adult human liver,[4] and have since investigated expression in a number of other fetal tissues. We found evidence of expression in tongue, brain, intestine, mandible, eye, sternum, pancreas, spleen, and in placenta and umbilical cord, but not in adrenals, thymus, skin, or lungs; high expression, however, was only observed in liver, intestine, and placenta.[13] This pattern makes its unlikely that expression of the 6 Kb HGF mRNA merely reflects haemopoiesis.

Finally, for completeness there are now two mRNA species for HGF, the most recently described being an alternatively spliced 1·5 Kb transcript with an identical 5 prime cDNA sequence for the first 856 nucleotides downstream of the initiation of translation site, but completely divergent at the 3 prime end.[14]

In summary, although the concept that only one growth factor is entirely responsible for liver regeneration is outmoded, the insights and implications of the HGF story seem likely to have an impact on our understanding of benign and perhaps malignant liver cell growth for many years to come.

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Is gastric emptying faster or slower in patients with early stage of non-insulin dependent diabetes mellitus?

SIR,—I have read with keen interest two recent reports on the effect of hyperglycaemia and gastric emptying.[1 2] Though these two studies differed in the subjects recruited and the techniques and design, they were centred on the same theme and, interestingly enough, the authors reached contrary conclusions.

Phillips *et al* showed much more rapid gastric emptying in patients with early non-insulin dependent diabetes mellitus (less than two years disease duration). Their study is based on scintigraphic measurement of the emptying rate of a liquid glucose meal from the stomach. The approach is straightforward and impeccable. The physiological response during the study period was not very different from the real-life situation in poorly controlled diabetes. However, their speculation on the role of rapid gastic emptying in the aetiology of non-insulin dependent diabetes mellitus is unfounded and too fanciful. It has been shown that insulin secretion is closely geared to the gastric emptying of a glucose load in healthy subjects.[3] Rapid gastric emptying, as in patients with dumping syndrome, definitely reduces the glycaemic responses but these patients are not more prone to diabetes unless risk factors such as obesity coexist.

Fraser *et al*,[2] based on localised gastroduodenal manometric measurement of healthy subjects in whom hyperglycaemia was induced with dextrose infusion, observed that hyperglycaemia stimulated pyloric contraction and suppressed antral motility. They concluded that hyperglycaemia delayed gastric emptying, but acknowledged that the motility of the proximal stomach, which was not assessed in the study, might play an important role in determining the rate of gastric emptying. Therefore, too many loopholes were left unfilled when the authors tried to generalise from data on localised motility and contraction to give an overall picture of gastric emptying. By the same token, caution must be exercised when results from acutely hyperglycaemic normal subjects are extrapolated to diabetic patients. Hyperinsulinaemia by itself will affect the motility of the gastrointestinal tract.[4 5]

Although the conclusions reached by these studies are exactly contrary, they do not necessarily contradict each other. The differences cannot be attributed to the consistency of the food or intraluminal acidic pH as these have either no effect on or may even delay gastric emptying time.[6-8] Fraser's work actually showed the predominantly suppressive effect of a raised blood glucose concentration on the vagal tone of the gastrointestinal tract, whereas Phillips's study included the effect on paracrinal control by the gut epithelium in response to an oral glucose load. These two mechanisms act in opposition, and presumably in non-insulin dependent diabetes mellitus patients the paracrinal control is more dominant. Continuous hyperglycaemia may partially blunt the acutely suppressive effect of a surge in blood sugar on the gut vagal tone. Hence the loss of the negative feedback to the stomach fails to 'brake' the massive outpouring of glucose into the intestine and further reduces the glycaemic response in diabetic patients.

Lastly, I would like to share my anecdotal observation of hyperglycaemia and diarrhoea in the early stage of the disease. I keep some alloxan induced diabetic rats in metabolic cages for microalbuminuria study. The rats with poorer metabolic control were incidentally found to suffer from diarrhoea (large daily output of loose stools with an offensive smell). Perhaps this dumping like syndrome may play some role in the diarrhoea of early diabetes.

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1 Phillips WT, Schwartz JG, McMahan CA. Rapid gastric emptying in patients with early non-insulin-dependent diabetes mellitus. *N Engl J Med* 1991; **324**: 130–1.
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Reply

SIR,—We believe that there is no discrepancy between the results reported in our study and those reported by Phillips *et al*[1] as they address different issues. The first concerns the motor effects of hyperglycaemia in healthy humans, while the second relates to the control of gastric emptying rates in patients with diabetes mellitus.

In the study by Phillips *et al*,[1] gastric emptying of a liquid meal was found to be accelerated in nine patients with type 2 diabetes mellitus. They did not comment on the selection criteria of the patients (there is a clear racial difference between the patients and controls), nor on the blood glucose concentrations during the study. Although gastric emptying of digestible solid and nutrient liquid meals is delayed in about 40% of patients with diabetes mellitus,[2-5] the initial emptying rate of liquid meals is accelerated in some patients.[2 4] It has been suggested that rapid liquid emptying in diabetes mellitus may reflect impaired proximal stomach adaptation to distension.[6] We have reported that in diabetes mellitus, gastric emptying is slower at increased blood glucose concentrations,[2 3 7] indicating that diabetic gastroparesis may result from poor glycaemic control and does not always reflect irreversible nerve damage. While this observation is not surprising (induced hyperglycaemia is known to slow gastric emptying in normal subjects),[8 9] it indicates that studies of gastric motility in diabetic patients should take into account blood glucose concentrations. Thus, while the report by Phillips *et al* is interesting, the data as presented in letter form do not allow evaluation, and their importance is difficult to interpret.

