Reply

EDITOR.—In reply, I would like to state that, while we agree that sphincter of Oddi hypertension may be an important contributor to the phenomenon of acalculous biliary pain, the purpose of the CCK provocation test is to select patients who might benefit from cholecystectomy. Whether subselection can be made on the basis of sphincter of Oddi testing remains to be seen but, certainly, the CCK provocation test should not be recommended as a selection tool for symptom relief after a cholecystectomy.

A W MAJEED

Department of Surgical and Anaesthetic Sciences,
Royal Hallamshire Hospital,
Sheffield S10 2JF, UK

Cholecystokinin infusion and gall bladder dysfunction

EDITOR.—We read with interest the commentary by Al-Musawi and Williamson (*Gut* 1998;43:454–5) and the paper in the same issue by Smythe *et al* (*Gut* 1998;43:571–8). We agree with Al-Musawi and Williamson that six months is an inadequate follow up time, that identification of cystic duct abnormalities is important and in particular that cholecystokinin (CCK) scintigraphy is a more accurate technique than either ultrasound or oral cholecystography. We however disagree with their view that the CCK provocation test, based solely on the reproduction of pain, is of diagnostic value.

The value and accuracy of CCK scintigraphy has been well documented by several groups^{1–4} including our own.^{5–7} The true positive rates for all these studies are in the range 94–97%. Our most recently reported data⁷ are from an eight year prospective study of 235 patients, with follow up (mean 4.5 years) of all patients, surgical and non-surgical, with both normal and abnormal gall bladder ejection fractions. This demonstrates 96% sensitivity, 92% specificity and 95% overall accuracy for CCK scintigraphy in predicting gall bladder dysfunction and long term clinical outcome. These findings are in agreement with the 6% false negative rate obtained by Fink-Bennett and colleagues¹ in a retrospective study. In our series, abnormal cystic ducts were found in 12% of patients who underwent surgery, all of whom were symptom-free on long term follow up.

In their introduction, Smythe *et al* state that Yap and colleagues⁸ and ourselves⁷ claim some efficacy for the CCK provocation test. This is incorrect. Both papers clearly describe the efficacy of CCK scintigraphy and the measurement of gall bladder ejection fraction. We have never advocated pain reproduction as an indicator of gall bladder dysfunction. Despite using a fast (three minutes) infusion of CCK,⁸ thought to be more likely to induce pain and cause spasm of the cystic duct, we have found no correlation between the reproduction of pain following CCK infusion and either gall bladder ejection fraction or subsequent surgical outcome.⁷ We agree with Smythe *et al* that pain reproduction following CCK infusion is not a diagnostic predictor.

Our experience of using CCK scintigraphy in over 300 patients over a 10 year period (manuscript in preparation) is that an abnormal gall bladder ejection fraction is highly predictive of gall bladder dysfunction and is a

good predictor of long term clinical outcome following surgery.

CCK scintigraphy is an accurate, objective technique and in our view should be the investigation of choice for suspected gall bladder dysfunction in patients without gallstones.

G W MIDDLETON

Principal Physicist,
Department of Medical Physics and Clinical Engineering,
University Hospital of Wales,
Heath Park,
Cardiff CF4 4XW, UK

J H WILLIAMS

Consultant Radiologist,
Department of Radiology,
Princess of Wales Hospital,
Coity Road,
Bridgend CF31 1RQ, UK

- 1 Fink-Bennett D, DeRidder P, Kolozsi WZ, *et al*. Cholecystokinin cholecystigraphy: detection of abnormal gallbladder motor function in patients with chronic acalculous gallbladder disease. *J Nucl Med* 1991;32:1695–9.
- 2 Misra DC, Blossom GB, Fink-Bennett D, *et al*. Results of surgical therapy for biliary dyskinesia. *Arch Surg* 1991;126:957–60.
- 3 Yap L, Wycherley AG, Morphet AD, *et al*. Acalculous biliary pain: cholecystectomy alleviates symptoms in patients with abnormal cholecystigraphy. *Gastroenterology* 1991;101:786–93.
- 4 Watson A, Better N, Kalfi V, *et al*. Cholecystokinin (CCK)-HIDA scintigraphy in patients with suspected gall-bladder dysfunction. *Australas Radiol* 1994;38:30–3.
- 5 Middleton GW, Williams JH. Is gall bladder ejection fraction a reliable predictor of acalculous gall bladder disease? *Nucl Med Commun* 1992;13:894–6.
- 6 Middleton GW, Williams JH. Detection of acalculous gall bladder disease using Tc^{99m} EHIDA imaging and cholecystokinin. *Eur Radiol* 1994;4:462–3.
- 7 Middleton GW, Williams JH. Diagnosis of acalculous cholecystitis using Tc^{99m} HIDA imaging – a long term follow-up study. *Eur Radiol* 1997;7:S84.
- 8 Middleton GW, Williams JH. Fast or slow cholecystokinin infusion Tc^{99m} HIDA imaging [letter]? *Australas Radiol* 1995;39:100.

