SOCIETY FOR ENDOCRINOLOGY, METABOLISM AND DIABETES OF SOUTHERN AFRICA: ABSTRACTS OF PAPERS

The following are abstracts of papers presented at the 10th Meeting of the Society for Endocrinology, Metabolism and Diabetes of Southern Africa held at the Athenaeum, Newlands, Cape, on 23 and 24 September 1970, during the 7th Biennial Scientific Congress of the Association of Physicians of South Africa:

EFFECT OF INSULIN ON SODIUM TRANSPORT AND WATER MOVEMENT ACROSS ISOLATED TOAD SKIN

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The effects of ox insulin (Wellcome) and glucagon-free insulin (Lilly Research Laboratories) on the transport of Na and water across toad skin (*Xenopus laevis*) were investigated. Na transport was quantitated by measurement of the short-circuit current (SCC); water movement in response to an osmotic gradient was observed directly. All toads were pretreated with deoxycorticosterone acetate.

Of 18 skins challenged with crystalline insulin (25 - 200 mU/ml), 12 responded after a latent period of up to 30 minutes, with a prolonged rise in SCC. In 9 instances, this was ac-

companied by a fall in transepithelial resistance. These effects were most marked where the insulin was added to the inner (corium) surface of the isolated skin. In 2 of 6 instances the effects were reversed within ½-hour of removal of the insulin.

Preliminary studies, on 3 skins, have shown (*a*) similar effects after the administration of glucagon-free insulin and (*b*) that the rise in SCC is accompanied by an increase in the rate of transfer of ^{22}Na from the skin to the inner bathing solution, i.e. increased activity of the sodium pump.

Both crystalline and glucagon-free insulin were found to be without effect on the osmotic permeability of toad skin (n=6).

These results confirm and extend those of previous workers.[1,2]

1. Herrera, F. C., Whittembury, G. and Planchart, A. (1963): Biochim. biophys. Acta (Amst.), **66**, 170.
2. Crabbé, J. and De Weer, P. (1969): Pflügers Arch. ges. Physiol., **313**, 197.

PLASMA RENIN ACTIVITY IN KWASHIORKOR

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The effective plasma renin activity and the level of angiotensinogen were measured by bio-assay in 76 children admitted consecutively to Harari Hospital with a main diagnosis of kwashiorkor. Fifteen of these children died in hospital. In these children, the effective renin activity was equivalent to 24 ng angiotensin/ml/4 h incubation at pH 5·5 and 37°C. This was significantly greater than in the surviving children (7 ng). There was no significant difference in the angiotensinogen level in the two groups (450 and 430 ng/ml). The children that died had a significantly lower plasma albumin than those that survived (1·6 compared with 2·3 g/100 ml), their packed cell volume was less (30 compared with 34%), their estimated weight loss was greater (35 compared with 28%) and the clinical assessment on admission placed them in a more severe grade (6 compared with 4). There was no significant difference between the groups with respect to sex, age, plasma globulin, potassium, sodium, magnesium or the presence of fever, infection, diarrhoea or vomiting. The best guide to prognosis appears to be the effective renin activity, but the plasma albumin, estimated weight loss and clinical assessment were also of value. It is suggested that there are three possible explanations for the high renin levels in kwashiorkor: hypoproteinaemia, agonal hypovolaemia and decreased hepatic inactivation.

ACTIONS OF THYROTROPIN AND DIBUTYRYL CYCLIC AMP ON RIBONUCLEIC ACID SYNTHESIS IN ISOLATED THYROID CELLS

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Previous work has shown that certain of the thyrotropin (TSH) stimulatory effects on isolated thyroid cells can be mimicked by dibutyryl cyclic AMP (DBC) and that these effects are essentially abolished by puromycin, cycloheximide and actinomycin D. Hence, at least one action of TSH may involve an increased synthesis of cyclic AMP which, in turn, may induce new protein formation by stimulating DNA-dependent RNA synthesis.

