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ABSTRACTS

CHANGES INDUCED IN BLOOD BASOPHILS BY CIGARETTE SMOKING.

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The cytological features of basophils in the peripheral blood were studied in twenty-seven healthy young male smokers before and ten minutes after the smoking of one to two cigarettes. Basophils were collected and concentrated from capillary blood samples using a millipore membrane filter and stained with toluidine blue. These cells were then classified into distinct categories. according to the staining characteristics and location of their cytoplasmic granules. This classification enabled us to differentiate the intact cells from the degranulated cells. A significant decrease ($P<0.001$) in the intact cells with a significant increase ($P<0.001$) in the degranulated cells was observed after smoking. Since basophil granules contain among other substances, histamine, which is a bronchoconstrictor agent, it is suggested that this might be a mechanism by which the immediate bronchoconstrictor response to cigarette smoking is mediated.

INTRACRANIAL CHANGES FOLLOWING HYPEROSMOLAR BICARBONATE INFUSION IN DOGS.

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Routine bicarbonate therapy has come into widespread use in correcting the acidosis especially in neonates and children. Though the acidosis is corrected, the controversy still exists as to the nature of the changes which occur in the brain and whether such changes are irreversible or not. Experiments were conducted in normal and hypoxemic dogs using both hypertonic $NaHCO_3$ (7.5%) and isotonic solution of Nacl (0.9%) by rapid and slow infusion. Blood was drawn before and after one hour for haemoglobin, hematocrit and serum electroytes. Autopsy and histopathological studies of the brain were done after the end of the experiments. It has been observed that hypertonic infusion in normal animals produces massive edema predo-

minantly in white matter. No haemorrhages were seen in slow infusion therapy, whereas in hypoxic animals it seems to aggravate the pre-existing damage.

Hypoxia and acidosis produce haemorrhages in the brain, hypertonic infusions further damage the brain if rapidly given. So one has to be cautious while correcting the acidosis with hypertonic solution.

MECHANISM OF GLUCOSE INDUCED INSULIN SECRETION. **S. Gunasekaran and P. Zachariah.** *Department of Physiology, Christian Medical College, Vellore.*

The specific role of glucose metaboslism in the different phases of glucose induced insulin secretion was studied in monkey islets isolated by modification of the collagenase digestion technique. The inhibition of glucose (300 *mg*%) induced insulin release by two inhibitors of glucose metabolism, viz. 2-Deoxy D-glucose (2DG) and D-Mannoheptulose (MH), was studied at time intervals corresponding to the well known initial and later phase of insulin release. The inhibitory concentrations of 2DG and MH were 100 to 300 *mg*% and 50 to 200 *mg*% respectively. By monitoring insulin secretion in four successive 15 minute periods, 2DG was found to inhibit the response to glucose nearly 40% in the first 15 min and by about 80% in the subsequent intervals. Similarly MH was found to inhibit the response to glucose by nearly 60% in the first 15 min and by about 85% in the subsequent intervals. These observations suggest that the initial and later phases of glucose induced insulin secretion have different characteristics. The later phase is more dependent on glucose metaboslim, whereas there is an important non-metabolic (probably glucoreceptor) component in the initial phase.

INTERSPECIFIC EFFECTS OF CRUSTACEAN HYPERGLYCEMIC HORMONE. **P. Sreenivasulu Reddy A. Bhagyalakshmi and R. Ramamurthy.** *Department of Zoology, S. V. University, Tirupati.*

The mode and site of action of hyperglycemic hormone in the eyestalks of crustaceans are well known. Our earlier work demonstrated interspecific action of curstacean hypergycemic hormone when tested on scorpions, insects and slug. The present work was undertaken to test the effect of hyperglycemic hormone obtained from crab, *Oziotelphusa senex senex* and prawn *Penaeus monodon* on some aspects of carbohydrate metabolism in the snail *Pila globosa*.

Administration of crustacean hyperglycemic principle significantly increased hemolymph sugar level and tissue phosphprylase activity in the snail. Tissue glycogen

registered a significant decrease which indicated that the source of hyperglycemia was the tissue glycogen. The results conclusively prove that the crustacean. hyperglycemic principle exerts influence on non-crustacean species also.

PREPARATION AND POST–OPERATIVE MANAGEMENT OF THIRRY–VELLA FISTULA IN THE ALBINO RAT. **R. E. Mendanha and K. N. Sudha.** *Department of Physiology, St. John's Medical College, Bangalore.*

The use of the rat Thirry-Vella (TV) loop model has many advantages over that of a dog. The emphasis of this paper is on the post-operative management and the procedure involved in ensuring maximum effectiveness of the preparation for a long period of time. These 12-15 week old Wistar strain rat of either sex were anaestetised by intraperitoneal injection of pentobarbitone sodium (30 *mg/kg*) for induction and maintained on ether. Through a midline abdominal incision a segment of the jejunum with the blood supply was isolated. The continuity of the intestine was restored by end to end anastomosis using 6/0 chromic catgut and continuous Lembert stitch. All the three layers of the intestine were sutured as one and a reinforcing layer of sutures were used. The two ends of the loop were exteriorized through 2 stab wounds on the anterior abdominal wall. The lips of the loop were widened, everted and stitched to the underlying fascia.

Post-operatively the animal was housed in a clean plastic cage and was fed with milk and glucose for 3 days. Subsequently it was fed on fine powdered chow, mixed with water. No post-operative antibiotic was used routinely. Saline was infused everyday in the direction of peristalsis using a No. 12 Foley's catheter. This keeps the loop patent preventing clogging by intestinal secretions. The success rate of the procedure was 74%. Two animals died due to breakdown of anastomsis, two died to post-operative infection, one due to possible thrombosis.

EFFECT OF IMMOBILIZATION STREES ON THE HIPPOCAMPUS OF *CALOTES VERSICOLOR*. **J.H. Sharieff, S. Kamath and Mahadi Hasan.** *St. John's Medical College, Bangalore and Brain Research Centre, J. N. Medical College, Aligarh Musium University, Aligarh.*

Twelve male Calotes versicolor in the range of 60–65 *gms* weights (6 control+6 experimental) were selected. Each animal was subjected to immobilization on a self designed wooden plank fitted with nails for securing for a duration of 24 hours. Animals

were sacrificed at the end of this period by perfusing through the heart with 10% Formalin/ Bouin's Solution under light chloroform anaesthesia. The gastric muscosa was examined for the appearance of ulcers. The brain with pineal complex was dissected out, processed and sectioned serially at 6 u thickness. It was stained with : 1) Haematoxylin and Eosin, 2) Kluver Borrera, 3) Gomori's Chrome - Alum and Haematoxylin and Phoxlin and 4) Acetic thionin.

