septal and preoptic regions resulted in a marked increase for about 40 days followed by a decrease almost to nil. The normal hormonal output reappeared on withdrawal of injection even in this animal.

Insertion of IUCD showed an increase in the estrogen output in one monkey studied so far. It was also observed that nialamide prevents release of prolactin through the participation of medial eminence of hypothalamus.

In the male monkeys prolonged captivity increases the threshold for electro-ejaculation. Some changes in the quality of semen thus obtained were also observed. Lesions of amygdala made the monkeys refractory to electro-ejaculation. Thus the interaction of central nervous system with the gonadal hormones is apparent and the excitability of the genital regions on the one hand and central nervous system on the other hand is influenced by local factors, as well as, circulating hormones.

EFFECT OF SUB-CORTICAL LESIONS ON FEEDING AND EMOTIONAL BEHAVIOUR. By **G.S. Chhina, S. Thomas, H.K. Kang, and B.K. Anand**, *Department of Physiology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi.*

Conflicting reports of the effects of nervous lesions of the caudate nucleus, putamen and globus pallidus on food intake have appeared in the literature. These structures also modify motor and emotional activity. Correlation of these changes with food intake is not defined clearly.

Studies were therefore undertaken to assess the effects of striatal lesions on feeding and emotional behaviour. Normal food, water and salt intake, as well as, emotional behaviour were studied in rats and the effects of localised stereotaxic lesions in the different parts of corpus striatum were observed. The emotional behaviour was determined quantitatively by emotionality rating scale of Brady and Nauta.

There was an increase in body weight of rats with bilateral lesions of the caudate nucleus, but it was not always accompanied by an increase in food intake. In fact in some cases there was no change in food intake, but only an increase in water intake. Unilateral caudate lesions had variable effects which were possibly related to the extent of damage to the other brain areas. Combined lesions of caudate and septal regions, and caudate and hippocampus produced an increase in food intake and body weight, but effects on the water and saline intake were variable.

Animals with lesions in different parts of globus pallidus died of anorexia within a week of the operation. The period of their survival ranged from 2 to 8 days. It was however, possible to make them live beyond this period, and sometimes to bring about complete recovery of food intake by tube feeding the animals.

Increase in the emotional activity was observed in those animals which had an increase in food intake. There was usually a decrease in the emotionality rating accompanying decrease in the food consumption. There, thus, seems to be some relationship between the changes in food intake and emotional behaviour and motor activity.

SOME FURTHER STUDIES ON THE PHYSIOLOGICAL CHANGES IN YOGIS. By **G.S. Chhina, B.K. Anand and Baldev Singh**, *Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Eight meditative and one Hatha Yogi were investigated. The effect of the meditation was recorded on EEG, respiration, heart rate, blood pressure and galvanic skin response. Two of these Yogis employed music for getting into meditation (Nad-Yogis). Since it was not possible to record their responses while they were playing instrumental music, tape-recording of their music was replayed and their responses were recorded when they were listening to their own music. One of these Yogis showed a well-modulated alpha activity which was not blocked by sensory stimuli while he was concentrating. The second subject could not restrain himself from playing and singing music along with the recorded music and therefore his responses could not be investigated. However, when this music was played for another meditative Yogi who

had been exposed to this music previously, he could easily go into meditation and showed well marked alpha activity which was not influenced by various sensory stimuli. Out of the other 6 meditative Yogis-5 showed marked alpha activity which was responsive to outside stimuli to different extents. One Yogi on the other hand showed low voltage, fast activity. In 7 Yogis, there was slowing of respiration and heart rate, fall in B.P., and decreased skin conductance, on the contrary one Yogi showed an increase in all these responses.

One Hatha Yogi, who practised swallowing of acid and nails, as well as, fire walking, showed marked muscle potentials accompanying swallowing and marked alpha activity when he was asked to imagine about his practise of fire-walking or acid-swallowing.

Meditative yogis thus were able to influence their brain functions and autonomic responses during the practice.