The latter possibility was investigated by studying the effects of TSH and DBC on the rate of incorporation of ^{14}C-labelled precursors into the RNA of isolated thyroid cells. The cells were incubated continuously with ^{14}C-adenine, ^{14}C-uridine or ^{3}H-UTP, in the presence of either TSH or DBC at concentrations giving maximal stimulatory effects. The RNA was isolated and its specific activity determined. The enhanced incorporation of the labels into RNA in each case was about 30% with TSH and about 50% with DBC. The stimulatory effects were relatively short-lived, and had almost disappeared after about 2 hours. Maximum stimulation occurred after about ½-hour in the presence of the nucleotide or nucleoside, but only after about 1 hour with the base. Both the uptake of the labels by the cells and the distribution of the labels in the acid-soluble fractions were determined, but no significant increases were found in either case.

These data indicate (*i*) that the action of TSH is mediated by cyclic AMP and (*ii*) that at least one of the effects of the elevated levels of cyclic AMP induced by TSH is to modify protein synthesis by enhancing DNA-dependent RNA synthesis.

ACTH REGULATION OF STEROIDIGENESIS

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ACTH regulation of steroidogenesis is superimposed upon pre-existing intra-adrenal regulatory mechanisms. Since little is known of intrinsic mechanisms it has retarded our understanding of the extrinsic regulatory process. Both intrinsic and extrinsic control mechanisms are likely to be unravelled simultaneously. When discussing the mechanism of ACTH control of steroidogenesis we implicitly refer to the events occurring in the approximately 1-minute interval between the arrival of ACTH at the adrenal and the observed increases in the rate of steroidogenesis. This may be too limited a statement of the problem.

Major theories concerned with the enhancement of steroidogenesis by ACTH include a consideration of: (*i*) the role of cyclic AMP (*ii*) the role of NADPH; (*iii*) the role of protein synthesis; and (*iv*) the role of membrane permeability barriers. These hypotheses are not mutually exclusive and more than one may operate.

An extension of the role of ACTH and cyclic AMP into the regulation of androgen as well as of corticosteroid synthesis will be presented. Furthermore cyclic AMP may be a means of setting an upper limit on the rate of corticosteroid secretion and may possibly have a similar role to play in androgen synthesis in the adrenal cortex.

ADENYL CYCLASE AS A POSSIBLE BETA-ADRENERGIC-LIKE RECEPTOR IN THE THYROID GLAND

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The adenyl cyclase-cyclic AMP system participates in the action of various hormones.[1] As a second messenger[2] the adenyl cyclase-cyclic AMP system is thought to act as a receiver and integrator of information and as an intracellular impulse generator, and thus fulfils the role of a receptor.

However, the receptor specificity of the adenyl cyclase to the hormones is incomplete and various degrees of overlap may occur, e.g. between catecholamines and thyrotropin in salivary glands, the pancreas and the thyroid.

The receptor-like role of the adenyl cyclase-cyclic AMP system in the thyroid gland was investigated using isolated bovine thyroid cells. It was observed that:

1. The biphasic action of TSH on the uptake of iodine was closely mimicked by DBC. This indicates that TSH acts via the adenyl cyclase-cyclic AMP system.
2. The stimulatory action of TSH on the iodide uptake was inhibited by propranolol at doses which caused specific receptor inhibition, but not by similar doses of phentolamine. This indicates that the activation of adenyl cyclase by TSH possibly involves a β-adrenergic-like receptor.
3. The action of DBC was not inhibited by specific receptor-blocking doses of propranolol. This suggests that the action of propranolol occurs at the plasma cell membrane and not at subsequent metabolic steps activated by cyclic AMP.
4. The inhibition of TSH action by propranolol varies with varying concentrations of TSH in the biophase, thus indicating a competitive inhibitory action of propranolol on the TSH receptor.

It is therefore concluded that TSH acts via a β-adrenergic-like receptor on, or in the vicinity of, the adenyl cyclase in the thyroid cell membrane. This action is competitively inhibited by the β-blocking agent propranolol, but not by phentolamine.

1. Robinson, G. A., Butcher, R. W. and Sutherland, E. W. (1968): Ann. Rev. Biochem., **37**, 149.
2. Sutherland, E. W., Robinson, G. A. and Butcher, R. W. (1968): Circulation, **3**, 279.