On studying the hippocampus, hypertrophy of the nuclei, accumulation of dense granules in axon hillock, and chromatolytic changes in the neurons were observed. Karyometrical study revealed increase in the size of nuclei of hippocampal neurons.

INFLUENCE OF AGE, SEX AND GROUPING ON CIRCADIAN VARIATION OF OXYGEN CONSUMPTION AND FOOD UTILIZATION IN *TILAPIA MOSSAMBICA* PETERS. **K. Nagarajan and V. Gopal.** *Division of Neurophysiology and Behaviour, Madras University PG Centre, Coimbatore.*

An animal is physiologically different organism at different stages of its life time. The changes in the physiological components of the body, infact, are the main causes for the aging in animals. There are reports in fowls and rats that sex is an influencing factor in modulating the circadian body temperature (Gopal and Srinivasan, 1979, Gopal and Indira, 1980). Apart from this, evidences are also available to show that the animal's behaviour is influenced by the interaction of another individual (Muller, 1978).

The fish *Tilapia mossambica* exhibits a differential pattern of oxygen consumption rhythm during different stages of its life time. The rates of feeding, absorption and conversion are decreased with increasing body weight on the fish. The pattern of oxygen consumption, rates of feeding, absorption and conversion are relatively unaffected in both the sexes of *T. mossambica.* When the fish is grouped along with its fellow individuals, it consumes comparatively more oxygen and food; but no significant difference in the conversion rate is observed. The results are discussed in the light of biological rhythms and economic considerations of fishing industry.

EFFECT OF IMMOBILIZATION STRESS ON THE PINEAL GLAND OF *CALOTES VERSICOLOR*. **J. Sharieff, S. Kamath and Mahadi Hasan.** *St John's Medical College, Bangalore and Brain Research Centre, J.N. Medical College, Aligarh Muslim University Aligarh.*

Twelve male Calotes versicolor (6 control + 6 experimental) weighng in the range

60 – 65 *gms* were selected. The animals were subjected to immobilization stress on a self deviced wooden plank for a duration of 24 hours. At the end of the period, the animals were sacrificed under light chloroform anaesthesia. Perfusion through the heart with 10% Formalin/Bouin's Solution was done. The gastric mucosa was examined for the presence of ulcers. Brain with pineal complex was removed and sectioned serially at 6 u. The successive slides were stained with : 1) Haematoxylin and Eosin 2) Kluver Barrera, 3) Gomori's Chrome – Alum and Haematoxylin and Phloxin and 4) Acetic thionin.

Hyperaemia of the gland and paraglandular accumulation of tissue which appeared to be adipose tissue were seen. No nuclear changes were observed.

PHYSIOLOGICAL SALINE FOR WHIP–SCORPION, *THELYPHONUS INDICUS*, STOLICZKA. **K.P. Rajashekar and Geetha Bali.** *Department of Zoology, Bangalore University, Bangalore.*

Whip - scorpion is an interesting specimen for neurophysiological studies because of the specialised behavioural traits exhibited by the animal and also due to the presence of specialised structures such as the central nervous system often needs dissected preparations and the use of physiological saline is indispensable for such studies.

Cellfree haemolymph of whip - scorpion, *Thelyphonus indicus*, was analysed for its major inorganic constituents. The concentrations of Na and K were estimated by flame photometry and the concentrations of Ca and Mg were estimated by atomic absorption spectrophotometer Chloride content was measured by the method of Van Slyke (1913). The pH was found to be 7 60. On the basis of these determinations, physiological saline was formulated. The pH of the saline was adjusted with Tris - HCl buffer.

The concentrations of various ions studied in the heamolymph of *T. indicus* as well as the haemolymph pH fall within the range of concentrations and pH values reported earlier for other arachnids.

STRUCTURAL CHANGES IN THE DENERVATED SARTORIUS MUSCLE OF FROG *RANA CYANOPHLICTIS*. **R. V. Krishnamoorthy and V. V. Subrahmanyam.** *Department of Zoology, University of Agricultural Sciences, GKVK Campus Bangalore.*

Electron micrographs of the ultra-thin (500 A) sections of the sartorious muscle of the frog showed subtle differences in the sarcomere pattern. Z-band organization

and interfibrillar position with reference to surgical denervation for one month. These changes were manifested when the sciatic nerve root was deprived in one leg of the frog, and when the innervated contralateral leg was used as control. The biochemical composition of the denervated muscle also showed significant changes. The collagenous proteins increased in content. The GTPase, ITPase and NTPase activities of the myosin were reduced Ca^{++}-binding properties of the muscle sarcoplasmic fraction increased on denervation; the Myosin/Actin ratios significantly increased. Lesser myosin with reference to actin content was noticed as indicative of denervation atrophy. The dense inter fibrillar patches observed in the micrographs in denervated muscle sections were correlated with increased alkali - soluble collagenous proteins.

ROLE OF CORTICOSTEROIDS IN THE METABOLISM OF VITAMIN B_6. **S. David and G. D. Kalyankar.** *Department of Biochemistry and Biophysics, St. John's Medical College, Bangalore.*

A close metabolic interrelationship between corticosteroids and vitamin B_6 is seen, in that the adrenocortical insufficiency increase the requirements of vitamin B_6. Many of the derangements of adrenocortical insufficiency (adrenalectomy) with respect to aminotransferases, amino acid decarboxylases glucose homeostasis could be minimized when the adrenalectomized rats are fed diet with excess B_6 (This conference, Sept 1980). Further studies showed that in adrenocortical insufficiency there is rapid decrease in the concentration of tissue B_6–compounds and decrease in vitamin B_6 metabolizing enzymes. They are (a) pyridoxol–kinase (pyridoxine–5'–phsphate synthesizing) and (b) pyridoxol–5'–phosphate oxidase (pyridoxal–5'–phosphate synthesizing). Many of these changes could be reversed by either feeding excess B_6 (2.0 *mg/rat/day*) or injecting corticosterone (2.5 *mg/rat* on alternate days). The data show the dependence of vitamin B_6 metabolism and its tissue retention on the adrenal status of the animal.

