In all instances the fall in blood glucose induced by this small dose of insulin was significantly increased by the administration of ACG, the change at 30 minutes being significant at less than the 1% level, and in five of the six volunteers the duration of the hypoglycaemia was prolonged. The difference in means at 70 and 80 minutes is significant at the 5% level.

DISCUSSION

The results show that under the conditions of the experiment—that is, prolonged fasting—ACG induces increased sensitivity of normal people to small amounts of intravenous insulin as measured by changes in blood glucose.

These conditions were deliberately chosen, since it was postulated that with the increased blood growth hormone levels induced by fasting ING² activity might be increased. Thus it would be expected that the effect of ACG in reversing ING inhibition might be more readily shown.

The results suggest that ING:ACG relationships may have a physiological role in glucose homeostasis, insulin acting to promote glucose entry into muscle and fat, and facilitating

glycogen synthesis in these tissues and the liver, while the relative ING:ACG activity exerts a modulating effect on the utilization of intracellular glucose and hence on insulin sensitivity. Variations in insulin sensitivity have been invoked as factors in determining glucose tolerance and the genesis of diabetes (Cerasi and Luft, 1967; Martin *et al.*, 1968), and the increased plasma insulin response after oral glucose in many diabetics may be a reflection of ING-induced resistance to insulin in these patients. The evidence reported here, suggesting the presence of ING in normal humans, makes more cogent the hypothesis that increased activity of this polypeptide or diminished activity of ACG might have a role in the genesis of diabetes mellitus, acting in the manner of the addition and compensation factors suggested by Cerasi and Luft (1967).

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²ING stands for inhibitory polypeptide-growth hormone. Experimentally it is capable of inhibiting glucose uptake and fatty acid synthesis and indirectly causing the mobilization of unesterified fatty acids from peripheral fat. It may be derived by either non-specific or specific hydrolysis of purified growth hormones.

Medical Memoranda

Renal Allograft with Massive Perirenal Accumulation of Lymph

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Complications of renal transplantation are protean (Starzl, 1964; Calne, 1967). Those associated with mechanical problems are of particular surgical interest. Recently we encountered a patient with chronic renal allograft rejection and the nephrotic syndrome (Harlan *et al.*, 1967). In addition a large amount of lymph had accumulated at the region of the transplant to produce the iliac compression syndrome. Review of the literature shows that this complication has received only passing mention (Hume, 1968).

CASE HISTORY

A 17-year-old Negro youth of blood group B, Rh-positive, presented in March 1966 with chronic glomerulonephritis and the nephrotic syndrome. By December 1967 he had to be supported by dialysis. Bilateral nephrectomy on 7 March 1968 confirmed the diagnosis.

On 1 May 1968 a kidney from a 40-year-old male Negro of blood group O, Rh-positive, who had died of brain injury, was transplanted into the patient. Lymphocyte antigen typing showed a C minus matching grade between donor and recipient (Lee *et al.*, 1967). The other donor kidney, weighing 290 g., was macroscopically and microscopically normal. Immunosuppression with prednisolone and azathioprine was given at the usual dosage (Straffon *et al.*, 1967). Local irradiation to the graft, with a total dosage of 900 rads, was given.

The immediate postoperative course was marked by acute tubular necrosis of two weeks' duration and urinary infection with *Escherichia coli*, which promptly subsided with kanamycin therapy. Renal function progressively improved during the first month—the serum creatinine decreased to 1.6 mg./100 ml., the 24-hour urine protein excretion stayed around 1 g., and the blood pressure fell to 160/80.

During the fifth postoperative week urinary infection with *E. coli* recurred. Proteinuria increased to 20 g./24 hours. An intravenous urogram showed enlargement of the graft. A renal arteriogram showed that the distal arterial branches were spaced far apart, a finding suggestive of intrarenal swelling or interstitial oedema (Hall and Holley, 1969). The urinary infection again responded to kanamycin treatment. Prednisolone was increased to 400 mg. daily for five days, and a course of actinomycin D was given because of

suspected rejection crisis. Local irradiation of the transplant, totalling 450 rads, was again instituted. No response to the above measures was noted. A renal biopsy examination showed moderate interstitial oedema and infiltration with mononuclear cells. The glomeruli showed some increase in P.A.S.-positive material in the mesangial region of the glomerular lobules.