EFFECTS OF MID-LOGNITUDINAL SECTION OF PONS ON SLEEP AND WAKEFULNESS. *By M. Mancia T. Desiraju and G.S. Chhina. Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

The influences of brain stem structures on the different phases of consciousness are well known. However, the role of the interconnections of neurones located in the two halves of the brainstem especially at the pontine level in modifying the sleep wakefulness pattern is not clear. In the present study longitudinal cuts of different extents in the mid line of the brainstem, as well as, bilater longitudinal cuts lateral to the midline were carried out in Monkeys. In some of these a part of the cerebellum was also removed, while in others it was just lifted for purposes of transection. Fronto-parietal EEG, neck muscle EMG, and EOG was recorded in these animals for several days continuously with brief rests every 6 hours.

Monkeys having midline sections of pons showed an increase in the total awake period during both night and day. Desynchronised sleep was affected more markedly than the synchronised sleep. In addition a characteristic EEG pattern was observed in some animals, consisting of presence of slow EEG and reduced cervical muscle tone with many slow and rapid vertical eye movement (REMS) resembling REMS of paradoxical sleep. Sometimes a desynchronised REMS of paradoxical sleep. Sometimes a desynchronised EEG with a very low EMG but without ocular movements was also observed. This mixed sleep pattern seems to be a compensatory phenomenon.

NERVOUS CONTROL OF EMOTIONAL BEHAVIOUR IN RATS. *By G.S., Chhina U. Nayar, and B.K. Anand, Department of Physiology, All India Institute of Medical Sciences, New Delhi.*

Changes in motor activity and food intake due to sub-cortical lesions are well known. The quantitative changes in emotional behaviour as a result of these lesions however, are not well documented. The studies therefore were undertaken in rats to assess their emotional behaviour quantitatively by the King's modification of the Brady and Nauta emotionality rating scale. The responses of rats to object presentation, disturbance in the cage, capturing

and handling were thus used to assess the variations in behaviour. Lesions were then made in frontal and temporal cortex, orbital surface of frontal lobes, caudate nucleus, globus pallidus, amygdala, hippocampus and medial eminence of hypothalamus in different rats. Lesions in the orbital surface of frontal lobe, caudate nucleus and amygdala showed a decrease in the emotional behaviour whereas, the lesions in septal region globus pallidus, temporal cortex and medial eminence of hypothalamus resulted in an increase. Damage restricted to hippocampus showed variable changes depending upon the extent of the lesions. The lesions of frontal cortex and sub-cortical regions outside the limbic system did not produce changes in the emotional behaviour of rats. Thus, the variations of different degrees in emotional behaviour can be produced from the nervous structures included in the limbic system.

BENZODIAZEPINE DERIVATIVES AS ANTI-STRESS AGENTS. By **S.R. Dasgupta** and **B.P. Mukherjee**
Department of Pharmacology, Institute of Basic Medical Sciences, University College of Medicine, Calcutta University, Calcutta.

Chlordiazepoxide (CDP), the first psychotherapeutic agent of the 1-4-Benzodiazepine series, with a broad pharmacological spectrum, has been recognized as a "specific agent against anxiety and tension" (1). A possible hypothalamic activity of CZP was reported by workers in this laboratory (2) which led to the investigations of effect of this group of drugs in different conditions of stress. The drugs studied were CDP, diazepam and nitrazepam. The following experimental studies were undertaken :—

The effect of benzodiazepine derivatives on:

- (i) eosinopenia of emotional stress in rabbits.
- (ii) stress induced ulcers in rabbit stomach,
- (iii) acute gastric ulcers in rats put under restraint,
- (iv) cortisone-induced lesions in rat stomach, and
- (v) anti-diuresis produced by nicotine in hydrated rats.

The most important outcome of these investigations was that these benzodiazepine derivatives were found to act in an antagonistic manner to two very important stress hormones, namely, the adrenocorticotrophic (ACTH) and antidiuretic (ADH) hormones. These drugs, however, were found to be ineffective against the effects of cortisone itself. The manner of antagonism of these drugs to ACTH and ADH, however, are not clear from the present experimental data.