THE EFFECT OF GROWTH HORMONE AND CORTISONE ON THYMIDINE KINASE ACTIVITY IN RAT ADIPOSE TISSUE

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Thymidine kinase activity in the adipose tissue of hypophysectomized male rats was increased approximately 10 times

after 2 days of injecting growth hormone. Simultaneous injections of cortisone prevented the stimulation by growth hormone. During 4 days of growth hormone administration thymidine kinase activity increased slightly after 1 day, rose sharply to a maximum at 2 days and decreased to about half the maximal value by the 4th day. Stimulation of DNA synthesis by growth hormone followed the same temporal pattern, and the increase of DNA synthesis was also inhibited by cortisone.

EFFECT OF HYPOPHYSECTOMY AND GH TREATMENT ON ALBUMIN SYNTHESIS AND CATABOLISM IN THE RAT

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Hypoalbuminaemia is a well-recognized consequence of hypophysectomy in a number of species of animals. Little data are, however, available to indicate the nature of the underlying changes in synthesis or catabolism responsible for the reduction in concentration. Partial restoration of the lowered albumin mass after hypophysectomy has been achieved by GH replacement therapy but there is no unanimity of opinion as to whether GH acts by stimulating albumin synthesis or by slowing catabolism.

Hitherto attempts at measuring albumin synthesis and catabolism under the above experimental conditions have been limited by the use of methods which have not entirely fulfilled the requirements for valid measurement in the unsteady state. Relatively recent technical advances in this field now permit valid measurement under non-steady conditions and a reinvestigation of the effects of hypophysectomy and GH replacement on albumin metabolism forms the basis of this paper.

Hypophysectomy has been shown to lower both albumin synthesis and catabolic rates. Furthermore these changes, as shown by pair feeding experiments, cannot be ascribed to a reduced food intake alone. GH has been shown to partially restore albumin synthesis and catabolic rates. On the basis of the data presented it is proposed that GH acts primarily by stimulating albumin synthesis and that catabolism is altered indirectly through changes in the intravascular albumin pool.

THYROXINE FORMATION IN A CONGENITAL GOITRE IN THE ABSENCE OF THYROGLOBULIN

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Thyroglobulin is not unique with respect to its ability to form thyroxine. Various non-thyroidal proteins will yield detectable amounts of thyroxine when iodinated non-enzymatically *in vitro*. The outstanding characteristics of the iodo amino acids of *in vitro* iodinated non-thyroidal proteins are a high MIT/DIT ratio and a low thyroxine content. The thyroxine content and the MIT/DIT ratio are determined by the available iodine, the tyrosine content of the protein and the tyrosine environment which, in turn, is a function of protein conformation.

A congenital goitre in Afrikander cattle has been investigated in which no thyroglobulin or thyroglobulin polymers were found. Yet, thyroxine was detected in the thyroid and in blood and the animals remained euthyroid with respect to growth and physiological processes such as reproduction.

Several unusual iodoproteins have been isolated from the goitre with sedimentation rates of 3·7S, 6·4S, 9S and 12S and with molecular weights of 110 000, 155 000, 185 000 and 330 000 respectively. The 3·7S possessed an asymmetric structure and contained only 0·036% of stable iodine while the 12S component showed partial immunological relationship with thyroglobulin and possessed the highest iodine content (0·2%). Sixteen and 21% of the total radioactivity in the 9S and 12S iodoproteins consisted of iodothyronines. MIT/DIT ratios in all proteins were higher than in native thyroglobulin.

It is concluded that thyroxine can be formed in non-thyroglobulin proteins in the thyroid to the extent that the goitre compensates for the complete absence of thyroglobulin and its polymers.

AMINO ACID TRANSPORT IN EXPERIMENTAL THYROTOXICOSIS

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Amino acid transport was measured by two *in vitro* systems in rats rendered thyrotoxic by a 15-day course of intraperitoneal injections of 0·3 mg thyroxine. Transport of L-alanine into everted gut segments and across everted loops of gut was inhibited in the thyrotoxic rats. Thus thyroxine appears to inhibit amino acid transport.

