Laboratory Tests in the Differential Diagnosis of Hyperamylasemia
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We evaluated the clinical utility of some recently developed laboratory methods, including total amylase by three methods; isoenzyme by inhibition and isoelectric focusing; lipase by pH-Stat and turbidimetry; and immunoreactive trypsin. All methods correlated highly positively with hyperamylasemia due to primary acute pancreatitis. Pancreatic-type isoenzyme determinations have the greatest clinical usefulness, because total amylase, lipase, and immunoreactive trypsin are increased in a relatively high percentage of other abdominal diseases. Increases in the last-mentioned enzymes in nonpancreatic abdominal disease may be the result of injuries to the pancreas secondary to the primary disease, which are being detected with these highly sensitive methods. Because of the high clinical sensitivity of lipase and immunoreactive trypsin determinations, a normal result tends to exclude acute pancreatitis. Hyperamylasemia seen in lung carcinoma is due to increase in an amylase isoenzyme similar to the salivary-type amylase. The method for pancreatic-type isoenzyme based on selective inhibition is satisfactory for routine clinical laboratory use.

Additional Keyphrases: pancreatitis • pancreatic disease • isoenzyme • diagnostic aids • "kit" methods

Diagnosis of acute pancreatitis is still a major diagnostic challenge, in part because the pancreas is located deep within the abdominal cavity, which makes this organ inaccessible for direct examination, and in part because of the limited usefulness of radiological studies. Imaging studies are expensive and are useful only in pancreatic disorders that are associated with anatomical changes. Commonly available laboratory tests have been helpful in the diagnostic process, but they lack adequate clinical sensitivity or specificity to allow establishment of a definitive diagnosis.

Among laboratory tests, measurement of α-amylase (EC 3.2.1.1) is the test most widely used in the diagnosis of acute pancreatitis. Unfortunately for such diagnosis, amylase activity in serum not only is increased in pancreatitis but also in some other pancreatic and in various nonpancreatic diseases (1). In addition, increases in the activity of amylase in serum in acute pancreatitis are not consistently observed. This lack of clinical specificity and sensitivity has led to a search for clinically more useful laboratory tests.

Urinary amylase measurements, as well as the measurements of the amylase/creatinine clearance ratio, are not specific (2, 3) and their use is now discouraged.

Measurement of triacylglycerol lipase (EC 3.1.1.3) in serum is useful in the diagnosis of pancreatitis, especially if used in conjunction with amylase measurements (4, 5). But this test has never been very popular in the United States, mainly because earlier methods were unsatisfactory, which resulted in conflicting reports regarding the clinical utility of lipase measurements (6). Such difficulties have largely been overcome by better and more specific techniques (6–8), and lipase is more commonly determined to confirm or rule out pancreatitis as a cause of hyperamylasemia.

Recently, measurements of amylase isoenzymes (9, 10) and immunoreactive trypsin (EC 3.4.21.4) (11, 12) have also been suggested as useful tests in the diagnosis of acute pancreatitis. Studies of the clinical utility of these newer techniques have mostly been limited to evaluation of an individual method, rather than comparative clinical evaluations of a battery of these newer tests, along with traditional laboratory tests. In addition, the subjects of most studies have been patients with "well-established" acute pancreatitis, without inclusion of an appropriate reference population with other abdominal diseases that clinically may resemble pancreatitis. For example, Ventrucci et al. (13), in their comparative study of pancreatic isoenzymes, lipase, and immunoreactive trypsin in serum, studied 16 patients with acute and 48 patients with chronic pancreatic disease and included 53 healthy control subjects, but none with other abdominal diseases. Kolars et al. (4) compared serum total amylase, isoenzyme, and lipase measurements in "seemingly clear-cut pancreatitis," with no data on a reference population. Thus, we have investigated the clinical utility of the above-mentioned techniques in the differential diagnosis of hyperamylasemia, not only in patients with acute and chronic pancreatic disease, but also in patients with various abdominal, nonpancreatic, and nonabdominal diseases and with renal failure.