On 26 June the patient complained of swelling of the right lower extremity. Femoral venography showed compression of the right external iliac vein (Fig. 1). Rapid deterioration of renal function with oliguria set in. Urine showed hyaline, granular, and waxy casts, together with oval fat bodies, and was sterile on culture. Leucocytosis was absent. Serum protein electrophoresis showed albumin 1.56, α_1 -globulin 0.35, α_2 -globulin 1.13, β -globulin 0.78, and γ -globulin 0.96 g./100 ml. Serum cholesterol was 330 mg./100 ml.

Venogram showing compression of right external iliac vein (arrowed) by accumulation of lymph.

A laparotomy on 3 July disclosed a massive collection of crystal-clear colourless fluid at the site of the transplant, totalling 900 ml. The lower urinary tract was shown by cystotomy to be in good order. Retrograde introduction of methylene blue showed the pelvis and ureter to be intact. The fluid was sterile on aerobic and anaerobic culture. It had a very similar content of urea, creatinine, sodium, potassium, and chloride to plasma, and was very different in composition from urine collected at the same time. Its protein content was 0.5 g./100 ml., calcium 2.2 mEq/l., and cholesterol 25 mg./100 ml., indicating a transudate by the criteria of Cantarow and Trumper (1962). An additional 600 ml. of the fluid was obtained from a suprapubic drain during the next few days.

On the second postoperative day indigo carmine given intravenously did not appear in the suprapubic drain, substantiating further the absence of any urinary leak. Postoperatively, though oedema of the right lower limb slowly subsided, oliguria and proteinuria persisted. Haemodialysis had to be restarted. Subsequently the wound became infected and drainage discontinued. A renal biopsy on 23 July showed progression of the findings previously noted. The antistreptolysin O titre at this time was 50 Todd units. Further decline of renal function necessitated nephrectomy a week later. The patient subsequently received a second renal transplant; this was functioning satisfactorily six months after transplantation.

Pathological Findings.—The transplant was grossly enlarged and oedematous, weighing 460 g. Thrombus was not found in the renal vein. Microscopically interstitial fibrosis was present, in addition to changes seen previously. All the glomeruli had con-

siderable focal irregular thickening of the basement membrane of the capillary wall by P.A.S.-positive material. Some of the tubules were greatly dilated and were full of eosinophilic fluid and casts. The small arteries were thickened and oedematous, with pronounced intimal proliferation and fibrosis. Scattered infarcts were found throughout the cortex.

DISCUSSION

This case presented the usual features of the chronic rejection process (Porter, 1964; Porter *et al.*, 1967). Clinically, chronic rejection was manifested by the nephrotic syndrome (Harlan *et al.*, 1967) associated with rapid and progressive renal failure.

The rejection phenomenon was associated with a massive perirenal collection of transudate. There are two possible sources for this fluid. The first is leakage from damaged lymphatic vessels around the iliac vessels at the site of the transplant. Ligation of all major lymphatic channels encountered at the time of freeing the iliac vessels to prevent the postoperative collection of lymph in the wound was recommended by Hume (1968). In our case lymphatic ligation was not performed. Although no immediate postoperative leakage of lymph from the wound was observed, it is possible that the accumulation was so slow that it did not appear clinically until three months after transplantation. The second explanation is the leakage of lymph from the oedematous organ at the time of rejection. The presence of oedema in a rejecting renal transplant (Porter, 1964; Williams *et al.*, 1964), due probably to a leakage of fluid through damaged capillary walls (Porter, 1964), is well known. It is conceivable that the lymph could have leaked from damaged capsular lymphatic vessels. On the other hand, it could have followed the lymphatic pathways of the organ to make its appearance through the hilum. Progressive accumulation of lymph ensued because the lymphatic vessels of the transplant were not in direct continuity with those of the recipient.

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