Work is currently in progress to investigate whether the inhibition of intestinal amino acid transport is due to the direct effect of thyroxine on amino acids or occurs as a secondary phenomenon consequent upon increased sugar transport.

A MODEL NORADRENALINE BINDING SITE

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The preparation of a specific antibody to noradrenaline has previously been reported. The antibody was shown to bind catecholamines strongly with association constants of the order of 07 1litre moles.[1]

Insolubilized derivates of the antiserum have been prepared and have been shown to bind noradrenaline and adrenaline. Investigations have been carried out with the possibility of using the system as a sensitive radio-immunoassay for the catecholamines.

1. Marlow, H. F. (1970): Brit. J. Pharmacol., **38**, 438.

RECENT PROGRESS ON THE EXTRACTION AND PURIFICATION OF HUMAN PLACENTAL LACTOGEN

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Various methods have been described[1-4] for the preparation of human placental lactogen from placentas, but the methods mainly used today are based on the discovery that fractions II and III, obtained as a byproduct in the preparation of human serum albumin from placentas at term contain the HPL. Starting with these fractions II and III, using a method initiated by Friesen[5] and modified by Catt *et al.*,[6] the HPL is further concentrated by absorption on DEAE-cellulose from dilute ammonium bicarbonate solution (0·50 - 0·1 M) and desorption with more concentrated ammonium bicarbonate solution. Purification of the HPL is then effected from this crude material by various chromatographic procedures.

Studies on this crude material in these laboratories have shown it to be extremely complex, containing at least 11 bands on polyacrylamide gel electrophoresis, and the presence of large quantities of fast running materials on Sephadex G-100 filtration, together with large quantities of albumin and haem-containing proteins makes the isolation of HPL by direct gel filtration extremely tedious, difficult and impractical, involving the use of large columns with small loadings.

It has now been found that precipitation at pH 4·8 effectively removes the bulk of the impurities, which are fast running on gel filtration, and that precipitation of the supernatant at this pH with alcohol, at a concentration of 11% v/v, gives a product which is free from albumin and haem-containing proteins and contains all the HPL.

This purified product is very amenable to simple Sephadex G-100 gel filtration and the HPL can be readily isolated in a form which is homogeneous on gel filtration analysis and which gives a single discrete band on polyacrylamide gel electrophoresis.

1. Josimovich, J. B. and MacLaren, J. A. (1962): Endocrinology, **71**, 209.
2. Cohen, H., Grumbach, M. M. and Kaplan, S. L. (1964): Proc. Soc. Exp. Biol (N.Y.), **117**, 438.
3. Friesen, H. (1965): Endocrinology, **76**, 369.
4. Turtle, J. R., Beck, P. and Daughaday, W. H. (1966): *Ibid.*, **79**, 187.
5. Friesen, H. (1965): Nature (Lond.), **208**, 1214.
6. Catt, K. J., Moffat, B., Niall, H. D. and Preston, B. N. (1967): Biochem. J., **102**, 27c.

METABOLIC FINDINGS IN SEVEN CASES OF HYPEROSMOLAR, NON-KETOTIC, DIABETIC STUPOR

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The clinical features of hyperosmolar, non-ketotic diabetic stupor have been comprehensively reviewed. There are, however, only a few reports of hormonal and free fatty acid (FFA) measurements during the acute stage of the syndrome; the interpretation of these findings has varied greatly.

In 7 cases, to be briefly described, opportunity was afforded to measure a wide range of relevant hormonal (i.e. immunoreactive insulin, growth hormone and cortisol) and biochemical values before treatment was begun.

With one exception, a consistent pattern of enhanced lipolysis, detectable levels of immunoreactive insulin and suppressed growth-hormone emerged; cortisol levels were uniformly raised. There was, in addition, evidence (elevated acute triglyceride levels) to indicate that the mobilized FFA were being taken up by the liver. The absence of ketosis in these cases might, therefore, have been due to completely effective, alternative mechanisms of FFA metabolism by the liver. Alternately, a block in intrahepatic ketone synthesis might have occurred. Differences in acute metabolic findings between non-ketotic, hyperosmolar diabetic stupor, and ketoacidosis are not well defined, although one that seems to emerge concerns the suppressibility of growth hormone.