In an emotional upsurge there is an increased secretion of both ACTH and ADH(3). The significance of these findings has been discussed and it has been concluded that these benzodiazepine derivatives possessed a strong anti-stress activity.

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STUDIES ON THE EFFECT OF BENZODIAZEPINE DERIVATIVES ON GUINEAPIG 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.

Chloriazepoxide (CDP), (a 1,4-Benzodiazepine derivative), has been reported to be effective in controlling symptoms and anxiety associated with epigastric and abdominal distress, food intolerance, spastic colon and duodenal ulcer in patients refractory to transquillizers and duodenal ulcer in patients refractory to tranquillizers and other medicines. Brown(1) and Rider and Moeller(2) observed remission of symptoms in both hospitalized and out patients with irritable colon, mucous colitis and other functional disorders of the gastrointestinal tract with CDP. CDP was employed by Elia(3) successfully for its calming effect in patients with cardio-spasm. In earlier communications the present authors have reported about the antagonistic activities of CDP and two other Benzodiazepine derivatives (diazepam, nitrazepam) on uterine spasmogens such as oxytocin, acetylcholine, carbachol and 5-hydroxytryptamine (4,5). In the widespread clinical applications of this group of drugs especially in conditions with associated visceral spasm, pharmacodynamic studies on smooth muscle were undertaken in our laboratory. With isolated guineapig ileum preparation it was found that diazepam, nitrazepam and CDP had anti-acetylcholine actions in decreasing order of potency. Similarly, against histamine, they showed the same pattern of antagonistic activity. Similar type of activity was also observed on isolated rabbit intestine. The significance of the findings have been discussed and it has been concluded that these observations may thus provide a pharmacological basis for the clinical effectiveness of these drugs. Moreover, the antistress activity of these drugs reported earlier(6,7,8) may, in addition, help in allaying the anxiety and emotional components associated with functional and neurogenic disorders of the gastrointestinal tract.

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BEHAVIOR OF ISOLATED FROG ATRIA IN SUCROSE MEDIA, By **H.R.K. Arora**, *Department of Pharmacology, Municipal Medical College, Ahmedabad.*

Isolated frog auricles maintained spontaneous contractions and response to electrical stimulation for a substantial length of time in a isotonic sucrose medium. After spontaneous contractions had stopped, these could be restored by changing to an isotonic sucrose 10 MM sodium bicarbonate medium. The response to electrical stimulation after it had been lost restored by changing to an isotonic sucrose medium containing either 10 mM sodium bicarbonate or 10 mM sodium chloride, the former being more effective. An analysis of the time course of changes in sucrose medium suggests that the maintenance of contractility in an electrolyte-free medium is due to the persistence of sodium close to the cell membrane, which is not readily could be removed even by repeated washing or on continuous perfusion with an electrolyte-free medium. Changes in pH markedly influenced the contractile response of atria, specially at pH value below 7.0. The chloride ions exerted an inhibitory effect on the contractile response of atria obtained in the presence of other electrolytes. The bicarbonate and phosphate ions, in comparison to the chloride ion, were more effective in restoring contractility of the frog atria. This effect was independent of the changes in pH. Compared to each other, the bicarbonate and the phosphate ions appeared to be equally effective in restoring the contractile response of the atria. However, the final recovery of atria in Ringer-Locke solution was better after bicarbonate perfusion than after phosphate perfusion.

CHOLINERGIC MECHANISM IN THE BRAIN. By **C.L. Malhotra, V.L. Mehta and S. Prasad**. *Department of Pharmacology, Lady Hardinge Medical College, New Delhi.*

Effect of different doses of chlorpromazine on acetylcholine content was seen after different time intervals on different areas of dog brain under ether anaesthesia. It was seen that both with CPZ 5 mg/kg and 10 mg/kg I.V., there was significant increase in the acetylcholine content of frontal cortex after 45 minutes and with CPZ 10 mg/kg, there was increase in acetylcholine content of frontal cortex both after 45 and 90 minutes, while the variations in the other areas studied were insignificant.

