example, a slide containing sarcosine oxidase, peroxidase, and peroxidase substrate could be used to correct for the presence of NEG, sarcosine, or any other such oxidizable substrate.

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References

Concentrations of Serotonin in Plasma—a Test for Appendicitis?

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We assessed the value of measuring serotonin (5-hydroxytryptamine) in plasma (by HPLC) in the diagnosis of acute appendicitis. Values for patients with subsequently confirmed appendicitis (11–145 nmol/L, median 70 nmol/L) significantly (P < 0.005) exceeded those for patients with abdominal pain in whom appendicitis was only a possible diagnosis (2–45 nmol/L, median 20 nmol/L). The results for appendicitis patients were bimodally distributed, with low results found in patients where surgery revealed gangrenous appendicitis with little viable appendicular tissue. We conclude that measuring serotonin may be of value in confirming or excluding the diagnosis of early acute appendicitis where the physical signs are equivocal, and thus helps reduce unnecessary appendectomies. However, serotonin is of little help in diagnosing gangrenous appendicitis, where physical signs are more likely to be clearcut.

Additional Keyphrases: gangrenous tissue · chromatography, liquid · electrochemical detection

"Suspected appendicitis" is the most common reason for an emergency surgical admission. More than 80 000 appendectomies are performed annually in the U.K. (1). Careful clinical assessment remains the cornerstone of diagnosis. Yet even after the most meticulous assessment, the initial diagnosis is erroneous (i.e., not supported by later histological examination) in ~25–30% of patients with suspected appendicitis (2–4).

Although various laboratory tests have been proposed to aid this diagnostic dilemma, their value is uncertain and no laboratory investigation is universally regarded at present as being of definite value in confirming the diagnosis when appendicitis is suspected.

Appendix tissue both contains and can secrete serotonin into the circulation (2, 5, 6). We designed this study to test our hypothesis that serotonin concentrations in plasma are increased during acute appendicitis.

Materials and Methods

Blood was sampled for plasma serotonin analysis, after informed consent from 24 consecutive patients presenting to the emergency room with acute abdominal pain, in whom appendicitis was a possible preliminary diagnosis. The patients were subsequently divided into two groups:

Group A: Appendectomy for acute appendicitis (diagnosed

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on histopathological grounds in each case): nine men, four women, mean age 23.6 (SEM 15.3, range 8-48) y.

Group B: Hospital admission with acute abdominal pain ascribable to causes other than appendicitis: two with normal appendix on appendectomy, and one each with small-bowel volvulus, pelvic inflammatory disease, peptic ulcer, pyelonephritis, gastroenteritis, peritonitis (no operation), subacute small-bowel obstruction, cholangitis, pancreatitis. The group comprised two men and nine women, mean age 48.9 (SEM 26.9, range 15-82) y.

We made no attempt to match the groups for age or sex. The Mann--Whitney U test was used to test for significant differences between the groups.

Preparation of blood samples. From each subject we slowly collected a 10-mL sample of venous blood, using a 21-gauge needle to minimize turbulence, which would cause release of platelet serotonin. The sample was then placed in a tube containing lithium heparin and mixed gently by rolling the tube to and fro. The sample was stored at 4 °C for no longer than 30 min, then centrifuged (4 °C, 25 min, 3000 × g). The supernatant platelet-poor plasma was carefully removed, put into 2-mL Eppendorf centrifuge tubes, and stored at −70 °C until analysis.

Assay. We measured serotonin by HPLC with electrochemical detection, using 3,4-dihydroxybenzylamine as internal standard. We extracted the serotonin from plasma by use of a strong cation-exchange resin, following the method of Ball and Inglis (7) for catecholamines. For the chromatography we used an ACS 300/02 pump (Applied Chromatography Services, Heapy St. Macclesfield, Cheshire, SK11 7JB, U.K.), a Jones ODS 3 column (Jones Chromatography Ltd., Llanbradach, Mid. Glamorgan CF8 3AA, U.K.), and a BAS LC 4A detector (Bioanalytical Systems, West Lafayette, IN 47906). The mobile phase contained, per liter, 0.1 mol of sodium dihydrogen phosphate, 0.1 mmol of EDTA, 5 mmol of 1-octanesulfonic acid, and 350 mL of methanol. The flow rate was 0.5 mL/min, the oxidizing potential 0.65 V. The solvents were "HPLC" grade. All reagents were analytical grade, obtained from British Drug Houses, Poole, Dorset, U.K. 5-Hydroxytryptamine creatinine sulfate, used as the standard, was from Sigma Chemical Co. Ltd., Poole, Dorset, BH17 7NE, U.K. The intra- and inter-assay coefficients of variation for plasma samples containing 20 nmol/L were 7.5% and 8.9%, respectively.