We included in our study three methods recently developed for measurement of total amylase activity in serum, in which maltotetraose, 4-nitrophophyl maltoheptaoside, and a mixture of 4-nitrophophyl maltopentaoside and -hexaose are the respective substrates. We also examined procedures for measurement of amylase isoenzymes by selective inhibition and isoelectric focusing, a procedure for the measurement of immunoreactive trypsin, and methods for the "pH-Stat" and turbidimetric measurement of lipase activity.

Materials and Methods

Specimens
All serum specimens studied, except for those from patients with lung tumors, were from hospital patients with hyperamylasemia, regardless of the clinical cause (Table 1). Serum specimens from patients with lung tumors were collected after the diagnosis had been established by biopsy.

Diagnoses were made on the basis of clinical presentation and objective findings. The latter included ultrasound or computed-tomography scan examinations of the pancreas, exploratory laparotomy, and, in two cases, autopsy. Patients without objective or clinical evidence of pancreatic disease were categorized in accordance with the clinical diagnosis (e.g., renal disease). If more than one diagnosis was present, the patient was classified under the disease which is known to be associated with hyperamylasemia.

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Methods for Amylase Activity Measurements

Amylase DS procedure (Beckman Instruments, Inc., Microbics Operation, Carlsbad, CA 92008) and SingleVial Amylase, UV Method (Boehringer Mannheim Diagnostics [BMD], Indianapolis, IN 46250). In both procedures is used the same enzyme-coupled reaction involving maltotetraose as substrate and the production of NADH in the indicator reaction. This and the following kit procedures were done as specified by the manufacturer in the kit insert.

Colorimetric a-amyrase procedure (Boehringer Mannheim Diagnostics). In this procedure 4-nitrophenyl-α-maltose is used as substrate and the coupled enzyme reaction involves α-glucosidase (EC 3.2.1.20); the 4-nitrophenol produced is measured at 405 nm according to the manufacturer’s instructions.

Pancrek E.K. a-amyrase procedure (Behring Diagnostics, previously Calbiochem–Behring Corp., La Jolla, CA 92037). The principle of this procedure is similar to that of the last-mentioned procedure, except that a mixture of 4-nitrophenyl-α-maltotetraose and maltotetraose is used as substrate.

Amylase Isoenzyme Determinations

Selective inhibition. This method involved use of an inhibitor isolated from wheat germ, as proposed by O’Donnell et al. (14). The procedure was adapted to the Beckman "Amylase-DS" and the BMD "SingleVial UV Amylase" procedures, as reported elsewhere (15). This inhibitor is commercially available from Sigma Chemical Co., St. Louis, MO.

Isoelectric focusing. For isoenzyme separations we used thin-layer polyacrylamide gels containing ampholytes (Ampholines) with a pH range of 5.5 to 8.5. We followed the procedure outlined in the gel package insert (cat. no. I-1804; LKB-Produkter AB, Bromma, Sweden) with the following exceptions:

Five to 10 μL of specimen, depending on its amylase activity, was applied to the test block and separated at 1200 V and 20 W at 4 °C for 4 h. The test blocks were removed after the first 45 min, and the separation was continued. The gel was removed and overlaid with filter paper that had previously been soaked with Beckman Amylase-DS or BMD UV reagent. After a 30-min incubation at 37 °C, the filter paper was removed, dried at 37 °C, and scanned in a densitometer (Model CDS-200, Beckman Instruments, Inc., Brea, CA 92621), utilizing an ultraviolet light source, the integrated areas being taken as a measure of the relative activity of the individual isoenzymes.