DIABETES AND RELATED VARIABLES IN A CAPE COLOURED COMMUNITY

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We have performed community studies for diabetes mellitus and related variables among the White, Bantu, Indian and Malay population of Cape Town. Similar studies among the Cape Coloured people are almost concluded. Outstanding features have included:

1. The extreme reluctance of this ethnic group to submit themselves to screening, leading to a recovery rate of under 50 g of glucose orally.
2. The frequency of high screening blood-glucose levels, many being over 300 mg/100 ml in asymptomatic individuals—approximately one-third of those tested screened 'positive', with glucose levels of over 160 mg one hour after 50g of glucose orally.
3. An 'already known' diabetes rate of 0·75% but a 'newly discovered' diabetes rate over 5%. Comparisons with the other ethnic groups will be made.

THE DIFFERENT EFFECTS OF ORAL SUCROSE AND GLUCOSE ON ALIMENTARY LIPAEMIA

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A formula breakfast containing protein, carbohydrate and fat was given on two occasions to 9 middle-aged male convalescent patients and to 10 young men. The meals differed only in the type of carbohydrate given—sucrose or an isocaloric amount of glucose. Following the formula meal containing glucose, the alimentary lipaemia was cleared more quickly than after the sucrose formula. The insulin response was greater after the meal containing glucose and appeared to be related to the larger glycaemic stimulus. Triglyceride clearing showed a significant correlation with insulin response. It is therefore suggested that the more rapid clearing of alimentary lipaemia following a meal containing glucose as compared with sucrose is related to the greater insulin response elicited by glucose.

RADIO-IMMUNOASSAY OF INSULIN

P. KELLER, I. G. O'REILLY AND L. SCHATZ, *Department of Medicine, University of Cape Town*

The principles underlying the radio-immunoassay technique for the determination of serum insulin concentrations, established by Hales and Randle, are described, and the routine application of the method to large numbers of specimens is discussed. The technique has been in use in this laboratory for nearly 6 years, and approximately 30 000 individual determinations have been carried out.

The normal fasting values as well as serial values established during oral glucose-tolerance tests compare well with those reported by other workers in the field. However, these data are not amenable to conventional statistical treatment due to the wide range of individual variations encountered even in normal fasting values. Presenting the values on a logarithmic scale does not resolve this problem, nor does the conversion of the insulin:glucose ratio to the 'insulinogenic index' although the latter procedure may produce additional information.

The results of our investigations have been used as one parameter in the assessment of the incidence of diabetes mellitus in various population groups; in the study of a selected group of potential prediabetics; in studies on genetic diabetes, and in the examination of a group of elderly people with or without patent impairment of carbohydrate metabolism.

Studies of insulin concentrations under varying test conditions, and the determination of insulin reserve under stimulation of the beta-cytotrophic system, have aided in the evaluation of the metabolic status of patients with chronic pancreatitis and subsequent secondary diabetes.

Detailed studies of serum insulin levels under varying test conditions in suspected cases of insulinoma have proved of value in the diagnosis of this condition. The clinical application of the quantitative determination of serum insulin concentrations in combination with other diagnostic criteria will be discussed.

OVINE METABOLIC ACIDOSIS

J. PROCOS, *Stock Disease Research Fund*, ANNETTE SCHUBERT AND B. J. BRIEL, *Veterinary Research Institute, Onderstepoort, Tvl*

Severe acidosis was induced in wethers by the infusion of hydrochloric as well as aceto-acetic and betahydroxybutyric acids. No clinical signs, apart from slight panting, were observed despite a fall in plasma glucose levels which occurred either spontaneously during the infusion of aceto-acetic acid, or artificially following administration of insulin in conjunction with hydrochloric acid infusions. It is suggested that acidosis *per se* is not immediately responsible for the induction of the nervous symptoms displayed by sheep suffering from pregnancy disease.