Results

Figure 1 shows our results for both groups, and the normal reference interval. In the patients with appendicitis the range of concentration of serotonin was 11–145 nmol/L, with a median value of 70 nmol/L. In patients with "other abdominal pains" the range was 2–45.4 nmol/L (median, 20.3 nmol/L).

The difference in values between the patients with appendicitis and those with "other abdominal pains" was significant (P = 0.005). However, Figure 1 shows that the appendicitis patients fell into two groups. In nine patients with non-gangrenous, non-perforated acute appendicitis, the plasma serotonin concentration was above normal in each case. In the other four patients, with gangrenous or perforated appendicitis, the plasma serotonin concentrations were similar to those observed in the "other abdominal pain" group. If we exclude the patients with gangrenous or perforated appendicitis, the differences between the appendicitis patients and those with "other abdominal pains" become highly significant (P < 0.001).

Discussion

We have postulated for some time that acute appendicitis may be associated with an increase in plasma serotonin, ever since the observation in the late 1960s that up to half of all patients with acute appendicitis, though afebrile, exhibit facial flushing (8). Serotonin-secreting carcinoid tumors occur most frequently in the appendix. Thus an acutely inflamed appendix with its increased blood flow may secrete measurable amounts of serotonin into the bloodstream.

Serotonin has been extensively investigated in relation to psychiatric disorders, peptic ulcer disease, liver diseases, and biliary tract disorders (9, 10, 11, 12), without significant disturbances being found. Sjolund and Nobin (13) demonstrated increased serotonin in patients with untreated celiac disease, the values declining with treatment. Their highest value (30 nmol/L) was much lower than in our appendicitis series. Alffan et al. (6) demonstrated that experimental low small-bowel obstruction in rats was followed by an increased gut-wall synthesis of serotonin with subsequent discharge into portal venous blood.

Dhillon and Rhode (2) used special stains to assess the serotonin content of appendices in two groups of patients, one group who underwent negative laperotomy for right iliac fossa pain and another group who had undergone incidental appendectomy during the course of another operation. They concluded that a painful, non-inflamed appendix secretes some serotonin into the circulation and that a continuation of this release would culminate in acute appendicitis.

Rødstrøm et al. (14) studied 20 patients with acute appendicitis (nine had above-normal serotonin concentrations in plasma) and 11 who had a normal appendix removed (only
Enzyme Abnormalities of Patients with Acquired Immunodeficiency Syndrome

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We determined the enzyme activities of glucose-6-phosphate isomerase, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase in serum from 23 normal controls, 27 anti-HIV seropositive individuals confirmed by Western blot, and 53 patients with acquired immunodeficiency syndrome (AIDS). There is a significant difference for all four enzyme activities among controls, HIV seropositive individuals, and patients with AIDS, the enzyme activities showing a progressive increase as the disease progresses. Evidently these enzyme measurements may be adjunctive biochemical markers for progression of AIDS.

The acquired immunodeficiency syndrome (AIDS) is thought to be caused by human immunodeficiency virus (HIV) and is characterized by a defect in cellular immunity (1–5). Significant weight loss, diarrhea, and fever frequently herald the development of infectious complication or malignancies. The progression of the disease usually is based on clinical evaluation and on the ratio of helper to suppressor T lymphocytes. The need for flow cytometric analysis of T lymphocyte subsets hampers their usefulness as a laboratory marker for follow-up testing. The concentrations of β₂-microglobulin, neopterin, and adenosine deaminase (EC 3.5.4.4) activity in serum have been suggested as prognostic biochemical markers for the development of AIDS (6–10). However, these tests are not routinely requested and, indeed, are not available from most laboratories.

Nutritional status as assessed by measurement of transthyretin (prealbumin) and albumin in serum has

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1Nonstandard abbreviations: AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LD, lactate dehydrogenase; PHI, phosphohexose isomerase; ANOVA, analysis of variance.