An example of a separation of various specimens and controls with increased total amylase activity, as obtained by the IEF method, is shown in Figure 1. Specimen 1 is a pancreatic extract showing two isoenzyme bands. Saliva (specimen 2) shows one major band and two minor bands. Serum specimens from a patient with acute pancreatitis (specimen 3) showed a major band in the pancreatic isoenzyme region of migration and minor bands in the salivary region. Serum sampled from a patient after oral surgery (specimen 4) showed predominance of S-type amylase, while serum from a patient with lung carcinoma (specimen 5) showed a migration pattern similar to that for specimen 4. Specimen 6 is a lipemic serum from a patient with severe

![Fig. 1. Isoelectric focusing patterns obtained with controls and patient specimens](image)
hemorrhagic pancreatitis. This specimen had been mailed to our laboratory and was not analyzed until seven days after the specimen was drawn. In this case, no isoenzyme bands could be observed, and the "streaking" may possibly be caused by partial digestion or deamination of the amylase, which affected the electrophoretic mobility without destroying the catalytic activity of the enzyme (see also "Comparison of Amylase Isoenzyme Methods").

Methods for Lipase Activity Measurements

*pH-Stat method.* This procedure was done as described elsewhere (7). An olive-oil emulsion is kept at a constant pH, 8.80, by continuously adding sodium hydroxide with the aid of a pH-Stat. The amount of sodium hydroxide consumed per unit of time is taken as a measure of lipase activity.

*Turbidimetric method.* The procedure is that described in the package insert of the "SingleVial Lipase Kit" supplied by Boehringer Mannheim Diagnostics. The reagents contain sodium deoxycholate and colipase, which increase the stability of the enzyme at the water-substrate interface and improve the specificity of the procedure. Lipase activity is determined on the basis of the decrease in absorbance that results from hydrolysis of a triolein emulsion.

Determination of Immunoreactive Trypsin

The method was used as described in the package insert of the "TRYSK" procedure supplied by International CIS (CEA [France], IRE [Belgium], and Sorin Biorema [Italy]), marketed in the United States by Deman Diagnostics, Needham Heights, MA 02194. With this procedure trypsinogen, trypsin, and the α1-antitrypsin--trypsin complex can be detected.

Results

Serum specimens from all patients with hyperamylasemia were tested with the methods just described. However, owing to the volume of specimen required for the various methods, some specimens could not be analyzed by the pH-Stat method.

Results are shown in Figures 2 and 3. We arbitrarily set the upper normal reference limit for each of the tests at 100%. Values exceeding the reference limits are expressed as relative percent of the upper reference limit, to best show the relative sensitivities of the individual procedures in various clinical conditions.

Results for total amylase in sera from patients with acute and chronic pancreatic disease are shown in Figure 2. Because all serum specimens used in this study were from patients with hyperamylasemia, total amylase activities ranged from 130 to 1800% of the upper reference range. The values for total amylase shown in Figure 2 were all obtained with the Beckman Amylase-DS Method, but all values obtained with the BMD colorimetric and the Behring Diagnostic amylase procedures showed similar increases in activity. In specimens from patients with hyperamylasemia due to pancreatic disease, the sensitivity of the BMD colorimetric method appears to be slightly higher than the sensitivity of the Beckman DS and Behring Diagnostic procedures. The mean relative increases observed with these three methods in acute (and chronic) pancreatic disease were 500 (250), 425 (236), and 388 (202)% respectively.

We also show our results for P-type amylase determinations in patients with acute (Figure 2, column 3) and chronic pancreatic disease (column 4) as measured by the inhibitor method. The correlation between the inhibitor method and the method involving isoelectric focusing is discussed below.

Because values for P-type isoamylase are expressed as percentage of total amylase activity (the upper normal reference limit for P-type amylase is thus 70%), the highest possible value that can be obtained is an increase of 143%, i.e., (100/70) × 100 = 143%. Samples from all but four patients in the acute pancreatic disease category showed P-type amylase activities above the upper reference limit. Two of four patients with normal values had a history of alcohol abuse; one had a normal image on ultrasound, the other a large, edematous pancreas. The latter had an increased P-type amylase with the IEF method. A third patient had idiopathic pancreatitis with a normal ultrasound image (marked in Figure 2 with a triangle), and the fourth showed a sonolucent mass in the region of the head of the pancreas and cholelithiasis on ultrasound. Three of these four patients with a normal percentage of P-type amylase had an
increased absolute value for this isoenzyme but an even higher increase of S-type amylase. Such increases in salivary isomylase in alcohol-abuse patients have been reported previously (16).