AGE RELATED EFFECT OF NUTRITIONAL PYRIDOXINE DEFICIENCY ON BRAIN FREE AMINO ACIDS OF THE GLUTAMATE GROUP. **T.S. Rajeswari and E. Radha.** *Department of Zoology, Bangalore University, Bangalore.*

Pyridoxine deficiency was induced in male rats aged 1 day (group 1) 21 days (group 2), 3, 12 and 24 months (groups 3, 4 and 5 respectively). Deficiency in all the groups studied resulted in significant decreases ($P < 0.001$) in the level of glutamic acid – 34% in groups 1 and 5 and 29%, 27% and 30% respectively in groups 2, 3 and 4. The level of GABA was more affected by the deficiency at all the ages compared to glutamic acid. Of the 5 groups, 2 and 3 appeared to be more resistant to deficiency showing

49% and 43% deficits while maximal deficit of 64% was observed in group 1 and 57% and 59% in groups 4 and 5, all the differences being highly significant ($P < 0.001$). Level of glutamine showed a highly significant 37% ($P < 0.001$) decrease in group 1 and a small but significant ($P<0.05$) 7% decrease in group 2. The other groups were not affected significantly. In the case of aspartic acid, deficits of 45% and 48% were observed in groups 1 and 2 and 23%, 33% and 30% in groups 3, 4 and 5. No significant age difference was observed for alanine – all the age groups showed significant increases of 23 to 28%. The ratio of glu. + asp./GABA + ala. decreased by 14% in deficient animals of group 1, by 9% in groups 2 and 3 and by 4% and 7% in groups 4 and 5. The results are discussed with reference to the importance of age in nutritional studies.

CORTICOSTEROID VITAMIN B_6-DEFICIENCY AND GLUCOSE HOMEOSTASIS. **G.D. Kalyankar, S.M. Saldanha and Usha Anand.** *Department of Biochemistry and Biophysics, St. John's Medical Collge, Bangalore.*

It has been shown that Vitamin B_6 - deficiency brings about changes in the adrenal functions, in that there is decrease in the secretion of corticosteroids and catecholamines and change in the ratio of E/NE. Further, there is decrease in the blood glucose level, glycogen and increase in muscle glycogen. These effects are reversed when these B_6 – deficient animals are fed either with excess B_6 or injected with corticosterone (Saldanha and Kalyankar, Reg. Conf. Abstracts, Sept. 1980). The work was extended to study the glucose homeostasis under adrenalectomized conditions. It was observed that in adrenalectomy (120 hrs after adrenalectomy) the blood glucose level decreases to 55.5 *mg/dl* from 88.0 *mg/dl* in normals. there is decrease in liver phosphorylase activity (733 $\mu g/g$ in controls to 488 $\mu g/g$), decrease in liver glycogen but increase in muscles. These changes of adrenalectomy are kept at normal levels or marginally increased by feeding-the adrenalectomized rats with added B_6 diets (2.0 *mg/rat/day*) or injecting corticosterone (2.5 *mg/rat* on alternate days). The data supports our earlier observations that vitamin B_6 status may influence glucose homeostasis.

EFFECT OF COLD ACCLIMATION ON THE ASCORBIC ACID CONTENT OF THE DENERVATED FROG MUSCLES. **T. Somasekhar and R. V. Krishnamurthy.** *Department of Zoology, University of Agricultural Science, GKVK, Bangalore.*

An attempt has been made to study the denervation atrophy with reference to cold acclimation in the selected muscles of frog *Rana cynaophlictis*. When denervated frog were adapted to cold significant retardation of atrophy in the muscles was noticed. The total Ascorbic acid (ASA) content increased on denervation in both sartorius and gas-

trocnemius muscles irrespective of cold adaptation. It is found that cold acclimation as well as denervation commonly increases the ASA levels in the muscles. Accumulation of of Ascorbic acid increased with progressive atrophy in both gastrocnemius and sartorius muscles of frogs maintained only at lab-temperature. But cold acclimation manifested in a different effect, in such a way that the relationship between the Ascorbic acid increase and muscle atrophy differed with the type of muscle. This progressive atrophy rapidly fell on cold acclimation in the case of sartorius muscle; in gastrocnemius it described a bell-shaped curve. The optimum ASA levels were obtained in gastrocnemius muscle when the muscle atrophy showed 3.5 per cent atrophy in the cold acclimated frogs.

The significant reduction in the denervation atrophy and changes in accumulation of ASA levels in the denervated muscles of frog on cold adapatation were discussed in the light of neurotrophic factors in the atrophying muscle.

LIPOPROTEIN PROFILE IN EXPERIMENTAL DIABETES. **P. T. Annamala and K.T. Augusti.** *Department of Biochemistry, University of Kerala, Trivandrum.*

Concentration of cholesterol in different lipoportein fractions were determined in alloxan diabetic rabbits treated with glibenclamide, tolbutamide and insulin. HDL - LDL and VLDL-cholesterol are found to be elevated in diabetic animals as compared to normal controls. Diabetic animals, on treatment with glibenclamide and toblbutamide showed a considerable decrease in the cholesterol concentration in all the lipoprotein fractions but the HDL/LDL cholesterol ratio, which is considered important in the development of cardiovascular complications, decreased significantly. On the other hand, insulin treatment resulted in a decrease in the cholesterol levels and an increase in the HDL/LDL cholesterol ratio. The effect of sulphonylureas on the HDL/LDL cholesterol ratio may probably explain the increased cardiovascular complication in diabetes treated with hypoglycemic agents.

EFFECT OF ACUTE STARVATION ON PROTEIN BINDING OF ACETYLSALICYLIC ACID. **Chanda Kulkarni, C. Adithan and Thangam Joseph.** *Department of Pharmacology, St. John's Medical College, Bangalore.*

This study was undertaken to investigate the effect of acute starvation (12, 24, 48 & 72 hrs) - on serum protein binding of Acetyle–Salicylic–acid (ASA). 120 albino rats of either sex were divided into groups of (15 control and test for each period of starvation. 1.5 *ml* of pooled serum (3 rats, of control and starved rats were subjected to equilibrium dialysis for ascertaining the protein binding of ASA. In addition the sera of the two groups were analysed for free fatty acids (FFA), total proteins (TP) and albumin

(Alb). FFAs increased during starvation though TP and Alb remained unaltered. Significant reduction in protein binding was observed with increase in FFA, however the relationship was not linear.

