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.

H J F HODGSON
A C SELDEN
Royal Postgraduate Medical School, London W12 0NN

1 Weidner KM, Arakaki J, Vandekerchove S, Weingart G, Hartmann H, Rieder C, *et al.* Evidence for the identity of human scatter factor and human hepatocyte growth factor. *Proc Natl Acad Sci* 1991 (in press).
2 Zarnegar R, DeFrances MC, Kost DP, Lindroos P, Michalopoulos GK. Expression of hepatocyte growth factor mRNA in regenerating rat liver after partial hepatectomy. *Biochem Biophys Res Commun* 1991; **177**: 559–65.
3 Okajima A, Miyazawa K, Kitamura N. Primary structure of rat hepatocyte growth factor and induction of its mRNA during liver regeneration following hepatic injury. *Eur J Biochem* 1990; **193**: 375–81.
4 Selden A, Jones M, Wade D, Hodgson HJF. Hepatotropin mRNA expression in human foetal liver development and in liver regeneration. *FEBS Lett* 1990; **270**: 81–4.
5 Bottaro DP, Rubin JS, Faletto DL, Chan AML, Kmiecik TE, Vande Woude GF, *et al.* Identification of the hepatocyte growth factor receptor as the c-met proto-oncogene product. *Science* 1991; **251**: 802–4.
6 Matsumoto K, Tajima H, Nakamura T. Hepatocyte growth factor is a potent stimulator of human melanocyte DNA synthesis and growth. *Biochem Biophys Res Commun* 1991; **176**: 45–51.
7 Naldini L, Vigna E, Narsimhan RP, Gaudino G, Zarnegar R, Michalopoulos GK, *et al.* Hepatocyte growth factor (HGF) stimulates the tyrosine kinase activity of the receptor encoded by the proto-oncogene c-MET. *Oncogene* 1991; **6**: 501-4.
8 Higuchi O, Nakamura T. Identification and change in the receptor for hepatocyte growth factor in rat liver after partial hepatectomy or induced hepatitis. *Biochem Biophys Res Commun* 1991; **176**: 599–607.
9 Zarnegar R, DeFrances MC, Oliver L, Michalopoulos GK. Identification and partial characterisation of receptor binding sites for HGF on rat hepatocytes. *Biochem Biophys Res Commun* 1990; **173**: 1179–85.
10 Laguda B, Selden C, Jones M, Hodgson HJF, Spurr NK. Assignment of the hepatocyte growth factor (HGF) to chromosome 7 q22-qter. *Ann Hum Genet* 1991; **51**: 213–6.
11 Dean M, Park M, Le Beau MM, Robins TS, Diaz MO, Rowley JD, *et al.* The human met oncogene is related to the tyrosine kinase oncogenes. *Nature* 1985; **318**: 385–8.
12 Collard JG, van de Poll M, Scheffer A, Roos E, Hopman AH, Geurts van Kessel ADHM, *et al.* Location of genes involved in invasion and metastasis on human chromosome 7. *Cancer Res* 1987; **47**: 6666–70.
13 Selden AC, Hodgson HJF. Role of hepatocyte growth factor in human ontogeny. *Clin Sci* 1990; **80**: 6P.
14 Miyazawa K, Kitamura A, Naka D, Kitamura N. Alternatively processed mRNA generated from human hepatocyte growth factor gene. *Eur J Biochem* 1991; **197**: 15–22.

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.

IVAN Y M CHUNG
Department of Applied Biology and Chemical Technology, Hong Kong Polytechnic, Hung Hom, Kowloon, Hong Kong

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.
2 Fraser R, Horowitz M, Dent J. Hyperglycaemia stimulates pyloric motility in normal subjects. *Gut* 1991; **32**: 475–8.
3 Ebert R. Gut signals for islet hormone release. *Eur J Clin Invest* 1990; **20** (suppl 1): S20–6.
4 Phaosawasdi K, Goppold R, Fisher R. Pyloric sphincter pressure response to insulin-induced hypoglycaemia in man. *Am J Physiol* 1981; **241**: G321–7.
5 Prasad K, Sarna S. The central and peripheral effects of insulin on migrating myoelectric complexes. [Abstract]. *Gastroenterology* 1988; **94**: 1589.
6 Cadiot G, Marrouche M, Sekra E, Paycha F, Rigaud D, Vatier J,*et al.* Is delayed gastric emptying due to alteration of pH-dependent regulatory mechanisms in gastro-esophageal reflux (GER)? *Gastroenterology* 1991; **100**: A38.
7 Hölzer HH, Raybould HE. Duodenal acid induced delay of gastric emptying in conscious rats. *Gastroenterology* 1991; **100**: A451.
8 Pallotta N, Biliotti D, Corazzian E, Torsoli A. Food consistency does not affect gastric emptying time of digestible caloric meals. *Gastroenterology* 1991; **100**: A479.

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