increased rapidly until reaching a plateau. These concentrations showed a significant age dependence \( (r = 0.7337 \) for men, 0.8143 for women). After a steady period, the hair strontium concentrations decreased rapidly, the decrease also showing a significant age dependence \( (r = 0.4902 \) for men, 0.6747 for women). During the plateau period, hair strontium concentration in men and women differed significantly, with higher values in the women \( (P < 0.001) \). The strontium also increased more rapidly and reached a plateau earlier in women than in men. At ages 1–20 years, the hair strontium concentrations in both sexes increased, whereas the concentration in both sexes decreased between ages 41 and 60 years. In other periods, it was unrelated to age.

Rates of metabolism increase and decrease during the life cycle. Paschal et al. \( (5) \) reported that the concentration of metals in the hair of a selected US population was age-dependent, and found that strontium increased up to about age 12–14 years. They proposed that this increase was a result of age-dependent excretion of alkaline metals in hair during skeletal growth and development. In fact, human skeletal growth is most rapid between ages 10 and 25 years. We suggest that the higher average hair strontium concentrations in women \( (12.59 \mu g/g) \) than in men \( (5.7 \mu g/g, P < 0.001) \) during this period are related to the reproductive period in women. Blakely \( (4) \) proposed that this difference was due to pregnancy and lactation, because calcium is used preferentially in the transport of ions to the placenta and mammary glands, and because pregnancy and lactation facilitate the absorption of alkaline earth metals from gut. Strontium, in contrast, may be preferentially excreted and accumulated in hair. Female hormone activity may result in increased strontium and decreased calcium concentrations in bone.

It is interesting to speculate whether the increased strontium in women during their reproductive years can prevent the occurrence of certain diseases that are seldom seen during that time. Besides the strontium requirement for activation of epidermal transglutaminase \( (2, 3) \), increased granulocyte strontium in inflammatory arthropides is related to the inflammatory activity \( (6) \). Therefore, it might be of interest to study the relation between strontium concentrations and certain diseases. Furukawa et al. \( (7) \) found that cultured keratinocytes stimulated with 1.0–3.0 mmol/L strontium showed higher viability and almost a twofold increase in number compared with those grown in a standard calcium concentration. They concluded that, for the culture of human keratinocytes in a serum-free medium, the addition of strontium could lead to a more uniform population of basloid cells with increased expression of surface fibronectin.

We conclude that our results, and those of others, may have some relevance to human nutrition as well as to disease and ageing.

References

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Analytical Interference Caused by Incompletely Clotted Serum Specimens

To the Editor:
Blood specimens received in the laboratory in clot tubes intended to yield defibrinated serum for analysis do not always clot fully and (or) promptly. Consequently, so-called serum specimens are not always fully defibrinated. Reasons for this include deficiencies of the blood clotting system, anticoagulant therapy, and contamination of the specimen with anticoagulant agents during collection. Such incompletely defibrinated specimens are sometimes recognized because clots or strands are seen in the storage tubes or sample cups the sera are being held in. Other times, the delayed clotting is not visible and detected only when there is a consequence such as a blocked line in an instrument or a sampling problem. In evaluating an automated immunoassay system (AIA1200; Tosoh Medics, San Francisco, CA), we observed some apparently spurious results, which the manufacturer thought might be due to fibrin formation in the reaction vessels inside the instrument. We investigated further by measuring follitropin (FSH) in specimens likely to have delayed clotting. We used replicate determinations to detect the effects of clotting, reasoning that clotting within the analytical system would cause variable interference and thus discordant results among replicates.

In measuring FSH in triplicate with the AIA1200, we observed spurious results in 9 of 40 potentially heparin-contaminated sera (during collection from an indwelling line), 9 of 13 serum specimens observed in the laboratory to be clotting (in the tube or sample cup or during some analysis), and 1 of 3 serum specimens from patients with a prolonged prothrombin time (PT). Thus, 19 of the total of 56 specimens we examined indeed exhibited evidence of interference. Table 1 lists the triplicate results obtained from the AIA1200 exhibiting interference. Some discords were quite large, e.g., in specimens 2, 8, and 12.