ORTHO—BETA—HYDROXY—LETHYL RUTOSIDE ON INCISION AND EXCISION WOUNDS. **Prakash V. Diwan and Dhruvaraj R. Kulkarni.** *Department of Pharmacology, J.N. Medical College, Belgaum.*

The phytochemical study of herb (tridax procumbens) revealed that it is rich in flavonoids. This plant had shown pro-healing property. Therefore, it was planned to observe the influence of a pure bioflavonoid on wound healing.

The incision and excision, dead space wound models in guineapigs and rats respectively were chosen for the study of rutoside. The tensile strength (incision wounds) in saline group of animals was 160.00 $\pm$ 11.9 *gms* while in the flavonoid animals, it was 236.00 $\pm$ 10.70 *gms*. The increase in the tensile strength by flavonoid is statistically highly significant ($P < 0.001$). Rutoside has failed to favour the excision wound healing studies. However, the early phase of healing has been influenced, i.e., upto 15 days. The study on dead space wound reveals that rutoside has an anti-inflammatory action. The importance of pro-healing properties of flavonoid will be discussed.

EFFECT OF ACUTE STARVATION ON PROTEIN BINDING OF PHENYLBUTAZONE IN RATS. **Babu S. Nema, C. Adithan and Thangam Joseph** *Department of Pharmacology, St. John's Medical College, Bangalore.*

Phenylbutazone is a drug with high protein binding capacity. It has been reported earlier that increasing fatty acids of serum *in vitro* decreases the protein binding of pheynlbutazone. It is well accepted that free fatty acids increases during starvation. Hence this study was undertaken to investigate the relationship between the protein binding of phenylbutazone and the increase in free fatty acids during starvation. Experiments were conducted in rats divided into two groups control and starved for periods of 12, 24, 48 and 72 hours. Though there was an increase in free fatty acid levels of serum during starvation, the protein binding capacity of Phenylbutazone was not affected. Neither the total protein and Albumin concentrations of serum were affected during acute starvation. The implications are discussed.

MONOCOMPONENT INSULIN (MC) IN DIABETES MELLITUS. **Mercy Paul, C.M. Joseph, S.S. Kumar and C.B. Sridhar.** *Department of Medicine, St. John's Medical College Hospital, Bangalore.*

Twelve Juvenile Diabetics admitted to the Medical Unit II of St. John's Medical College Hospital were given the benefit of therapy with MC insulin (Monotard). These patients were fully evaluated with the conventional tests; add complications associated with Diabetes were excluded. Diet instruction was given with the help of dietician; and, they were trained to take their own injection; and, test urine for sugar when in the ward. They were commenced on lente insulin; and dose increased depending upon value checked at 4 p.m. All the twelve patients received lente insulin in the dose ranging from *70 to 96 units* with a mean of around *84 units*. This brought down the blood sugar from *700 - 800 mg%* (*mean 740 mg%*) to *180 to 220 mg%* (*mean of 210 mg%*).

After explaining to the patient the insulin therapy was discontinued under observation for the next few days. Over the subsequent 3 to 5 days, the blood sugar rose upto an average of above *500 mg%*. The patients were commenced on M.C. insulin (Monotard) starting from 10 units/day, gradually increasing the dose till the Random Sugar value tested around 3 to 4 p.m. showed a mean value of *200 mg%*. This was achieved over a period of 5 to 7 days on an insulin dose ranging from 24 units to 30 units/ (mean *28 units*) days given as a single dose in the morning. On this dose they did not reveal rising trend in blood sugar over the next 3 weeks period.

To conclude, in this preliminary communication we have shown that the severity of Diabetic State as regards Hyperglycemia can be brought under an effective, control with Monocomponent insulin on one-third the dose of conventional lente insulin.

M.C. insulin (Monotard) was generously supplied by Messrs. Ranbaxy (Pvt.) Ltd, Sole distributors for M.C. Insulin Novo Industries, Denmark.

INFLUENCE OF INDOMETHACIN ON TOLBUTAMIDE HYPOGLYCEMIA. **Prakash V. Diwan, Laxman D. Tilloo and Dhruvaraj R. Kulkarni**. *Department of Pharmacology, J.N. Medical College, Belgaum.*

Maturity onset diabetics who are on tolbutamide may be required to take anti-inflammatory agents sometime or other. Anti-inflammatory agents such as aspirin, phenylbutazone potentiate the hypoglycemic effect of toblbutamide. In the present

study, the interaction between non-steroidal anti-inflammatory agent (indomethacin) and tolbutamide was investigated.

The study was done in normal rabbit of either sex weighing between 1.5 to 1.75 *kg*. Animals were fasted for 18 hrs but were allowed water. Some animals received indomethacin 5 *mg/kg* p.o. and remaining received only the vehicle. An hour later, all the animals received tolbutamide 250 *mg/kg* p.o. Four hours later, the blood samples were collected. The blood sugar was estimated by the method of Follin Wu. The percent decrease in fasting blood glucose level was noted.

In tolbutamide treated animals (n=9) there was 25.46 ± 2.85% reduction in blood sugar level from the fasting levels, whereas, in animals receiving both indomethacin and tolbutamide (n=12), the percent decrease was 14.08 ± 3.92. These results clearly show that indomethacin has interfered with hypoglycemic action of tolbutamide.

EFFECTS OF SUMITHION ON INORGANIC CONSTITUENTS IN THE FRESH-WATER APPLE SNAIL, *PILA GLOBOSA* SWAINSON. **M. Balavenkatasubbaiah, A. Bhagyalakshmi and Ramanurthi.** *Department of Zoology, S.V. University, Tirupati.*

The lethal (Lc_{50}/48 hrs=2 ppm) and sub-lethal (1 & 7 day periods=0.2 ppm) concentrations of sumithion (Fenitrothion: O-O dimethyl 3-methyl-4-nitrophenyl phosphorothiate) exposure caused significant changes in the ionic composition (Na^+, K^+ and Ca^{++}) of the tissues of the snail, *Pila, globosa*. In the haemolymph all the three ions registered a significant increase whereas in hepatopancreas except sodium, the other ions were decreased after sumithion exposure. In the foot muscle also all the three ions were decreased. The significance of these changes in the ionic composition in the tissues of sumithion exposed snails are discussed in the light of literature available.