Effect of reserpine (0.5 mg/kg I.V.) on release of acetylcholine from parietal cortex of dog was seen by push pull cannula technique as well as by cup method. With push pull cannula, it was seen that release of acetylcholine was greater with pentobarbitone sodium than with ether, both under control conditions and after reserpine. By cup method, it was seen that the release of acetylcholine from the parietal cortex was less under ether than under sodium pentobarbitone anaesthesia though the difference is not significant. After reserpine, there was significant increase in spontaneous release of acetylcholine from parietal cortex in the first sample though insignificant in successive samples. The release with reserpine was more under ether than sodium pentobarbitone anaesthesia.

PHARMACOLOGICAL STUDY OF COMPOUND II'' By V.S. Murthy, S.L. Agarwal, C.B. Seth, R. Vijayavargiya. *Department of Pharmacology, M.G.M. Medical College, Indore, M.P.*

Effect of compound II was studied on neuromuscular junction and on the cholinesterase activity by Warburg's technique.

Compound II in low doses (1-2/ $\mu\text{g/ml}$) potentiated the acetylcholine induced contractures on frog rectus abdominus muscle. It caused potentiation of indirectly as well as directly stimulated twitch responses of phrenic nerve diaphragm preparation of rat, and lowered the tetanic threshold in doses of 10 $\mu\text{g/ml}$.

In higher doses 50/ $\mu\text{g/ml}$., it caused inhibition of acetylcholine as well as KCl induced contractures of frog rectus and also of all the directly as well as indirectly stimulated twitch responses of phrenic nerve diaphragm preparation.

The potentiation was due to anticholinesterase activity of compound II as it did not occur where cholinesterase was inhibited by eserine before using compound II.

Invitro studies on cholinesterase activity confirmed that compound II inhibits true and pseudocholinesterase and it is as potent as neostigmine though has a short lasting effect than the later.

MECHANISM OF PROLONGATION OF BARBITAL AND CHLORALHYDRATE ANAESTHESIA IN MICE. By N.M. Tiwari, K.J. Namaji, B.K. Joshi and N.L. Sadre. *Department of Pharmacology, Medical College, Miraj*

Chloral hydrate anaesthesia has been shown to be potentiated by histamine and chlorpromazine (Sadre and Tiwari). The effect of pretreatment with histamine and chlorpromazine shows summation of potentiation effects. It was thus inferred that mechanism is not due to antihistaminic action of chlorpromazine. Adrenaline depleting agents-reserpine guanethidine, alpha methyl DOPA, tyramine and bretylium tosylate in suitable doses were injected in mice and the potentiation effect studied. The results highly suggest that the potentiation effect may be related to adrenaline depleting action.

EFFECT OF ANABOLIC STEROIDS AND ADRENALINE DEPLETING AGENTS ON INSULIN INDUCED HYPOGYCAEMIA By N.M. Tiwari, K.J. Namaji, B.K. Joshi and N.L. Sadre. *Department of Pharmacology, Medical College, Miraj*

Reserpine and chlorpromazine have been shown to potentiate insulin induced hypoglycemia (Tiwari et al). It was inferred that this may either be due to adrenaline depleting action or some other action. A screening study or pretreatment with anabolic steroids and adrenaline depleting agents in potentiating insulin induced hypoglycaemia in rats shows that the mechanism of potentiation of insulin induced hypoglycemia is not due to its adrenaline depleting action or anabolic action.

BLOCKADE OF SYMPATHOMIMETIC AMINES ON ISOLATED AURICLES. By **N.M. Tiwari, K.J. Namaji, B.K. Joshi and N.L. Sadre.** *Department of Pharmacology, Medical College, Miraj*

Effect of chlorpromazine, prochlorpromazine, chlorpheniramine and antazoline methane sulfonate on chronotropic responses of sympathomimetic amines on isolated rat atria were studied. It was observed that chlorpromazine and other antihistaminics depress the chronotropic responses of the rat atria to sympathomimetic amines but chlorpromazine alone produces marked depressant effect on the nodal activity and its effects are not washed out by change of Ringer solution. Other antihistaminics used do not produce such depression of nodal activities. Antazoline methano sulphate produces potentiation of chronotropic response of rat atria to adrenaline. All the above drugs have an established antiarrhythmic action. It is thus inferred that antiadrenaline effect is not correlated to their antiarrhythmic effects.