In the chronic pancreatic disease category (column 4), only one of six patients had an abnormal P-type amylase. This patient had chronic fibrotic pancreatitis with interstitial fibrosis, as determined by surgery. 

**Immunoreactive trypsin activity** (Figure 2, columns 5 and 6) was consistently increased in the patient groups with acute and chronic pancreatitis, with only one exception in the former and one exception in the latter disease category. The patient in the acute category (marked with a triangle) is the previously mentioned patient with idiopathic pancreatitis. The patient in the chronic category (marked with a circle) had near-complete destruction of the pancreas, confirmed at autopsy.

Results obtained with the BMD turbidimetric lipase method (Figure 2, columns 7 and 8) showed increases in all but one patient with acute and two patients with chronic pancreatic disease. The patient in the acute category (marked with a triangle) is the previously mentioned patient with idiopathic pancreatitis. One of the exceptions in the chronic disease group is the patient with destruction of the pancreas mentioned above (marked by a circle), and the other exception is a patient with a mass in the tail of the pancreas (marked with a square). These same two patients also had normal values with the pH-Stat lipase method (Figure 2, column 10). All patients in the acute category on whom the pH-Stat method was performed, had increased values (Figure 2, column 9). The relatively high percentage of enzyme activity increases in the chronic pancreatic disease group, compared with previous studies by other authors, can be explained by the fact that we included in our study only patients with hyperamylasemia.

All patients with hepatobiliary and bowel disease had increased total amylase activity (Figure 3A). P-type amylase was increased in only two of eight patients. One of these (triangle) had a melanoma with metastases to hepatic, biliary, and other sites, and the other (circle) had a small bowel obstruction. The relatively great number of elevations in immunoreactive trypsin (column 3) and lipase (columns 4 and 5) in this disease group could be due to the relatively high sensitivity of these methods, which allows detection of small amounts of enzymes released into the circulation. For the mechanism of such enzyme elevations, see "Discussion and Conclusions."

Although such laboratory findings may be of some clinical importance, they would be of no help in pinpointing the primary diagnosis in this group of patients. Since P-type amylase is increased in acute pancreatitis with high frequency, normal P-type amylase determinations are most informative in excluding primary pancreatic disease as the cause of hyperamylasemia. On the other hand, increased immunoreactive trypsin and lipase determinations in the presence of normal P-type amylase are helpful in determining the presence of secondary pancreatic pathology. These findings also suggest that the sensitivity of a test for a given enzyme, such as lipase, may be as important as the type of enzyme tested. If a less-sensitive lipase method were to be used, the clinical specificity might increase, but at the expense of sensitivity.

Figure 3B shows our results for patients with miscellaneous nonpancreatic diseases (rib fracture, gastrointestinal bleeding, peptic ulcer, and oral surgery). Ten of the 12 patients had normal P-type amylase (column 2); only one patient had a borderline value, and one had an increased value. One of these patients (triangle) had a systemic viral infection which could have invaded the pancreas, while the other had malnutrition and volume depletion (circle). Five of the 12 patients showed increased concentrations of immunoreactive trypsin (column 3). Lipase measured with the turbidimetric method (column 4) showed increased values in six of 12 patients, and the pH-Stat method (column 5) showed increased values in four of seven patients. Thus, these findings confirm our earlier statement that normal findings of P-type amylase are useful in excluding pancreatic disease as the primary diagnosis in this group of patients.