APPLIED MELOTHESIA: TIME FACTOR IN PHYSIOLOGY AND MEDICINE. **C.S. Narayana Setty.** *Department of Physiology, Ambedkar, Medical College, Bangalore.*

Melothesia as per Encylopaedia Britannica (Vol-II 1961 Edition), refers to Cosmic Physiology. Moon rotates around its own axis (28 days) and around the Earth (29.5 days) constituting New Moon and Full Moon. The earth rotates around the Sun (365 days) generating seasons. Earth rotates on its own axis, causing Day-night cycle. Among others Biorhythms offer evidence in favour of melothesia. There are day-night, seasonal, 11.3 years, motonic (19 years period) cycles. Each of them affects living orga-

nisms. Day--night cycle affects human body function. Time is generated by earth rotation. The body function vary during this period quantitied by Acrophase (maximum intensity at a particular time). The period of Circadian rhythm is 22–28 hours. In the human, EEG, epidermal mitotic rate, urinary chemicals, Blood Cells and electrolytes, body temperature, plasma constituents, Body physical vigour, weight, Heart rate, Blood pressure, Expiratory Peak flow rate, Respiratory Rate, Blood microfilarial count, tooth pain, birth death due to surgery (Accidents and miscellaneous causes), Absorption of certain drugs, Immunisation effectiveness, Digestive enzyme activity have all been shown to follow a circadian rhythm. Disturbances of human circadian rhythm manifest as 1) Jet fatigue, in transmeridianal flights across several time zones, 2) Morbidity in shift workers unable to adjust to the schedule. In these two cases, the environment and body are out of phase, 3) Insomnia (day-night cycle disturbed) 4) lack of mitotic rhythm in early cancer, 5) MLD_{50} of certain drugs, toxins threshold of audiogenic seizures, effect of Anoxia, differs at 8 A.M. and 6. P.M. 6) Asthma, histamine reaction and night mares are common during nights when the cortisol in the body is at the lowest. 7) Epileptic seizures in human as investigated from hospital records cluster towards morning. Traditional belief describe increase in epileptic seizures on days of full moon and new moon.

SPHINCTERIC MECHANISMS OF THE TERMINAL PORTION OF THE PAROTID DUCT AND THEIR ROLE IN THE ETIOLOGY OF PAROTITIS AND PNEUMOPAROTITIS.

Warren D. Lobo and Sylvia Kamath. *Department of Anatomy, St. John's Medical College, Bangalore.*

A study of the terminal portion of the Parotid duct was undertaken for the possible presence of a Sphincteric mechanism which may play a role in the prevention of regurgitation of air and infective material into the parotid system in the normal individual during increased intra-oral pressures. Two cases of Pneumoparotitis were subjected to (a) Clinical & (b) X--Ray Examination. The terminal 1 cm of the Parotid ducts in 6 cadavers was studied histologically. A study of the prevalance of Parotitis in relation to oral hygiene was carried out in a rural community.

From the study it is concluded that no intrinsic involuntary sphincter is present and the duct appears to be closed at all times by both the tone of the buccinator muscle and active contraction of the muscle. Flow of saliva through the duct is due to mounting pressure in the parotid gland which overcomes the tone of the "Buccinator Sphincter".

Damage to the "buccinator sphincter" may be responsible for the regurgitation of air and infective material into the duct, resulting in Pneumoparotitis and recurrent bacterial parotitis.

FINGER CLUBBING - ITS QUANTIFICATION AND SIGNIFICANCE IN GASTRO-INTESTINAL MALIGNANCIES. **V. Srinivas, V. Jayanthi, R. Chandrasekar and G. Krishnamurthi**, *Department of Physiology, Kilpauk Medical College, Madras.*

Clubbing is an invaluable clinical sign occurring in many diseased states, particularly characteristic of certain pulmonary and circulatory disorders. A rapid simple device to quantify the degree of clubbing has not been successfully attempted so far.

An instrument named "CLUBBOMETER" has been devised in this project to provide quantitative measurement of the hyponychial angle and profile angles from which the angle of nail elevation can be calculated.

A fully developed "Clubbometer" is a protrator over which a rotatable angle marker is fixed. The protractor is calibrated in degrees. A convex lens is used for magnification.

The measurement of the angle of nail elevation was found for all the ten fingers of the two hands in 30 normal individuals including 12 male and 18 females (about 600 readings repeated twice by two different observers).

The measurement were repeated similarly in 26 patients (18 males and females) suffering from malignancy of the gastro-intestinal tract. In this condition not complicated by circulatory and respiratory disorders, the angle of the nail was elevated greatly in all the fingers and more than 100% in most of the 8 fingers. The significance of the findings are presented for discussion

EFFECT OF MEAL-TIME RESTRICTION ON WATER INTAKE. **V. N. Prabhu, A. Thomas and B. S. Rao.** *Department of Physiology, St. John's Medical College, Bangalore.*

Two groups of adult male rats housed in individual cages are used. Gr. I was free feeding whereas Gr II feeding time was restricted to 3 hr. Both groups had *ad lib* water. Gr. I water intake in 3 hr (2.3±0.15 *ml*/100 *gm* bw) and in 24 hr (14.1 0.2 *ml*/100 *gm* bw) was directly proportional to respective 3 hr (1.8±0.06 *gm*/100 *gm* bw) and 24 hr (12.3±0.13 *gm*/100 *gm* bw) food intake as indicated by water-to-food (w/f) ratio (3 hr, 1.3±0.02, 24 hr 1.2±0.09). Gr. II 24 hr w/f

(1.4±0.04) was similar to Gr. I w/f. However, Gr II 3 hr w/f (0.5±0.02) was decreased because increased food intake (9.4±0.19 *gm*/100 *gm* gw) was unattended by matching increase in water intake (4.6=0.14 *ml*/100 *gm* bw). Results indicated temporary attenuation of Gr. II 3 hr food-induced thirst and hence delayed water intake. However, normal ADH release simultaneous with thirst may have decreased Gr II urine output (0.6±0.08 *ml*/100 *gm* bw) as compared to Gr I urine output (2.2±0.22 *ml*/100 *gm* bw). Similarly of estiated water % in Gr I and Gr II tissues substantiate rigidity of input-output water controls defending tissues water homeostasis.