Ductal dilatation and stenting for residual hepatolithiasis

EDITOR.—Sheen-Chen *et al* (*Gut* 1998;42:708–10) have advocated the use of ductal dilatation and stenting through a T-tube tract followed by choledochoscopic stone retrieval in patients with residual postoperative hepatolithiasis and intrahepatic strictures. The total number of procedures (percutaneous duct dilatation, stent placement and choledochoscopic stone extraction) per patient ranged from four to 11 (median 8). No mention is made of the length of time, length of hospital stay or total cost from initial surgery to completion of the above procedures and ultimate stone clearance. Surprisingly, the authors have not cited their two previous papers on the technique.^{1,2} While undergoing repeated percutaneous biliary intervention, patients have the discomfort and inconvenience of external T-tubes and stoma appliances to control the invariable and distressing bile leakage around the external catheters. The strategy proposed by Sheen *et al* also does not provide access to the intrahepatic ducts if recurrent calculi develop later after removal of the T-tube.

In order to avoid these hazards and minimise the incidence of incomplete operative stone removal and to facilitate extraction of recurrent intrahepatic stones, we have used meticulous intra-operative techniques to clear stones and create a biliary access loop to

Figure 1 Jejunal access loop marked with metal clips.

deal with recurrent stones. Full exposure of the hepatic duct bifurcation is obtained at operation and intra-operative ultrasound, cholangiography and cholangioscopy are used to locate and map the site and extent of segmental duct stones. Accessible segmental duct strictures are widened by surgical ductoplasty and impacted stones extracted.³ When peripheral segmental ducts beyond the reach of conventional operative cholangioscopy are involved, intra-operative radiological manipulation with a balloon to dilate strictures and a basket to extract recalcitrant stones is used. If substantial parenchymal atrophy has occurred, or multiple cholangitic abscesses are present, the involved segment or lobe is resected in addition to duct drainage and creation of the access loop. Usually only a left lateral segmental resection is required.

Percutaneous transjejunal biliary intervention has become an integral part of the multidisciplinary management of complex intrahepatic strictures and stones since the initial descriptions by Fang and Chou,⁴ Barker and Winkler⁵ and Hutson *et al*.⁶ The original cutaneous stoma has been replaced by a subparietal jejunal loop.⁷ In 21 patients with residual or recurrent intrahepatic stones we achieved successful intrahepatic biliary access in 95 (98%) of 97 puncture attempts.⁸ Several technical points in the jejunal loop construction are useful to create a loop which is easy to identify and enter. The access limb should be short and straight between the hepaticojejunal anastomosis and site of subparietal fixation. The terminal 4 cm of the bowel is sutured to the peritoneum of the anterior abdominal wall and marked with a parallel row of metal clips to provide "runway lights" for radiological identification and puncture (fig 1). The subparietal attachment and clear marking of the loop simplify identification and allow consistently successful percutaneous entry. In difficult cases the use of high frequency ultrasound facilitates identification of the surgical clips and the needle tip during entry into the access loop. Two additional clips on either side of the hepaticojejunostomy are useful to identify the site of the anastomosis.⁷

As an alternative to expensive electrohydraulic lithotripsy a vascular snare used as a cheese-cutter facilitates stone fragmentation and removal in patients with soft calculi. If stones recur, as they often do, the entire

sequence described by Sheen *et al* needs to be repeated after operative T-tube replacement. A jejunal biliary access loop eliminates the need for prolonged external tubes and is readily available for re-usage without the need for further surgery if stones or strictures recur.

J E J KRIGE

I J BECKINGHAM

J TERBLANCHE

Department of Surgery,
University of Cape Town Medical School,
Anzio Road,
Observatory 7925 Cape Town,
South Africa

S J BENINGFIELD

Department of Radiology,
University of Cape Town Medical School,
Anzio Road,
Observatory 7925 Cape Town,
South Africa