In the group of patients with renal failure (Figure 3C), significant elevations were seen with immunoreactive trypsin (column 3) and lipase (columns 4 and 5), as had been described in previous reports (17, 18). On the other hand, most patients' samples (18 of 21) gave normal results with the P-type amylase method (column 2).

**Lung cancer** has been described as a cause for hyperamylasemia (19, 20). Only two of our 15 patients with confirmed bronchogenic carcinoma showed increased total amylase activity. Amylase isoenzyme determinations showed predominance of an isoenzyme similar to the S-type amylase in these two patients; P-type amylase was normal with both methods. P-type amylase determinations evidently are helpful in excluding a pancreatic cause for the hyperamylasemia and they indicate that the prevalence of hyperamylasemia in patients with lung cancer is much less than expected from literature reports (19, 20).
Comparison of Amylase Isoenzyme Methods

A comparison of results obtained for all disease groups by both isoamylase methods (Figure 4) showed a correlation of $r = 0.86$, while the coefficient of correlation of results from patients with pancreatic disease only (Figure 4) was $r = 0.87$. The only exceptions were a sample from a previously mentioned patient with hemorrhagic pancreatitis and two specimens from patients with pancreatic disease resulting from ethanol abuse. In the first case, the inhibitor method was found to agree with the clinical diagnosis, while in the other two cases, the inhibitor method was found to be normal, while the IEF method indicated increased P-type amylase isoenzyme. The absolute amount of P-type amylase, however, was increased but in the presence of an even greater increase in S-type amylase. Other discrepant observations were well within the normal range for both methods and thus are of little significance in the context of our discussion.

The close correlation between results by these two methods indicates that the isoamylase method by selective inhibition, which is much simpler and faster than the IEF method, is suitable for use in a service laboratory.

Activity Ratios for Methods Measuring Total Amylase

The calculation of the activity ratio for different methods for total amylase activity used on the same specimen gives some indication as to the isoenzyme bias of the methods used. The activity ratios for the BMD colorimetric to the Beckman DS method showed a significantly higher ratio for specimens from patients with pancreatic diseases as compared with specimens from patients with nonpancreatic diseases (Table 2). These differences become more obvious if the patients are separated into groups with an increase in P-type amylase and an increase in S-type amylase, or if pancreatic extracts and saliva are analyzed.

These findings suggest that the BMD colorimetric method shows greater preference for P-type amylase than does the Beckman DS procedure. However, it is doubtful that this difference—although statistically significant ($p < 0.005$)—is of diagnostic help, because values from the different diagnostic groups overlap so much.

### Table 2. Activity Ratio: BMD Colorimetric/Beckman DS Method

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>X</th>
<th>1 SD</th>
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</thead>
<tbody>
<tr>
<td>Pancreatic diseases</td>
<td>35</td>
<td>1.86</td>
<td>0.24</td>
</tr>
<tr>
<td>Non-pancreatic diseases</td>
<td>12</td>
<td>1.67</td>
<td>0.27</td>
</tr>
<tr>
<td>Hepatobiliary &amp; bowel disorders</td>
<td>8</td>
<td>1.62</td>
<td>0.34</td>
</tr>
<tr>
<td>Renal failure</td>
<td>21</td>
<td>1.67</td>
<td>0.25</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>2</td>
<td>2.20</td>
<td></td>
</tr>
<tr>
<td>Patients with P-type</td>
<td>33</td>
<td>1.96</td>
<td>0.21</td>
</tr>
<tr>
<td>Patients with S-type</td>
<td>16</td>
<td>1.56</td>
<td>0.17</td>
</tr>
<tr>
<td>Pancreatic extract</td>
<td>1</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td>Saliva</td>
<td>1</td>
<td>1.40</td>
<td></td>
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</table>

The significantly different ratio obtained for patients with hyperamylasemia ascribable to lung cancer was remarkable (2.20 vs 1.67 for nonpancreatic and 1.86 for pancreatic diseases), suggesting that the isoenzyme type observed in patients with lung cancer may not be the S-type. This finding is supported by the observation of Sudo and Kanno (21) that the dissociation constants of the tumor amylase for several substrates were smaller than those for pancreatic and salivary amylase; that tumor amylase did not hydrolyze maltotriose; that tumor amylase has minor differences in sialic acid content; and that neuraminidase treatment results in different electrophoretic mobility of tumor amylase.

