ent distance. I know medicine and clinical chemistry from "both sides of the clouds."

The AACC, especially through Clinical Chemistry, has markedly improved the status of this profession, in my own judgment of what it can and should do to improve and prolong life and the quality of life in the clinical environment. However, I am unsure whether today a "clinical chemist" is a hospital-associated person who directs the chemistry laboratory and serves as a consultant, is involved only with the technology of laboratory operation and methodology development, or is an industrial person whose role is to develop saleable services and products for use in the clinical laboratory.

References

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Fluorescein Interference with Urinary Creatinine and Protein Measurements

To the Editor:

We report that fluorescein interferes with the Du Pont aca and Beckman Astra analyses for creatinine and protein in urine. Although fluorescein interferences with other analytes have been previously reported (J–5), this is an important observation and clinical laboratories should be aware of its existence.

In our hospital, 5 mL of 100 g/L fluorescein sodium solution is injected rapidly into patients for the diagnosis of diabetic retinopathies and retinal vasculopathies. Many of these patients have already been diagnosed and are under treatment for renal, diabetic, and hypertensive disorders. A common concurrent biochemical investigation in these patients is an assay of 24-h urinary protein and creatinine.

In this study, nine patients were injected with fluorescein sodium (Fluorescite® Injection, NDC 0065-0082-05; Alcon Labe., Inc., Fort Worth, TX 76194), as described above. With the patients' consent, urine samples were collected before the injection and 5, 10, 20, 60, and 120 min afterwards. All patients also submitted a urine samp-ple 20–25 h after the fluorescein angiogram.

In addition, we added various volumes of fluorescein sodium solution, 100 g/L, to normal urine to produce samples with fluorescein concentrations of 0.0001, 0.01, 0.1, 0.5, 1, 8, 10, 17, 20, 25, 33, and 50 g/L. All samples were then analyzed by both the Astra and aca analyzers for creatinine and by the aca for protein, according to the manufacturers' recommended procedures. The urinary protein procedure used on the aca is an endpoint turbidimetric method (540 nm) in which benzethonium chloride precipitates urinary protein in an alkaline medium. A blank is also measured. Both creatinine assays employ a kinetic Jaffé reaction (Astra = 520 nm; aca = 510 nm).

In both the Astra and the aca assays, fluorescein interfered with creatinine measurements (Figure 1, right). At high fluorescein concentrations, the instruments report no creatinine results. With the Astra, fluorescein produced a biphasic result, as shown in the shaded insert in the Figure. A small negative interference is present at fluorescein concentrations of 0.5–5.0 g/L but reverses its effect within a short concentration range (6–8 g/L), becoming positive (>100%), then sharply reverses again between 8 and 9 g/L. These concentrations are likely to be encountered in the urine of patients who received fluorescein 1–2 h before the analyses.

Fluorescein increases urinary protein measured with the aca (Figure 1, right). At fluorescein concentrations >10 g/L, results reported by the analyzer exceed the assay's linear range, thus alerting the operator of a possible interference problem. Interference at lower concentrations might not be noticed, however.

The timed urine samples submitted by our patients show similar results (Figure 1, left), indicating that fluorescein is excreted at a rapid rate. Unless samples are collected before injection, urinary collections should be delayed at least 24 h or samples should be collected within the first 5 min after injection.

We attempted to visually identify fluorescein concentrations <0.01 g/L, but this was difficult to do and therefore is not recommended.

In conclusion, if fluorescein is to be administered to a patient, body fluids (blood, urine) for laboratory tests should be collected either before fluorescein is given or at least 24 h later.

References

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Utility of Serum Phospholipase A Measurements

To the Editor:

I read with interest that Kazmierczak et al. (1) recently confirmed some of our previous findings concerning
serum phospholipase A (PLA), e.g., the normal range of up to 10 U/L (2), the clinical decision limit of about 40 U/L (3), the independence of serum lipase and amylose (2, 4), and, last but not least, the practicability and reproducibility of our photometric assay (5, 6). Their implications about the utility of PLA measurements require, however, some critical comments.

They compared two patient populations with and without pancreatitis, but they did not assess the severity of the disease. As a consequence, their data cannot be used to refute the prognostic statements of other authors (7–9), including those of our own group (3, 4, 10). Our main objection is that the authors failed to distinguish between edematous and necrotizing forms of pancreatitis (4, 7, 8) in their study. Regarding the observation that a reasonable prognostic sensitivity and specificity quoad viam requires that PLA values exceed 40 U/L for several days (3), it is inadequate to state that PLA was unexpectedly low immediately before death in three cases of lethal pancreatitis and 10 lethal cases of the control group, especially when the authors admit that they performed only single PLA measurements in 30 of 161 patients.

The report of Kazmierczak et al. (1) confirms previous observations that serum PLA—measured with our photometric assay at pH 6—is not suitable for the diagnosis of pancreatitis (for reviews, see 11, 12). Incidentally, serum PLA usually exhibits a broad pH optimum, ranging from about 6.5 to 8 (for examples, see Figure 1), whereas the pH optimum of the pancreatic isoenzyme is clearly acidic (2, 11). For future studies on the role of pancreatic phospholipase A2 we therefore recommend the use of 100 mmol/L acetate buffer, pH 6, with calcium chloride, 4 mmol/L instead of the commercial buffer solution (Boehringer, Mannheim, F.R.G.; cat. no. 1056239).

Because nonpancreatic serum phospholipase A2 is also active at acid pH (Figure 1), we further suggest the use of antibodies against the pancreatic isoenzyme, as recently described by Escola et al. (13).

References


Georg Hoffmann

Dr. Kazmierczak et al. respond:

To the Editor:

We thank Dr. Hoffmann for his interest in our work and wish to address his comments regarding the utility of phospholipase A (PLA) as a prognostic indicator of disease severity in patients with acute pancreatitis. Our interest in PLA was aroused by the numerous reports, including those mentioned by Dr. Hoffmann, citing the excellent prognostic utility of PLA measurements in patients with pancreatitis as well as nonpancreatic diseases (1–7). Unfortunately, in our opinion, these studies were deficient with respect to the use of a suitable control population.

We designed our study to test the utility of PLA measurements in all patients who were evaluated for suspected pancreatitis and had amylase or lipase tests ordered by the physician. PLA measurements were thus performed only on those samples ordered by the physician for amylase or lipase. Thus, the timing and number of samples obtained for each patient depended on how often amylase or lipase was ordered by the physician caring for the patient. Patients identified for inclusion in our study by this system showed increased PLA in pancreatic as well as a wide variety of nonpancreatic diseases. We found it difficult to differentiate patients with acute pancreatitis from those having nonpancreatic diseases by using PLA.

Fig. 1. Time courses of serum phospholipase A activity measured at three different pH values in five patients with severe inflammatory diseases: ○, pH 6.5 (Tris maleate); ⨁, pH 8.0 (Tris · HCl); — — —, pH 7.4 (Tris · HCl)

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