A STUDY OF DETMATOGLYPHICS IN CANCER CERVIX PATIENTS. **V. Jayanthi, V. Srinivas, R. Chandrasekhar and G. Krishnamurthy.** *Department of Physiology, Kilpauk Medical College, Madras.*

The study of dermal ridge patterns has become an useful clinical tool in the diagnosis of diseases. The fascination for dermatoglyphics lies in the possibility of predicting a disease before any of the earliest clinical signs and symptoms has appeared. It is felt that a reasonable degree of predictability of malignant diseases based on dermatoglyphics can form the base for mass screening programmes. The commenest malignant condition prevalent in the female, namely, cancer of the cervix of the uterus was chosen for this study.

The hand prints of 76 normal females and 106 patients suffering from cancer cervix of various stages confirmed by biopsy were taken and analysed. The prints were taken of the palm and all the ten fingers individually by the routine finger rolling technique using printer's ink. The four basic patterns namely, the arch the ulnar loop, the radial loop and the whorl were identified and recorded for each finger print. The percentage of each of the four patterns occurring in a single finger was calculated for each of the ten fingers separately in the normals and the cancer cervix patients. The probability index was obtained by the ratio of the values of incidence for all the ten fingers in cancer cervix patients compared to the normals and these values were converted to logarithmic values. The product of the probability indices of all the ten fingers of an individuals gives the digital index and this is obtained conveniently by algebraic addition of the logarithmic values.

The histograms of the digital index against the frequency of occurrance in the normal and cancer cervix patients separately for fingers of th eleft hand and right hand and for all the ten fingers of both hands are prepared. The histograms show that the patients suffering from cancer cervix are a distinct subgroup of the general population.

The significance of the dermatoglyphic findings in cancer cervix in terms of mass screening of the population is presented for discussion.

PYROGEN INDUCED CHANGES IN FOOD AND WATER INTAKE. **Nandini Mullatti and P. S. Shetty.** *Department of Physiology, St. John's Medical College, Bangalore.*

It is generally assumed that anorexia is a concomitant feature of Pyrexia although the magnitude, degree and the mechanisms responsible for the reduction in food intake are not well established. Male, albino rats were used in this study; rectal temperature, food and water intake were monitored at 4 hourly intervals for 24 hrs prior to and after administration of the Pyrogen (Cholera Vaccine). Injection of the Pyrogen was associated with a decrease in 24 hr cummulative food intake (–12.4% ; $P < 0.05$) compared to sham injected days in the same animal. The reduction in food intake was maximal at 12 hrs (–23.3% $P<0.01$) associated with a reduction in warer intake (– 8.8% ; $P<0.05$) and the maximal rise in body temperature. Although Pyrogen induced changes in food intake are unlikely to be related to a behavioural thermoregularly response from this preliminary study, it is difficult to conclude that both the rise in body temperature and the reduction in food intake are mediated by the Pyrogen.

(NM acknowledges receipt of ICMR Research Studentship).

GUEST LECTURES :

PROBLEMS OF STRESS – MANAGEMENT AND TREATMENT. **Sarada Subrahmanyma.** *Madras.*

Stress plays a vital role in mental and physical ilinesses. Psychic trauma can lead to maladaptive physiological stimulations in a susceptible individual by interaction with the environment triggers a chain of events that may eventually lead to psychiatric disorders. Stressful stimuli are received by different centres in the brain were the informations are coded, analysed, integrated and respond and in a few exaggerated.

One of the primary factors concerned in behaviour is the delicate balance between the different neurotransmitters (Sarada Subrahmanyam and Porkodi 1980). Any upset in their coding may cause behavioural problems. Here and attempt is made to evaluate the role of brain monoamines in the etiology of certain affective disorders and the effect

of different kinds of treatments like medical, surgical, non-volitional biofeed back and yoga and mediation. The cases selected were depression, aggression, schizophrenia and epilepsy.

Clinical, psychological, biochemical and EEG studies were done in all the groups before, during and after treatment. In blood, in addition to routine parameters cortisol was assayed. In the CSF and urine the metabolites of NA, DA and 5-HT were estimated.

There were definite alterations in the amine levels in all the groups. The different types of treatment tend to restore the balance in varying degrees thereby improving behaviour.

AN APPROACH TO BETA CELL PHYSIOLOGY THROUGH STREPTOZOTOCIN. **P. Zachariah.** *Christian Medical College, Vellore.*

The following inferences concerning the beta cells of the pancreatic islets have emerged, or have been strengthened, from the study of a wide range of factors affecting the action of streptozotocin (SZN); 1) The beta cell membrane has a glucose carrier system which can transport SZN also. 2) This carrier system demonstrates competitive inhibition as well as facilitation by counterflow. 3) The rate of entry of glucose into beta cells is a limiting factor in the insulinogenic action of sugar; this suggests a significant intracellular action for glucose in insulin release. 4) Beta cell activity is under continuous modulation by alpha and beta adrenegic activity. 5) The beta adrenergic receptor on the beta cell is of the beta two type. 6) All agents (except glucose) which stimulate insulin release, enhance the susceptibility of beta cell to SZN. All agents which inhibit insulin release have the opposite action. It is conceivable that the process of the secretion of insulin enhances beta cell permeability. 7) Exogenous insulin enhances SZN action suggesting that beta cells are susceptible to insulin action. 8) Induction of diabetes by a combined action of SZN and certain viruses suggest a multifactorial mechanism for pancreatic diabetes involving adverse environmental conditions and betatoxic viruses.