Increase in Test Results in Pancreatic and Nonpancreatic Conditions

We calculated the percentage of cases that showed increases in the values for P-type amylase, immunoreactive trypsin, turbidimetric lipase, and pH-Stat lipase test results in pancreatic and nonpancreatic diseases. Renal disease was excluded since it interferes with all test procedures considered in our investigation and can easily be recognized on clinical grounds and by appropriate laboratory procedures. The least interference by renal disease was observed with P-type amylase (three of 21 patients), as shown in Figure 3C. We excluded total amylase from these calculations, because the selection of our samples was based on an increased amylase activity.

The results (Table 3) indicate that the highest percentage of increased values in patients with acute pancreatic disease was obtained with the pH-Stat lipase method, followed by the turbidimetric lipase, immunoreactive trypsin, and P-type amylase methods. The results are in fair agreement with reports by Ventrucci et al. (13), who found nearly equal diagnostic sensitivity for serum lipase, P-type amylase, and immunoreactive trypsin values. Kolars et al. (4) found the highest sensitivity was that for lipase, followed closely by P-type amylase. As expected, the percentage increase for all test procedures was considerably less for patients with chronic pancreatic disease. In addition, average increases in laboratory results were much higher in acute pancreatic disease compared with all nonpancreatic diseases (Table 4).

The percentage of increased values in the hepatobiliary and bowel disease category was highest with the immunoreactive trypsin test, followed by both lipase procedures. The lowest percentage (25%) was found with P-type amylase, indicating the highest specificity for this test. For the miscellaneous non-pancreatic disease group, lipase gave the highest number of increased values, followed by immunoreactive trypsin and P-type amylase. The relatively high specificity for P-type amylase was expected, but the specificity for lipase determinations was less than expected from results of other studies. However, this is not too surprising if
Table 3. Percentage Increase in Test Results in Pancreatic and Nonpancreatic Disease

<table>
<thead>
<tr>
<th></th>
<th>P-Amylase increased values, %</th>
<th>Immunoreactive trypsin increased values, %</th>
<th>Lipase, turbidimetric increased values, %</th>
<th>Lipase, pH-Stat increased values, %</th>
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<tr>
<td>Acute pancreatitis</td>
<td>86.2</td>
<td>96.5</td>
<td>96.5</td>
<td>100</td>
</tr>
<tr>
<td>n = 29</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Chronic pancreatitis</td>
<td>16.7</td>
<td>83.3</td>
<td>66.7</td>
<td>60</td>
</tr>
<tr>
<td>n = 6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary &amp; bowel diseases</td>
<td>25</td>
<td>87.5</td>
<td>62.5</td>
<td>60</td>
</tr>
<tr>
<td>n = 8</td>
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<tr>
<td>Miscellaneous</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>nonpancreatic diseases</td>
<td>16.7</td>
<td>41.7</td>
<td>50</td>
<td>57.1</td>
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<tr>
<td>n = 12</td>
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Table 4. Laboratory Results Relative to Upper Reference Limit

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<th>Acute</th>
<th>Chronic</th>
<th>All nonpancreatic diseases</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>X</td>
<td>Range</td>
</tr>
<tr>
<td>Total amylase (Beckman)</td>
<td>29</td>
<td>425</td>
<td>130–1800</td>
</tr>
<tr>
<td>P-type amylase (inhibitor)</td>
<td>25</td>
<td>132</td>
<td>101–143</td>
</tr>
<tr>
<td>Immunoreactive trypsin</td>
<td>28</td>
<td>1,006</td>
<td>162–9245</td>
</tr>
<tr>
<td>Turbidimetric lipase</td>
<td>28</td>
<td>1,744</td>
<td>126–19633</td>
</tr>
<tr>
<td>pH-Stat lipase</td>
<td>23</td>
<td>1,436</td>
<td>149–8796</td>
</tr>
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</table>