NUTRITIONAL VITAMIN-D DEFICIENT OSTEOMALACIA IN AN ADULT

C. WEINKOVE, B. PIMSTONE AND W. P. U. JACKSON, *Endocrine Clinic, Groote Schuur Hospital, Cape Town*

A middle-aged spinster presented with backache and multiple fractures. There was a past history of an inadequate diet and psychogenic vomiting. Radiologically she showed Looser's zones and undermineralization of the skeleton. The only biochemical abnormality was a persistently low serum phosphorus with a normal serum calcium and alkaline phosphatase. Osteomalacia was confirmed by 4-hour calcium retention and strontium kinetics as well as histology and microradiography of undecalcified bone. Investigations for malabsorption were negative. Her good clinical and biochemical response to small doses of oral vitamin D confirmed the suspicion that her osteomalacia was nutritional.

HYPEROSMOLAR, HYPERGLYCAEMIC, NON-KETOTIC COMA AFTER THE REMOVAL OF A CHROMOPHOBE ADENOMA IN AN ACROMEGALIC

W. P. U. JACKSON AND B. L. PIMSTONE, *Endocrine Clinic, Groote Schuur Hospital, Cape Town*

A hypophysectomized, previously non-diabetic acromegalic came into hospital totally unconscious, cyanotic, grossly dehydrated and hyperglycaemic and soon went into status epilepticus. She recovered from this episode and became appa-

rently non-diabetic. Problems posed by this and other patients regarding the pathogenesis of this condition will be discussed.

CUSHING'S SYNDROME DUE TO ACTH PRODUCTION FROM A BENIGN THYMOMA

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A 32-year old White male presented with Cushing's syndrome of recent onset. The elevated urinary 17-oxogenic steroids were dexamethasone non-suppressible, yet responded excessively to exogenous ACTH. X-ray of the chest at the time was thought to be normal. Laparotomy showed bilateral adrenal hyperplasia, and a total adrenalectomy was performed, the patient being maintained on cortisol and fluorohydrocortisone. One year later X-ray of the chest showed a large rounded superior mediastinal mass, which grew very rapidly over 4 months. On thoracotomy, a benign thymic neoplasm was removed which had high concentrations of ACTH on radioimmunoassay (1·4 μg/g tumour). Electron-microscopy of the tumour showed secretory granules. The rapid growth of the benign neoplasm after adrenalectomy suggests a possible restraining effect of the previously high cortisol levels on thymic growth.

AMENORRHOEA IN THE FEEDING DISORDERS WITH SPECIAL REFERENCE TO ANOREXIA NERVOSA

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Studies on patients with anorexia nervosa demonstrate that food restriction and weight loss give rise to a general reduction in gonadotrophin excretion and amenorrhoea. By itself, however, weight loss does not account for the loss of the cyclical pattern of gonadotrophin activity. This loss of rhythmicity is an important feature of anorexia nervosa. Its precise causation is unknown: it may be related to the profound psychiatric disturbance which accompanies the illness. The present state of knowledge in the human does not permit us to come to further conclusions. Speculation on the basis of animal studies may lead us to guess that the endocrine disturbance in anorexia nervosa might be due to a failure of the anterior hypothalmic mechanisms concerned with the rhythmic control of gonadotrophin secretion.

THE EFFECTS OF PROTEIN-CALORIE MALNUTRITION (PCM) ON INSULIN SECRETION IN CHILDREN

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Insulin secretion was measured after oral and/or intravenous glucose loading in 54 children with kwashiorkor and marasmus. Tests were repeated immediately after clinical recovery and, in certain cases, again after some months of feeding.

Insulin responses were expressed quantitatively as insulin-glucose ratios. In addition, individual patterns of insulin response were assessed. Quantitatively impaired pancreatic insulin secretion is virtually the rule in PCM, in many cases returning to normal only after many months. Other abnormal patterns were noted—these include a delayed peak insulin response and sustained secretion after glucose. Based on these data it is suggested that impairment of pancreatic insulin release is not the sole abnormality. Gut betacytotrophic factors and insulin antagonism clearly play a role in individual cases.