IMMUNOLOGY OF CANCER. **D.M. Vasudevan.** *Regional Cancer Centre, Trivandrum.*

The immunological system of man is capable of mounting an attack against non-self antigens. Concomitant with the transformation of a normal cell into a malignant one, there will be alterations in the surface characteristics which will be expressed as neo-antigens or tumor associated antigens. Most of the tumour antigens isolated

from human cancers are of embryonal in nature and are called onco-fetal antigens. The best examples are the carcin-embryonic antigen originally isolated from gut cancers and the alpha-feto protein first detected in hepatomas. Chemical carcinogens produce antigenically different tumours. Viruses usually produce the same antigen irrespective of the type of host cell. Herpes simplex viruses are associated with oral and cervical cancers. EB-virus is know to produce Burkitt's lymphoma under appropriate conditions. The tumour associated antigens thus produced could elicit an immunological response in man. The most important effector arm against malignancy is the Cell-mediated immunity or the direct cytolysis by sensitised T cells. Lymphocytes passing through thymus are called the T cells. The sensitised T cells can directly lyse the target tumour cells. The second effector mechanism is the complement dependent antibody mediated immunity, otherwise called the humoral immunity. This mechanism is very important in checking the blood born metastasis. The third mechanism is the antibody dependent cell mediated cytolysis which is independent of complement activity. Inside the tissues, where antibody concentration is minimal, the K cells can effectively kill the malignant cells. Even though the body is mounting an immune attack against the cancer cells, often this seems inadequate, as is evident from the growth of the tumour mass. This concomitant immunity is mainly due to the blocking effect of circulating antigens. The antigens released by the tumour cells will combine the receptor sites of the active lymphocytes, thus depressing the lymphocyte activity. This inhibotory activity is seen as long as the tumour is growing, and these factors are decreased when the tumour mass is removed. A population of T cells function as suppressors to immunological mechanism. This suppressor cell activ ty is increased in cancer patients. When the supressor cells are removed, the resultant lymphocyte population showed increased activity against cancer cells. Conventional methods of cancer treatment leave many cancer cells which are capable to grow and form recurrence. Immunotherapy is aimed to eradicate these residual tumour cells. Non-specific immunotherapy by BCG and other drugs, though simple, has failed to produce substantially good results. Active immunisation with tumour specific antigen is the method of choice. Tumour specific antigen from oral cancer is being isolated at the Regional Cancer Centre, Trivandrum which may be useful for immunotherapy.

NUTRITION AND THE IMMUNE RESPONSE. **S.G. Srikantia.** *Mysore University, Mysore.*

Among important environmental factors which influence health are nutrition and infection. The synergistic action of these two factors has long been recognised. Altered

nutritional status is known to modify susceptibility to infection and modify the course of the disease, while infection is known to adversely affect nutritional status. Although epidemiological and Clinical evidence points to this interrelationship, it is only in recent years, that systematic studies have been undertaken to define the biochemical basis of this interrelationship. Malnutrition interferes with a number of immune mechanisms. The Phagolytic and bactericidal capacity of circulating leucocytes is impaired, antibody production to specific antigens sub-optimal, concentrations of immunoglobulins concerned with local immunity law and the cell mediated immune status altered. Several nutrient deficiencies impair the immune response and in man, Protein- Energy inadequacy, anaemia and Vitamin A deficiency have been studied in some depth. Not all deficiencies impair all responses; also the plane of malnutrition appears to be a critical determinant. These findings are not only of academic interest, but have practical implications.

INTRODUCTION AND OVERVIEW. **P.G. Talwalkar.** *Franco-Indian Pharmaceuticals, Bombay.*

The impact of the H_2 antagonists on medical community has been dramatic and there has been world wide outpouring of publications now numbering more than 3,000, and CIMETIDINE, the first H_2-antagonist to be marketed, is available in more than 100 countries. It is estimated that more than 11 million patients were treated with it until 1980. It is, therefore, appropriate at this time to review our current state of knowledge on CIMETIDINE. I can think of no better way to do this than a multidiciplinary syposium of this type in which eminent Physiologists, Pharmacologists and Clinicians will participate in free and open review.

CIMETIDINE has created tremendous interest in all these medical specialities. A Clinician is interested because it has offered him a mode of treatment much more efficacious than any of the conventional medical therapies. Basic scientists such as Physiologists and Pharmacologists are interested because CIMETIDINE is not a new drug from the same family but its mechanism of action involves a totally new concept (i.e. H_2-receptor) and their antagonists.

It was known that histamine could stimulate gastric acid secretion but although many antihistamines existed, none of these conventional histamine blockers had the ability to inhibit gastric secretory to histamine.

Prof. J.W. Black postulated that histamine provoked gastric acid secretion by acting upon an unrecognised type of histamine receptor which was not susceptible to blockage by conventional antihistamines. A term "H_2 - receptor" was coined for these receptors. The work to find out therapeutically useful H_2 - receptor antagonists was started in 1964 and in 1972, after screening 700 compounds, the first agent (Burimamide) which could competitively inhibit the stimulatory effect of histamine on acid secretion was developed.

Burimamide was active parenterally. In 1973, the first orally acting H_2 - blocker (Metiamide) was developed. It produced reversible agranulocytosis in five patients on whom it was tried experimentally. The research work continued further and ultimately in 1975, safe orally acting H_2 - blocker, Cimetidine was developed by Brimblecomb *et al.*

GENESIS OF H_2 - RECEPTOR CONCEPT. **Dhruvaraj R. Kulkarni.** *Department of Pharmacology, J.N. Medical College, Belgaum.*

Since the days of Langley who coined the term "receptor substance" through those of Ehrlich and Clark whose works indirectly supported the concept, receptors have largely remained as hypothetical structure on/in cells. Recent advances including radio ligand binding studies have thrown much light on as to what receptor are and how they function. Yet almost every receptor that has been identified so far, has behaved like 'a beautiful but remote lady' of Dejongh (1964) till relentless researcher has coaxed her to reveal glimpses of her beauty. And H-2 receptors have not been any exception.

The idea of any receptor has to start as a conjectural proposition based on available circumstantial evidences to be followed by identification and characterisation of this 'imagined' receptor on well accepted methods. Such methods of receptor study include indirect ones like. potency–ranking of analogues and demonstrating of anatagonist selectivity and direct ones like radioligand binding studies. In so far as H–2 receptor is concerned the indirect methods have been employed.