- 1 Sheen-Chen SM, Chou FF, Lee CM, *et al*. The management of complicated hepatolithiasis with intrahepatic biliary stricture by the combination of T-tube tract dilation and endoscopic electrohydraulic lithotripsy. *Gastrointest Endosc* 1993;39:168-71.
- 2 Sheen-Chen SM, Cheng YF, Chou FF, *et al*. Ductal dilatation and stenting make routine hepatectomy unnecessary for left hepatolithiasis with intrahepatic biliary stricture. *Surgery* 1995;117:32-6.
- 3 Krige JEJ, Benningfield SJ. Surgery and interventional radiology for benign bile duct strictures. *HPB Surg* 1993;7:94-7.
- 4 Fang K, Chou T. Subcutaneous blind loop in a new type of hepaticocolochojunostomy for bilateral calculi. *Clin Med J* 1977;3:361-8.
- 5 Barker EM, Winkler M. Permanent access hepaticocolochojunostomy. *Br J Surg* 1984;71:188-91.
- 6 Hutson DG, Russell E, Schiff E, *et al*. Balloon dilatation of biliary strictures through a choledochocolochojunostomy fistula. *Ann Surg* 1984;199:637-47.
- 7 Krige JEJ, Bornman PC, Harries-Jones EP, *et al*. Modified hepaticocolochojunostomy for permanent biliary access. *Br J Surg* 1987;74:612-13.
- 8 Beckingham IJ, Krige JEJ, Benningfield SJ, *et al*. Subparietal hepaticocolochojunostomy for the long-term management of intrahepatic stones. *Br J Surg* 1998;85:1360-3.

The *Helicobacter pylori* breath test: a surrogate marker for peptic ulcer disease in dyspeptic patients

EDITOR,—We read with great interest the paper by McColl and colleagues (*Gut* 1997;40:302-6) reporting the usefulness of the non-invasive *Helicobacter pylori* ¹⁴C-urea breath test (¹⁴C-UBT) in predicting underlying ulcer disease in patients with dyspepsia. By administering 0.4 MBq ¹⁴C-urea after the test meal, the cut off values calculated by the authors at 20 minutes seem to be very high—namely, above 40 kg% dose/mmol CO₂ for *H pylori* positive and less than 20 kg% dose/mmol CO₂ for *H pylori* negative patients. The values between 20 to 40 are suggested to be equivocal. The authors have not given the basis for obtaining these cut off values. We have used the ¹⁴C-UBT routinely since 1990 and so far have performed this test on almost 500 patients using a wide variety of test protocols. Based on our initial data, the cut off value for *H pylori* positive patients was calculated to be above 0.6% dose/mmol CO₂ × kg (body weight) 15 minutes after oral administration of 185 kBq ¹⁴C-urea without giving a test meal or cold substrate.¹ Similarly, a theoretical value of 0.585% can be obtained at 15 minutes by multiplying the body weight of an average adult human (65 kg) by the cut off value of 0.009% dose/mmol CO₂ reported earlier by us and used to confirm eradication of *H pylori*.^{2,3} Raju and others have also

reported a cut off value of 0.55% at 20 minutes using 37 kBq ¹⁴C-urea after an overnight fast.⁴ Most recently, a cut off value of 1.0% dose/mmol CO₂ × kg at 10 minutes has been reported after administration of 185 kBq of tracer without capsule.⁵

In view of the literature cited above, the cut off values for the ¹⁴C-UBT reported by McColl and colleagues seem to be very high and may be the result of a calculation error or technical problem. If these values are taken as a reference by others, analysis of their ¹⁴C-UBT data may not distinguish accurately *H pylori* infected from non-infected patients.

To minimise decomposition, it is recommended that stock of ¹⁴C-urea be stored at -20°C in a freeze-dried solid form. Repeated thawing of the aqueous solution of the tracer causes it to decompose. We have found a drastic reduction in the count rate from 213 793 to 5487 dpm in 20 lambda solution when the tracer was thawed more than 25 times over 109 days; the count rate declined to almost 50% of the original—namely, from 323 000 to 156 499 dpm, when a different solution of tracer was thawed nine times over 112 days. Therefore, ideally the standard should always be prepared from the same stock solution which is administered to the patients. It is likely that the high cut off values obtained by McColl and colleagues resulted from the preparation of standard taken from stock solution which might have been thawed repeatedly, whereas the tracer dose administered to the patients was thawed once or twice only.

As the ¹⁴C-UBT is a simple, quick, non-traumatic, highly reliable, and cost effective test, it is used for screening, follow up, and for epidemiological purposes. Different authors have reported different cut off values with variable units depending on the test protocols they have followed, and the results are also expressed in different units.⁶ To avoid unnecessary confusion in the interpretation of ¹⁴C-UBT data, now there is an urgent need for a standard test protocol.

