January 9, 1990

Dear Editor:

Clavien and colleagues are to be congratulated on their excellent paper 'Acute pancreatitis and normoamylaseamia' (Ann Surg 1989; 210:614–20). We concur entirely that computerized tomography (CT) scanning should be used in cases of doubtful or negative enzymatic results. They state that 19% incidence of normoamylaseamia found in their series is '... significantly higher than commonly admitted,' and that '... future classifications of pancreatitis [should] mention the fact hyperamylaseamia is not a necessary condition for the diagnosis of AP [acute pancreatitis].'

We see some difficulties, however, in extrapolating their data into a general context. The results of different series will be flavored by referral patterns and the prevalence of different etiologies. To illustrate we examined serial amylase levels in 339 patients with AP (259 with mainly gallstone etiology and 82 with an alcoholic cause), 99% of whom were admitted within 24 hours of the attack and mostly included in other studies.[1–4] Amylase was measured by the Phadebas method, our diagnostic level for AP being more than 1000 IU/L (normal range, 70 to 300 IU/L). On admission hyperamylasemia was present in 99.1% (diagnostic level reached in 94.4%); at 24 hours this was 96.7% (71.7%); at 48 hours it was 72.3% (35.1%); at 72 hours it was 47.6% (7.2%); and at 1 week it was 25.1% (8.2%). Thus it is apparent that the greater the delay in patient admission after the onset of the attack, the greater the likelihood of a normal amylase. Thus the unusually high incidence of normoamylaseamia in the authors' results is partly explained by a considerable delay in the admission of most of their patients.

Even with this proviso, the finding that 58% of 132 alcoholic patients had a normal amylase level seems remarkably high. In our experience 98.8% of alcoholic patients had an amylase level of more than 300 IU/L and this was more than 1000 IU/L in 84.1%.

Perhaps Clavien and colleagues have included in their analysis a proportion of patients with exacerbations of chronic pancreatitis rather than acute pancreatitis *per se*. Clinical judgment and CT scanning are not, in themselves, always sufficient to exclude chronic pancreatitis, as the authors imply. It would have been helpful to know more about the actual outcome of these patients during hospital admission and their subsequent investigation, including endoscopic retrograde cholangiopancreatography. It is difficult to appreciate how it is possible to differentiate by CT alone between acute and chronic pancreatitis in a patient with a normal serum amylase level and who, on CT scanning, has no more than a moderately enlarged pancreas. Certainly in these patients we would endorse the wider use of serum lipase determinations.

The authors state that 'the CT scan appears to be the gold standard in AP'; surely histopathology is the gold standard. This seems to be borne out by the statement that CT in their hands has a sensitivity rate of 92%, which is similar to our own figure of 94%.[2]

Internationally accepted strict criteria for the diagnosis of acute pancreatitis need to be adhered to for comparison of results between different centers and for the undertaking of prospective randomized trials. At a time when general improvements in supportive care and more precise methods of intervention clearly have resulted in improved outcome, it will be difficult to show new advances if series of acute pancreatitis are diluted by cases with chronic pancreatitis alone (enlarged pancreas and normal amylase level), or patients with gallstone disease alone (raised amylase and normal pancreas). It is noteworthy that Clavien and colleagues have presented a large series of patients in whom a diagnostic level of amylase, other than a level above the upper limit of normal, is not even discussed.

While agreeing with their general conclusions, two points must be emphasized. First that where elevated enzyme levels are used without confirmatory CT or histologic examination these should be set at several standard deviations above the normal and include a time definition. Second where CT scanning is used as the main diagnostic investigation in alcohol-related disease, additional criteria are required to exclude chronic pancreatitis or alternatively to confirm an acute attack superimposed on a chronic condition. In the latter case, CT criteria alone may be applicable in some but not all cases. We would entirely endorse the inference of Clavien and colleagues that an improved classification of acute pancreatitis is warranted given the recent advances in diagnostic CT.

References

1. London NJM, Neoptolemos JP, Lavelle J, et al. Contrast-enhanced abdominal computed tomography scanning and prediction of severity of acute pancreatitis: a prospective study. Br J Surg 1989; 76:268–272.
2. London NJM, Neoptolemos JP, Lavelle J, et al. Serial computed tomography scanning in acute pancreatitis: a prospective study. Gut 1989; 30:397–403.
3. Neoptolemos JP, Carr-Locke DL, London NJ, et al. Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. Lancet 1989; ii:979–983.
4. Goodman AJ, Neoptolemos JP, Carr-Locke DL, et al. Detection of gallstones after acute pancreatitis. Gut 1985; 26:125–132.

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Dear Editor:

We are grateful for the interest shown by Drs. Neoptolemos and London in our recent prospective study on acute pancreatitis (AP). They doubt the general nature of our observation that a significant proportion of patients with AP have normal amylase values on admission to hospital. They based their objections on the level of amylase selected as the cut-off point for normality in our study, on their suggestion that some of our patients may have had chronic pancreatitis, and on the results of their own studies.[1,2]

The purpose of our study was to define the incidence of normoamylasemia on admission in patients with suspected AP by

the systematic use of contrast-enhanced CT scan, regardless of amylase values. All patients with serum amylase levels less than 160 IU/L were considered to be normoamylasemic because this value is 3SD above the mean and, by definition, includes 99% of normal individuals. Keeping the purpose of the study in mind, is the choice of an amylase level that is the upper limit of normal really questionable? Neoptolemos and London suggest that a higher level of amylase should have been regarded as the cut-off in our study. If so the percentage of patients with 'normal' amylase levels would have been even greater, and the resulting sensitivity worse.