EFFECT OF INTRA-CEREBROVENTRICULAR ADMINISTRATION OF NICOTINE AND ISOMETHYL NICOTINUM BROMIDE ON THE ACETYLCHOLINE CONTENT OF THE RABBIT BRAIN By **I.C. Bhattacharya.** *Physiology and Pharmacology Laboratories, Department of Pharmaceutics, Banaras Hindu University, Varanasi*

In a previous study of the central effects of nicotine it was postulated that similar to its effects on the peripheral nervous system, the central responses originate through involvement of some cholinergic mechanism in the CNS. Acute intraperitoneal injections of nicotine produced a higher acetylcholine (Ach) content in the rabbit brain after single and repeated administrations.

In the present study the level of Ach content in the rabbit brain after acute and chronic intra-cerebroventricular (ICV) injections of nicotine hydrogen tartrate (Nic) and isomethyl nicotinum bromide (IMN) have been estimated and compared with the effects of i.v. and i.p. injections. A single i.v. injection of Nic 200ug/Kg increased the Ach content by 342.5 per cent after 20-30 min. Administration of 100 ug into the left lateral ventricle showed a similar quantitative increase. IMN was less effective in altering Ach content after i.v. or ICV injections. Atropine pretreatment 5mg/kg i.p., 15 min. before Nic injections, was ineffective in blocking the increase of Ach while 20mg/Kg i.p. blocked the increase by i.v. injections but was only about 50 per cent effective against ICV injections. A dose of 5mg/Kg i.p. of atropine methyl nitrate was ineffective in blocking the Nic effect. Subcutaneous injection of eserine 0.1 mg/Kg increased the Ach content by 43.6 3.1 per cent. An ICV injection of 100ug serine produced quantitatively similar effect as Nic but was quicker in increasing the Ach levels. Similar values were obtained when 100ug ICV administration of Nic was followed by an ICV injection of eserine 100ug. However, when three such injection of Nic were administered after every 15 min preceded by a single ICV injection of eserine, the Ach content was raised significantly and compared well with the effect of 0.5mg/Kg i.v. Nic. These results have been compared with the effect of Nic on acute and chronically treated rat brains. The study indicates the possibility that Nic, like eserine, releases Ach from the presynaptic region probably from the synaptosomes. It may also inhibit the ChE or decrease the sensitivity of the receptors for binding and uptake process of liberated or newly synthesised Ach.

THE EFFECT OF PROTEIN MALNUTRITION ON ENDOCRINE GLANDS IN YOUNG MALE AND FEMALE ALBINO RATS By **R.N. Banerjee, J. Nacchaudhuri, T.C. Gupta,*** *Department of Physiology College of Medical Sciences, Banaras Hindu University, Varanasi*

The present investigation had been undertaken to study the effect of protein deficiency, produced by 5% casein (animal) and 5% ground nut flour (vegetable) diets on the different endocrine and sex glands in young male and female albino rats. Weekly body weight of the animals were recorded. One group of animals were sacrificed at the end of 2 weeks of treatment and the other at the end of 4 weeks. The fresh weight of the adrenal, thyroid, pituitary, testes, prestage, seminal vesicles, ovary and uterus had been recorded and their histological study had been done. It was observed that during protein deficiency there was significant fall in the growth of the animals. Also some significant changes in the weight and histological structures of the above mentioned tissues were also observed. It was observed that the deleterious effect of protein deficiency was more pronounced in 4 weeks series and markedly in 5% ground nut flour fed animals. The female animals were more susceptible to this protein depletion than male. Histologically it was observed that these glands were atrophied and disorganised. Particularly the primary and accessory sex organs were more susceptible to protein malnutrition in comparison to other endocrine glands. Blood glucose, serum inorganic phosphate and total cholesterol level and electro-phoretic pattern of the serum protein fractions of these animals were also studied. A significant fall in total cholesterol and albumin was observed in the sera of the deficient animals.

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