In our recent study,[10] induced hyperglycaemia resulted in a pattern of antropyloroduodenal motility known to be associated with slow gastric emptying in normal subjects.[11] It seems reasonable to suggest that hyperglycaemia may account for

reduced antral pressure waves[12] and increased pyloric pressure waves[13] observed in diabetic patients with symptomatic gastroparesis, but we agree that this hypothesis requires confirmation.

The mechanisms by which hyperglycaemia influences gastric motility are uncertain and may be indirect and multifactorial. A recent study performed by our group suggests that hyperinsulinaemia does not influence antropyloric motility.[14]

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1 Phillips WT, Schwartz JG, McMahan CA. Rapid gastric emptying in patients with early non-insulin-dependent diabetes mellitus. *N Engl J Med* 1991; **324:** 130–1.
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Prospective clinical and manometric study comparing pneumatic dilatation and sublingual nifedipine in the treatment of oesophageal achalasia

SIR,—Dr Coccia and colleagues (*Gut 1991;* **32:** 604–6) conclude that sublingual nifedipine is as good a treatment as pneumatic dilatation of the gastrooesophageal sphincter in patients with stage I or II oesophageal achalasia. This conclusion is based on manometric investigations as well as clinical evaluation. Regarding the manometric study it is difficult to see whether the manometric technique is sufficient as the diameter of the pressure probe and their normal values are not stated. Further, it might be assumed that the tube is in a fixed position during the nifedipine treatment. If that is the case how did the authors make sure that it was maximal sphincter pressure they measured?

There is no mention of the relaxation of the sphincter in relation to swallowing and as achalasia means lack of relaxation that important parameter is missing. Also there was no information about the peristaltic response of the oesophageal body.

From a clinical point of view there is obviously no difference in the two treatment groups, but the possibility of a type II error is not calculated and these patients were only followed for a short period of time. It is important to know whether the stage I or II of achalasia progresses under the treatment with nifedipine or after dilatation.

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Reply

SIR,—As the patients are their own controls, the diameter of the probe should be irrelevant. The probe diameter is 4·7 mm, however, and the values recorded in normal subjects are: lower oesophageal sphincter pressure = 19 (4·5) mm Hg (×(SD) and pressure waves amplitude = 80 (15) mm Hg. The probe position was controlled periodically during the examination to make certain that it measured the maximal lower oesophageal sphincter pressure.

The question about lower oesophageal sphincter relaxation and return of peristalsis is very interesting. In fact, in some cases peristalsis returned and the postdeglutitive relaxation of the lower oesophageal sphincter was improved. This is, however, the subject of other research which is in progress.

The absence of differences between the two treatment groups is not limited to a clinical point of view, but is also based on radiologic and manometric criteria (see Methods and Results sections). The duration of our follow up period is between that of Traube (*Gastroenterology* 1986; **90:** 1670) and of Gelfond (*Gastroenterology* 1982; **83:** 963) and the improvement observed at the final control is against a possible progression of the disease.

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NOTES

Study Day on Management of Pancreatic Cancer

This will be held on 24 March 1992 at the University of Southampton. Further details from Mrs J Daniels, University Surgical Unit, F Level Centre Block, Southampton General Hospital, Tremona Road, Southampton SO9 4XY (Tel: 0703 796144; fax: 0703 794020).

International Association for the Study of the Liver – Biennial Scientific Meeting

The Biennial Scientific Meeting of the International Association for the Study of the Liver will be held in Brighton from 3–6 June 1992. For further information please contact the IASL Conference Secretariat, 145 Islingword Road, Brighton, Sussex BN2 2SH, UK (Tel: (0) 273 623123; fax: (0) 273 622944).

C A Ewald Prize

The German Gastroenterology Society (Deutsche Gesellschaft für Verdauungs- und Stoffwechselkrankheiten) announces the C A Ewald Prize for outstanding scientific work on the topic 'Pathogenesis of peptic ulcer'. The applicant's work may be unpublished or published in 1990 to 1991 and should be written in German or English. The applicant is asked to submit five copies of his application as follows: (1) Scientific work, (2) Curriculum vitae, (3) List of all previous publications.

The C A Ewald Prize is sponsored by the Cascan Company, Wiesbaden, and amounts to 10 000 DM. The prize can be awarded only to applicants not older than 40 years. Applications should be sent not later than 30 April 1992 to: Professor Dr M Manns, Med. Hochschule Hannover, Abt Gastroenterologie, Konstanty-Gutschow-Str 8, 3000 Hannover 61.

European Workshop on Therapeutic Digestive Endoscopy

The Xth European workshop on therapeutic digestive endoscopy will take place at Erasme Hospital, ULB, Brussels, Belgium from June 16 to 18 1992. For further information please contact André Van Gossum, MD, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B–1070, Brussels (Phone: 32 2 555 37 12; fax: 32 2 555 46 97).

European Pancreatic Club

The XXIV Meeting will be held from 11–14 October 1992 at Ulm, Germany. For further information please contact the EPC Scientific Secretariat, Mrs M Wild, Department of General Surgery, University of Ulm, Steinhoevelstrasse 9, 7900 Ulm, Germany (Phone +731/1 79–2200, 2201; fax +731/179–2466).

The European Association for the Study of the Liver (EASL)

The annual meeting will be held in Vienna, 25–29 August 1992. For information contact the Secretary of EASL, Dr P L M Jansen, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands (Fax: 31.20.691 7033).