DEFECTIVE RENAL HANDLING OF INSULIN IN KIDNEY DISEASE

R. RABKIN, N. M. SIMON, S. STEINER AND J. A. COLWELL, *Groote Schuur Hospital, Cape Town*

Renal handling of insulin was studied over plasma insulin levels of 6 - 40 μU/ml in 13 patients by renal-vein catheterization. The kidney in normal subjects and 7 patients with moderate renal insufficiency—glomerular filtration rate (GFR) over 22·5 ml/min per kidney per 1·73 m^2—removed 39 $\pm$ 4% (SD) of the insulin from arterial plasma. Severe renal insufficiency (GFR$<$6) reduced insulin uptake to 9% in 4 subjects, 2 with diabetic glomerulosclerosis. Mean GFR in normal subjects was 61 $\pm$ 11 (SD) and renal insulin extraction —renal plasma flow $\times$ % uptake—was 106 $\pm$ 28 (SD) ml/min.

These findings suggest that a decreased uptake of insulin by damaged kidneys accounts in part for the diminished insulin requirements seen in patients with diabetic glomerulosclerosis and that all the renal uptake of insulin cannot be explained by glomerular filtration alone.

INVESTIGATION OF ENDOCRINE FUNCTION IN CHRONIC CALCIFIC PANCREATITIS

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Tests for the measurement of exocrine pancreatic function in chronic pancreatitis are fairly well established. Until recently, relatively little attention has been given to the assessment of endocrine function beyond estimation of glucose tolerance. The introduction of hormonal radio-immunoassay techniques has added a new impetus to this area of investigation.

In the present study, involving a group of patients with unequivocal features of severe chronic pancreatitis (all showing radiological evidence of pancreatic calcification), insulin reserve was firstly investigated. The provocative stimuli employed were: intensive beta-cell stimulation with combined glucose, glucagon and tolbutamide; intravenous tolbutamide alone; and intravenous arginine infusion. After each stimulus, the mean immunoreactive insulin response in the pancreatitis patients was significantly lower than that of matched healthy controls. The degree of impairment seemed to be proportional to the degree of glucose intolerance.

Related to insulin determination, it was of interest to measure, also, growth-hormone (HGH) responses in the *diabetic* subgroup, since their beta-cell failure was—in a sense —acquired. Standard insulin-tolerance tests showed that, despite induced hypoglycaemia of a magnitude not significantly different from control subjects at 30 minutes, and significantly greater at 45 and 60 minutes, their peak growth-hormone responses were significantly blunted. This was compared with the HGH responses elicited after the intravenous arginine infusion, and a similar secretory impairment emerged.

Finally, an attempt was made to assess the glucagon secretory capacity of the pancreatic alpha-cells—again during the arginine infusion test.

PITUITARY-ADRENAL FUNCTION TESTS IN PATIENTS WITH HYPOPITUITARISM

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The pituitary-adrenal function of patients with suspected hypopituitarism has been assessed by the response of plasma 11-hydroxycorticosteroids to insulin-induced hypoglycaemia, lysine-vasopressin and corticotrophin and by the response of urinary total 17-oxogenic steroids to metyrapone. On the basis of these results recommendations are proposed for a rational approach to the selection of pituitary-adrenal function tests.

A CLINICAL COMPARISON OF THE SHORT-TERM EFFECTS OF PROPRANOLOL AND PRACTOLOL IN THYROTOXICOSIS

S. EPSTEIN AND B. L. PIMSTONE, *Thyroid Clinic, Groote Schuur Hospital, Cape Town*

Fifteen patients with proved thyrotoxicosis were placed on either practolol or propranolol for 1 month in a single-blind cross-over study. Symptoms and signs were recorded at the initial visit and thereafter at 2-weekly intervals. The effect of short-term therapy with each of these drugs was compared. Propranolol had no advantage over practolol which was considered safer and could be used in asthmatics without increasing bronchospasm. Where propranolol was ineffective, practolol was of little benefit in controlling thyrotoxicosis. In a few patients with myopathy practolol had no effect whereas, when changed to propranolol, the myopathy improved dramatically; the reasons for this will be considered.