It is well recognised that conventional antihistamines like mepyramine block some (e.g. ileal stimulation, broncho–constriction) but not other (e.g. acid secretion, cardiac chronotropism) actions of histamine. This differential blocking effect of mepyramine–like agents suggests the existence of mepyramine- insensitive histamine receptors. This idea was systematically investigated by Ash and Schild (1966). Employing indirect methods like potency- ranking of histamine analogues and antagonist selectivity, they demonstrated that rat- gastric secretion and rat uterus inhibition effects of histamine analogues were well correlated potency-wise and that these effects were mepyramine insensitive. On the other hand, receptors mediating histamine action on guineapig ileum were potency-

wise different and were also mepyramine sensitive. They suggested the term 'H–1 receptor' for those mediating mepyramine sensitive actions of histamine on guinea pig ileum. The other receptors not sensitive to mepyramine were simply called as 'non H–1' receptors.

The credit of defining these non–H–1 receptors goes to Black and associates (1972). They systematically studied several histamine agonists and antagonist on H–1 and Non–H–1 responses by employing test systems like, rat stomach, guineapig ileum (both H–1) and rat gastric acid secretion, rat uterus and guineapig ileum (all non-H-1). By potency ranking, antagonist selectivity and PA_2 values analysis of their data, they established two sets of histamine receptors, one histamine and 2-methyl histamine sensitive and mepyramine susceptible, the other 4–methy histamine & histamine sensitive and burimamide (a poineer member of a new class of antihistamine-H2 blockers- developed by Black *et al.*)susceptible. The former class of (Mepyramine susceptible) reportors was already named as H-1 receptor by Ash and Schild, hence, the latter was called as H-2 receptor. This brilliant exposition later lead to mapping of H-1 & H-2 receptors and selective clinical uses of anatagonists and agonists, and further understanding of their functions.

It is believed that imidazole nucleus is essential both for agonists and antagonists for H-2 receptor recognition. Exception like dimaprit (an agonist) and ranitidine (an antagonist) perhaps prove the rule.

DEVELOPMENT OF H-2 RECEPTOR ANTAGONISTS. **Molly Thomas.** *Christian Medical College, Vellore-2.*

The relative ineffectiveness of H-1 receptor antagonists–the so-called classical antihistamines–to block all the effects of histamine, such as effects on gastric acid secretion, relaxation of uterine muscle etc. suggested that these actions of histamine may be mediated through a second and a different receptor. Till 1972, no H–2 specific antagonists were available. However, research work at S.K.F. Laboratories yielded a clue, that like the adrenergic blockers, antagonists could be developed and the break-through came when it was found that N α guanyl histamine induced gastric acid secretion. This was the basis for the development of H-2 antagonists; further studies showed that guanidine groups in presence of imidazole groups were necessary for the blocking effect.

Substitution of guanidine with amidine and thio ureas yielded better partial agonist effect. These compounds were all strong bases which at physiological pH accept a proton and become positively charged- thus having a strong resemblance to histamine. In an attempt to separate the histamino-mimetic and antagonist properties, the strongly basic guanidine group was replaced by thiourea groups which though polar, were uncharged. From these beginnings, extending the length of alkylene side chains resulted in Burimamide

which was 100 times. active than N guanyl histamine. Further modification of burimamide gave metamide which had no clininal usefulness due to the bone marrow depressant effect. The offending group was considered to be thiourea and later replaced with nitro-guanidine and cyano guanidine analogues which were found to be very effective, of which cyano guanidine is found more potent and has been studied in detail. The compound available and extensively used is known as cimetidine.

The search for a better and more effective H-2 specific antogonist, is still going on and the number of compounds such as ipromidine, and other SKF investigational drugs are on the increase.

CLINICAL PHARMACOLOGY OF RECEPTORS AND ANATAGONISTS. **V. Vijasekeran.** *Madras Medical College, Madras.*

Though H_2–receptors are widely distributed in the body clinically important receptors are on the gastric parietal cells. Clinically useful H_2–receptor antagonists are cimetidine and Ranitidine but Burimamide and Metiamide have given the lead to development of clinically useful drugs.

Cimetidine is a specific and selective H_2–receptor antagonist. The blockade is reversible being competitive in nature. Cimetidine inhibits histamine evoked gastric acid secretion in a dose-dependent manner. It also inhibits to varying extent acid secretions induced by other endogenous and exogenous secretogogues. The breadth of action on gastric acid secretion of H_2–receptor blockers suggest that histamine may be the final common path through which acid secretion is mediated. Alternative hypothesis is that histamine may potentiate the action of Acetylcholine and gastrin. Cimetidine reduces both the volume of gastric acid and H_1 on concentration. It is quite likely that basal secretion of intrinsic factor is also reduced. Although the concentration of pepsin is not reduced the total amount secreted falls because the volume of gastric juice is less. Gastrin basal secretion remains unaltered. Limited clinical studies suggest a therapeuctic effect of restoration of immune function for cimetidine.

Cimetidine is effective orally. A single dose yields therapeutic concentration for about 4 hours. It is widely distributed except in the brain. It crosses the placental barrier and secreted in milk. It is excreted mostly in the urine and to some extent in the bile.

It is generally well tolerated. Side effects are infrequent and minor. CNS manifestations are seen in some patients. The week anti–androgenic effect is seen in men and women on long term treatment. There is no rebound effect on withdrawal of cimetidine. Though cimetidine may be given in emergency iv or im, the route of choice is oral. 200--300 *mgs* thrice with meals and a further 400 *mgs*, at bedtime is a satisfactory

dosage schedule. 8 weeks treatment may be adequate to complete a course of therapy. There are different long term prophylatic regimen.

Cimetidine has proven value in duodenal ulcer. Other hyper–secretory states which may benefit are Zollinger–Ellison Syndrome, Systemic mastocytosis etc. In certain conditions like reflex oesophagitis it is used without evidence of benefit. Ranitidine is a newer H_2–receptor blocker under clinical evaluation with promising therapeutic value.

CLINICAL EXPERIENCE WITH H_2–RECEPTOR ANTAGONISTS. **Stanley Macaden.**
Baptist Hospital, Bangalore.

Development of H_2 receptor antagonists could be termed as the major pharmacological breakthrough of the past decade. It has helped in our understanding of the important role of Histamine in gastric secretion and has now materialised into a new approach in the treatment of Peptic ulceration, the most common cause of morbidity of the gastro–intestinal tract. However, this new concept must ultimately have rational clinical application, without which it loses its effectiveness. Therefore, the need for placing the use of H_2–receptor antagonists in its right perspective.