# Disordered gastric motor function in diabetes mellitus

Horowitz and Fraser [1] elegantly discuss impaired gastric motility in diabetic patients. Recent work [2–4] may add some useful information to this comprehensive review [1].

We investigated the actions of an antilipolytic drug, GR 79236 (Glaxo Group Research, Greenford, Middlesex, UK), in the diabetic ketoacidotic (DKA) rat [2]. Stomach weights were significantly ($p < 0.002$) lighter in the animals with markedly lower serum non-esterified fatty acid (NEFA) concentrations. Thus, stomach weights, expressed as median and (range), were 3.0 (2.5–10.0) and 9.8 (7.0–15.0) g in the GR 79236-treated and control groups, respectively. Both groups studied were deprived of food for the preceding 10 h. In contrast, blood glucose levels were significantly ($p < 0.04$) higher in the GR 79236 group (22.0; 18.8–31.3 mmol/l) than in controls (15.1; 10.8–29.6). These observations suggest that high blood NEFA levels slow gastric emptying. However, we cannot exclude a role for changes in the other biochemical variables (e.g. pH, serum acetoacetate or calcium) which occurred [2]. Our findings however, are compatible with the evidence [1] that insulin, with/without hypoglycaemia, increases gastric emptying.

DKA in the rat was also associated with elevated serum creatine kinase (CK) activity [2, 4], an effect reversed by GR 79236 [2, 4]. We did not establish the source(s) of CK, but this enzyme may well be 'leaking' from virtually every muscle tissue [4]. Whether such an effect affects gastric muscle function remains to be established.

GR 79236 could be used, at least in animal experiments, to investigate the role of NEFA-related variables (independently of blood glucose) on gastric motility. GR 79236 may also have synergistic actions with insulin [3] and may therefore be a useful tool in non-ketonuric diabetes where insulin is present in the circulation. In humans, gastric function could be evaluated during transient elevations in plasma NEFA concentrations following the intravenous injection of ACTH [5] or heparin [6]. Similarly, investigators could benefit from using lipid-lowering fibric acid derivatives, e.g. bezafibrate, which can reduce plasma NEFA concentrations in diabetic patients [7].

If this 'NEFA hypothesis' is correct, new options for the treatment of impaired gastric motility in diabetic patients must be considered.

Yours sincerely,
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# Increased expression of type III and type IV collagen in diabetic nephropathy

Dear Sir,
With interest, we read the recent article published in your journal by Tamsma et al. [1] regarding the distribution of extracellular matrix components in human diabetic nephropathy. We would like to present our own experience on this subject. Overproduction of extracellular matrix is considered to be primarily responsible for both glomerular and tubulointerstitial changes in diabetic nephropathy (DN). We used immunohistochemistry and non-isotopic in situ hybridization techniques to examine the possible role of interstitial type III collagen and type IV basement membrane collagen in diabetic glomerulosclerosis and tubulointerstitial damage in ten DN patients and ten normal control subjects.

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Compared to the control cases, higher immunostaining for type IV collagen was recorded in the glomerular sclerotic matrix, whereas immunostaining for type III collagen was noted only in the late stage of global sclerosis [2]. However, in the damaged tubulointerstitium of DN, increased immunostaining for both type III and type IV collagens were found.

To determine the origin of these collagens in both glomerulosclerosis and tubulointerstitial damage, non-radioactive in situ hybridization was performed utilizing thymine-thymine (T-T) dimerized synthetic oligonucleotides complementary to either human pro α (1) III chain or pro α (1) IV chain mRNAs as probe. Like Prigent et al. [3], we could not detect any type III collagen mRNA or protein in normal glomerulus [4]. Also no mRNA-positive cells were found in the normal tubular epithelium. Nevertheless, the appearance of pro α (1) III mRNA positive cells in the sclerotic glomeruli [5] and damaged tubules with accumulation of its protein suggested de novo synthesis of interstitial type III collagen by the intraglomerular and tubular cells in DN. In contrast, compared to the control subjects, increased synthesis of type IV collagen by intraglomerular cells in diabetic glomerulosclerosis [5] and