1. Intestinal hormones and plasma insulin.
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Glucose absorbed from the gut induces a greater rise in plasma insulin than glucose administered intravenously (McIntyre et al., 1964; Elrick et al., 1964) and it has been suggested that a hormone (“incretin”), released from the gut may augment the glucose stimulus to the islets of Langerhans. In the experiments to be reported, the effects of purified secretin and 2. pancreozymin/cholecystokinin alone and with glucose upon venous plasma insulin levels in human subjects have been investigated. In addition, the effect of endogenous secretin, stimulated by infusion of acid into the duodenum, upon plasma levels of insulin has been studied. The results are discussed in relation to the “incretin” hypothesis.

2. Immunoreactive glucagons in human pancreas, gut and plasma.
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Using a radio-immunoassay procedure and serial dilutions of neutralized acid-ethanol extracts of human tissues, and extracted or unextracted human plasma, the cross-reaction between crystalline beef-pork (pancreatic) glucagon and human pancreatic glucagon was identical. Immunoreactive “glucagons” were widely distributed in the human gut. Cross-reactivity with pancreatic glucagon was complete in the case of colonic “glucagon” and became progressively less in jejunum, duodenum and stomach, in that order. Normal fasting human plasma frequently contained non-pancreatic immunoreactive “glucagon”. Alimentary administration of glucose, but not intravenous glucose, stimulated secretion of pancreatic (for immunochromic and quantitative reasons) glucagon. Supra-normal quantitative, pancreatic glucagon response, often associated with a supranormal augmentation of insulin release, was obtained with the rapid entry of glucose into the small intestine e.g. after rapid intrajejunal infusion of glucose in controls or after oral glucose in post-gastrectomy subjects. Alimentary galactose, but not intravenous galactose, produced a considerable rise in plasma insulin and pancreatic glucagon. A humoral stimulus to pancreatic glucagon secretion may be released by alimentary glucagon and galactose.

Prolonged starvation caused no rise in plasma pancreatic glucagon levels, but occasionally produced a non-quantitative increase in immuno-reactive “glucagon” of non-pancreatic origin.
It is suggested that in man, under physiological conditions, pancreatic glucagon is primarily insulinogenic and only secondarily hyperglycaemic, and that nonpancreatic "glucagons" are primarily hyperglycaemic (or lipolytic).

3. The role of calcium in insulin secretion in vitro.  

Extracellular calcium is essential for a number of excitatory phenomena (muscle contraction, secretion of adrenaline, oxytocin and zymogens). Studies have been carried out to determine whether the stimulation of the insulin secretion in pieces of rabbit pancreas incubated in vitro is also dependent on the presence of calcium in the extracellular fluid. The stimulation of insulin secretion by an increase in glucose concentration, tolbutamide or glucagon was prevented by the omission of calcium from the incubation medium. Replacement of calcium in the same experiment reversed the inhibition. In experiments on glucose-stimulated insulin secretion in which the calcium concentration of the medium was varied in the range 0--5 mM there was found to be an optimum calcium concentration for insulin secretion at 2.5 mM.

4. The Effects of Glucagon and Tolbutamide on Ketogenesis.  
P. D. Bevers and J. Ashmore. Aberdeen, and Dept. of Pharmacology, University School of Medicine, Indianapolis.

The intraperitoneal administration of glucagon (1 mg/kg) to rats, 30 minutes before they were killed, caused an increased production of ketone bodies by liver slices prepared from these animals. Increased ketogenesis occurred when either glucagon or cyclic AMP was added to homogenised liver, and in vitro injection of glucagon to rats increased the rate of lipolysis in the livers removed 30 minutes later. It is suggested that the effect of glucagon on ketogenesis may be through activation of a hormone-sensitive hepatic lipase. Tolbutamide (0.1 and 0.5 mg/ml) reduced ketogenesis in vitro, and also depressed liver lipase activity, whereas insulin deficiency increased the lipase activity.

5. Lipolytic Action of Human Placental Lactogen.  
J. R. Turtle, G. K. Littleton and D. M. Kipnis. Washington University, St. Louis.

6. The Effect of diabetes on lipid storage in muscle.  

Triglyceride (TG) and phospholipid (PL) concentrations have been measured in rat heart and gastrocnemius muscles perfused briefly with physiological saline media to remove blood lipids. In the normal animal the concentrations, in mg/100 g dry muscle were in heart, TG 12.0 ± 1.3 and PL 171 ± 1.8 and in gastrocnemius TG 12.0 ± 1.5 and PL 64 ± 2. In the alloxan-diabetic rat the triglyceride concentration in both muscles was approximately doubled but the phospholipid concentration did not change. The accumulation of triglyceride in these muscles in diabetes was shown to be dependent upon glucose and adrenal corticosteroid. In hypophysectomised animals, diabetes did not change the triglyceride concentration unless the animals were treated with growth hormone and cortisol. The accumulation of triglyceride did not involve dietary lipid because similar changes were seen in diabetic rats fed on a fat-free diet and also in normal rats starved for 48 hr.

The rate of triglyceride synthesis in the rat heart in vitro has been calculated from measurements of the incorporation of radioactivity from U(14C)-glucose into the glycerol moiety of triglyceride and into free glycerol. This rate is increased in the diabetic heart. It is thought that triglyceride accumulates in the diabetic muscle because mobilization of lipid from adipose tissue increases the plasma concentration of free fatty acids and that this leads in turn to an increase in the rate of triglyceride synthesis in muscle.

7. The Effect of Insulin on the Glucose and Free Fatty Acid (FFA) Flux.  
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The effects of insulin on the entry and exit rates into and from the plasma of glucose and free fatty acid (FFA) were studied in non-diabetics and maturity-onset diabetics by simultaneous infusion of U(14C)-glucose and palmitic acid-1-14C. No relationship could be established between insulin-induced changes in glucose outflow and FFA inflow. The decrease in FFA entry following insulin was not significantly different in diabetics and nondiabetics; thus, the antilipolytic effect of the hormone appears to be retained in diabetes. Insulin decreased FFA inflow, determining thereby the extent of the fall in circulating levels, while the outflow, was dependent on the FFA concentration. These findings do not support the suggestion that insulin unresponsiveness in terms of glucose utilization is due to the diminished effect of the hormone on FFA release.

8. Glycosuria as an Index of Control and Diabetic Retinopathy.  

An analysis has been made of 3907 observations by ophthalmologists on the eyes of 2184 diabetics, of whom 990 had more than one observation. Control of diabetes has been measured from the "glycosuria percentage" (percentage of urine tests at routine clinic attendances showing glycosuria of 2% or more). The patients have been divided into those with a "glycosuria percentage" of 19% or less and those with 20% or more. The lower "glycosuria percentage" is associated with a significantly lower incidence and chance of development of retinopathy, but only in patients under 60 at diagnosis of diabetes. Estimates of chances of progression and regression of retinopathy are essentially unrelated to "glycosuria percentage". It is suggested that control of diabetes may only affect the early stages of the development of retinopathy, and that other factors may predominate when retinopathy is established.

9. Myopia and Diabetic Retinopathy.  

The observation that diabetic retinopathy is uncommon in patients with high degrees of myopia has been investigated from the records of 104 ophthalmologist examinations of 47 diabetics with high myopia. Retinopathy was present in 28% of these examinations; this is significantly less than the 42% expected on the basis of age at diagnosis and duration of diabetes. 10 of the 15 patients with retinopathy had mild or moderate changes, usually non-progressive, but 5 had one or more vitreous haemorrhages. The probable reasons for the increased frequency of vitreous haemorrhages and the decreased frequency of simple retinopathy are discussed.