C M PATHAK

K L KHANDUJA

Department of Biophysics,
Postgraduate Institute of Medical Education and
Research,
Chandigarh-160 012, India

D K BHASIN

B C SHARMA

Department of Gastroenterology,
Postgraduate Institute of Medical Education and
Research,
Chandigarh-160 012, India

Correspondence to: Dr Pathak (email: medinst@pgi.chd.nic.in)

- 1 Pathak CM, Panigrahi D, Bhasin DK, *et al*. Advantage of use of DPM for ¹⁴C-urea breath test for the detection of *Helicobacter pylori*. *Am J Gastroenterol* 1992;87:1887-8.
- 2 Pathak CM, Bhasin DK, Panigrahi D, *et al*. Evaluation of ¹⁴C-urinary excretion and its comparison with ¹⁴CO₂ in breath after ¹⁴C-urea administration in *Helicobacter pylori* infection. *Am J Gastroenterol* 1994;89:734-8.
- 3 Sharma BC, Bhasin DK, Pathak CM, *et al*. ¹⁴C-urea breath test to confirm eradication of *Helicobacter pylori*. *Ind J Gastroenterol* 1997;16(suppl 2):A27.
- 4 Raju GS, Smith MJ, Morton D, *et al*. Mini-dose (1-μCi) ¹⁴C-urea breath test for the detection of *Helicobacter pylori*. *Am J Gastroenterol* 1994;89:1027-31.
- 5 Lerang F, Haug JB, Moum B, *et al*. Accuracy of IgG serology and other tests in confirming *Helicobacter pylori* eradication. *Scand J Gastroenterol* 1998;33:710-15.
- 6 Ormand JE, Talley NJ, Carpenter HA, *et al*. [¹⁴C] urea breath test for the diagnosis of *Helicobacter pylori*. *Dig Dis Sci* 1990;35:879-84.

Reply

EDITOR,—Our 20 minute breath test result is in fact expressed in terms of 100 × kg% dose/mmol CO₂, but the factor of “100” was omitted in error in the original publication. This explains why our results are much greater than those stated by Pathak and colleagues. The basis for our cut off values as presented in the paper is to be found in an early publication¹ but in light of further experience with the breath test, it is now our practice to take a result of >30 as positive.² This corresponds to a cut off value of 0.3 in the units used by Pathak and colleagues. The sensitivity and specificity in the determination of *Helicobacter pylori* status with this cut off value are 98% and 100% respectively.²

We agree with Pathak and colleagues regarding the desirability of standardising the test protocol. In addition to the list of variables they have detailed, which influence the test result, there is the matter of assaying the ¹⁴C content of the test sample. If adequate correction is not made for luminescence, this can lead to a falsely raised result, a problem which could be significant with test doses at the lower end of the reported activity range.

The question of preparation, storage and stability of the ¹⁴C-urea is interesting. Several different approaches have been published—the test dose may be produced in capsule form,³ stored at -20°C and thawed just before use,⁴ sterilised and stored at 2-4°C,⁵ or withdrawn, just before use, from a stock solution stored at 2-4°C.⁶ In some cases the main concern has been to ensure that test doses are sterilised before storage, thus preventing any decomposition by urease producing bacteria.⁷ Analysis of the test dose of ¹⁴C urea after several weeks⁸ or six months' storage^{4,5} has shown no significant deterioration of the product. In our protocol, the original freeze dried ¹⁴C-urea is dissolved in sterile water, from which individual test doses are dispensed into screw-capped containers and stored for up to six weeks at 2-4°C. We have not experienced any problems with decomposition of the product. In terms of convenience, use of a screw-capped container to contain the test dose is less convenient than use of a capsule, but more practical than use of a sealed sterile vial or ampoule. We are currently investigating the use of benzyl alcohol as an antimicrobial preservative to allow longer storage of test doses. From the work of Pathak and colleagues it is clearly inadvisable to freeze and thaw a stock solution of ¹⁴C urea repeatedly.

T E HILDITCH

Department of Clinical Physics and Bio-Engineering,
Western Infirmary, Glasgow G11 6NT, UK

K E L MCCOLL

University Department of Medicine and Therapeutics,
Western Infirmary, Glasgow G11 6NT, UK

- 1 Neithercut WD, Milne A, Chittajallu RS, *et al*. Detection of *Helicobacter pylori* infection of the gastric mucosa by measurement of gastric aspirate ammonium and urea concentrations. *Gut* 1991;32:973-6.
- 2 Mowatt C, Murray LS, Hilditch TE, *et al*. Comparison of helical rapid blood test and ¹⁴C-urea breath test in determining *Helicobacter pylori* status and predicting ulcer disease in dyspeptic patients. *Am J Gastroenterol* 1998;93:20-5.
- 3 Peura DA, Pambianco DJ, Dye KR, *et al*. Microdose ¹⁴C-urea breath test offers diagnosis of *Helicobacter pylori* in 10 minutes. *Am J Gastroenterol* 1996;91:233-8.
- 4 Clarkson A, Millar AM. Validation of a technique for the preparation of individual patient doses of ¹⁴C-urea. *Nucl Med Commun* 1997;18:57-9.