Turning to their contention that our results might be explained by the inclusion of patients with chronic pancreatitis, we believe there is abundant evidence in our paper that this is not so. All of the patients had suspected AP on clinical grounds. None of the patients had pancreatic calcifications or pancreatic duct dilatation on CT scan, or evidence of exocrine insufficiency. A large proportion (68%) of the normoamylasemic patients had elevated serum lipase, a strong argument in favor of the diagnosis of AP.[3] Furthermore, in Figure 1 of our paper, there were data available showing that even in more severe forms of AP (*i.e.*, CT groups II and III, phlegmon extending in at least one extra-pancreatic area), normoamylasemia was present in 14% of the cases on admission. On the other hand, by excluding all patients with previously documented bouts of pancreatitis and similar painful episodes, the incidence of normoamylasemia is still 15.6%. Regarding their remark that studies on AP will be diluted by patients with chronic pancreatitis, if CT standards are adopted, they do not seem to have considered that the omission of normoamylasemic patients may be much more damaging to validity of those studies. Incidently we did not state that '58% of 132 alcoholic patients had normal amylase,' but that of all normoamylasemic patients 58% had evidence of alcohol abuse. Our interpretation of the term 'gold standard' means the best available standard; in Geneva, at least, histology of the pancreas in AP is rarely available.[4]

Next, examining their objections based on their own work, it is critical to note that they define AP in terms of elevated serum amylase level, *i.e.*, 'serum amylase level of greater than 1000 IU/L in the presence of a compatible clinical picture.'[1,2] Of course almost 100% of their AP patients have serum amylase levels greater than 300 IU/L. In fact, given their definition of AP, it is surprising that all patients do not have elevated amylase. Although most authors include hyperamylasemia in their diagnostic criteria of AP, to our knowledge none has used the data to identify the rate of normoamylasemic pancreatitis.[3] Neoptolemos and London take us to task for 'considerable delay in the admission of most patients,' while stating that 99% of their patients were admitted within 24 hours of the onset of an attack. But by defining AP in terms of serum amylase, one might miss the diagnosis in patients arriving later with normoamylasemic AP. By their own figures, almost 30% of patients at 48 hours were normoamylasemic. Have they considered that some patients might arrive at their hospital only when they reach this stage of the disease and, as a result, are not identified as having AP? Their comments about whether our results reflect the 'general context' are conjectural. We will only know about the pertinence and general applicability of the Geneva experience when other centers have examined nomoamylasemia in acute pancreatitis using the approach presented in our study. The percentage of AP patients with normoamylasemia in the area of England studied by Neoptolemos and London may indeed be less than the 19% in the Geneva study, but until they do the study they cannot know the figure. We believe they might be surprised.

References

1. London NJM, Neoptolemos JP, Lavelle J, et al. Serial computed tomography scanning in acute pancreatitis: a prospective study. Gut 1989; 30:397–403.
2. London NJM, Neoptolemos JP, Lavelle J, et al. Contrast-enhanced abdominal computed tomography scanning and prediction of severity of acute pancreatitis. A prospective study. Br J Surg 1989; 76:268–272.
3. Clavien PA, Burgan S, Moossa AR. Serum enzymes and other laboratory tests in acute pancreatitis. Review. Br J Surg 1989, 76: 1234–1243.
4. Clavien PA, Hauser H, Meyer P, Rohner A. The value of contrast-enhanced computerized tomography in the early diagnosis and prognosis of acute pancreatitis. A prospective study of 202 patients. Am J Surg 1988; 155:457–466.

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Dear Editor:

We have read with great interest the paper of Drs. Dubois and colleagues, 'Coelioscopic Cholecystectomy,' in the January 1990 issue.[1] The same authors reported, at a later stage, 200 laparoscopic cholecystectomies (LC) of 19 patients were converted at the same session to open surgery. In 16 cases this was due to adhesions or technical difficulties and in three cases because of bleeding. In two patients a 'chole-peritoneum' or bile collection developed, probably due to leakage requiring drainage.[2] Dubois and colleagues should be commended for their contribution.

This intriguing technique has created more controversy and excitement in the surgical community than the publication of Langenbuch's first cholecystectomy[3] or Sauerbruch et al.'s extracorporeal gall stone lithotripsy.[4] In the United States, Reddick and Olsen[5] published their first results. In our institution five surgeons, including us, are performing LC.

We are extremely concerned about patient safety because iatrogenic injuries may occur with this procedure. Clearly competence in diagnostic laparoscopy is a prerequisite to learning how to perform LC. Courses to teach LC are mushrooming and are booked months ahead. Some of these lack a proper curriculum or experienced teachers and many provide limited hands-on experience. Laparoscopic cholecystectomy is one of the most complex endoscopic procedures and needs a great degree of skill to perform it safely and well.

We train residents under supervision for 3 years to do open cholecystectomies before they may sit for their Board examinations. Although LCs do not require years of training, poorly structured crash courses lacking proper endorsement from specific surgical societies or authorities can be extremely harmful.

In addition, there are no guidelines to hospital credentialing or privileging committees and consequently many surgeons without adequate training are performing this procedure. What is more disturbing is that physicians in other disciplines, including gynecology, are performing LCs with or without surgical assistance. There is an urgent need for surgical authorities to issue guidelines to surgeons and hospitals. Biliary surgery was