Discussion and Conclusions

One considers the high sensitivity of the newer methods for lipase and immunoreactive trypsin, which detect small increases in these enzymes, and if one further considers the type of patient population included in this study (alcoholics, postsurgery patients, and patients with peptic ulcer and other abdominal diseases).

Our inclusion of these patients challenges the test procedures included in our study and sets the study apart from those investigations that included only patients with confirmed pancreatitis. However, we believe that this makes our study specifically helpful, because clinicians frequently are confronted with the differential diagnosis of hyperamylasemia in patients with clinical signs similar to those observed in acute pancreatic disease.

Results obtained with both lipase methods were similar. Abnormal results were obtained in 60 to 63% of patients with biliary and bowel disease and 50 to 57% of patients with miscellaneous nonpancreatic diseases. The inclusion in our study of patients with a mixture of various pancreatic and nonpancreatic abdominal diseases appears to be responsible for the relatively high percentage of above-normal values for lipase and immunoreactive trypsin, both of which are generally thought of as being relatively organ specific (13). Literature reports and autopsy findings suggest several mechanisms by which such increases may occur. We have already referred to the possible silent invasion of the pancreas by microorganisms (23). Bowel obstruction has been found to be associated with increases in lipase and amylase (24). McCutcheon (24) speculates that reflux of duodenal content containing enterokinase activates pancreatic enzymes, which diffuse across the duct wall into the interstitial tissue; there they cause vascular damage that leads to changes that vary in intensity from edema and hemorrhage to frank infarction. Liver disease is said to cause synthesis of pancreatic trypsinogen in excess of trypsin inhibitor and thus may lead to intraductal activation of trypsinogen (25). Furthermore, focal, subclinical pancreatitis may be the result of intestinal obstruction, vascular disease, uremia, dehydration, or hypovolemia (26–28). In all these cases, acute pancreatitis was not the primary diagnosis and yet increased pancreatic enzyme values were observed and, when tested, were found to have subsided after the primary disease cleared up.

Despite these difficulties, individual enzyme tests or test combinations may be an aid in the differential diagnosis of abdominal diseases. For confirming acute pancreatitis as the primary cause of the disease, P-type amylase determinations seem to be most helpful because of the relatively high number of true positive and the low number of false positive tests. Normal values for lipase and immunoreactive trypsin (if performed with the methods in this study) tend to rule out acute pancreatitis. For the detection of secondary, subclinical pancreatic injury in the presence of a primary nonpancreatic abdominal disease, enzyme panels consisting
of P-type amylase and lipase or immunoreactive trypsin may offer additional diagnostic help. A normal P-type amylase in these situations tends to rule out acute pancreatitis as a primary diagnosis. The relative increases in immunoreactive trypsin and lipase in pancreatic vs nonpancreatic diseases may also be of some diagnostic assistance. Lipase and immunoreactive trypsin in acute pancreatitis are considerably more elevated than in chronic pancreatic disease and in nonpancreatic diseases with suspected secondary pancreatic injury (see Table 4). However, difficulties remain in fully assessing the diagnostic value of these procedures and are linked in part to our inability to diagnose acute pancreatitis definitively and to differentiate it from other abdominal diseases with subclinical secondary pancreatic injury.

Colorimetric α-amylase test kits and Single Vial Lipase test kits were obtained through the courtesy of BMC, Tutzing, F.R.G. Patrak S.K. α-amylase test kits were received through the courtesy of Behring Diagnostics. The selective inhibitor isolated from wheat germ that we used in determining amylase isoenzymes was kindly supplied by Dr. K. F. McGeeney.

References