We also studied the IMx (Abbott Laboratories, Abbott Park, IL), finding spurious results (in triplicate determinations) in two of nine sera observed to be clotting in the laboratory but not in the one serum specimen from a patient with a prolonged PT. These discords within the IMx were less dramatic than those seen with the Tosoh, the replicates being 29, 16, and 12 IU/L and 22, 11, and 11 IU/L. One of five other sera potentially contaminated with heparin during collection yielded questionable results when assayed in duplicate (64 and 73 IU/L). Among the 13 sera exhibiting no suspicious results on the IMx, 10 gave spurious results on the AIA1200; and 1 of the 2 sera with spurious results by IMx gave spurious results by the AIA1200.

To test the hypothesis that continued fibrin formation could be causing the interference, we added excess heparin to block subsequent clotting and thus the interference. We did this in two ways: (a) by transferring aliquots
of serum specimens contaminated with heparin (from indwelling lines) into heparin-containing Vacutainer Tubes (Becton Dickinson, Rutherford, NJ), and (b) by adding heparin (final concentration, 25–50 kIU/L) to the diluent used on the Tosoh AIA1200. The results are shown in Table 1. Interference was judged to be eliminated if triplicates were no longer discordant. Addition of excess heparin did appear to end or reduce the interference, except for specimen 17. Notice that spurious results were either high (specimens 12, 13, and 16), or low (specimens 11, 14, 15, and 19). For specimen 10, however, results for the replicates themselves were not discordant; rather, the interference was revealed by the change in results due to heparin treatment. This indicates that discordance among replicates does not necessarily reveal this problem. In fact, among the other 18 triplicate results, most have pairs that would be considered acceptable duplicates (e.g., specimens 1, 7, 9, 13, 14, 16, 19).

Serum protein electrophoresis indicated that fibrinogen was present in every specimen we examined that exhibited interference. It is possible that clotting in the sample cup (rather than within the instrument) could cause short sampling. However, this would produce results that are spuriously decreased, not increased (as we observed both), and would not be remedied by addition of heparin to the Tosoh diluent as we found. We conclude that fibrin formation within the Tosoh reagent vessel was the most likely cause of the artificially high or low results observed with that assay system. Because of the limited data we have for the IMx, we can only note that interference from fibrin may occur but we cannot suggest a mechanism or location.

Although we encountered this interference in patients' specimens infrequently (our estimate of prevalence is ≤1%), the problem cannot be ignored. A laboratory receiving a few hundred specimens per day may risk several spurious results daily if using susceptible instrumentation.

The wider significance of our observation is that, in addition to tests with completely clotted and completely anticoagulated plasma specimens, incompletely clotted serum specimens—whether from coagulation factor deficiencies or the presence of anticoagulants—should also be considered when evaluating new methods and instruments.

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Glucose Interference in Jaffé Creatinine Method: Effect of Calcium from Peritoneal Dialysate

To the Editor:

Measurement of creatinine in peritoneal dialysate is used in the peritoneal equilibration test to assess the performance of ambulatory peritoneal dialysis (1). Because peritoneal dialysate solutions often contain glucose, which interferes in the Jaffé creatinine measurement, Farrel and Bailey proposed the following correction equation to account for the interference (J):

\[ \text{corr. Cr} = \{\text{meas. Cr} - \text{F[gluc]} \}

where F is an analyzer-dependent constant.

We found, however, that the correction equation failed to predict the spurious creatinine results produced by unused peritoneal dialysate solutions. Moreover, we found significant discrepancies between creatinine results for the unused peritoneal dialysate solutions and for glucose solutions with the same glucose concentration; e.g., spurious creatinine values were 86 μmol/L for 236 mmol/L glucose solution and 154 μmol/L for unused dialysate solution at the same glucose concentration.

Trying to uncover the cause of this discrepancy, we further analyzed the interference of the constituents of the unused peritoneal dialysate solutions. The dialysate Dianead™ (with glucose 42.5 g/L) was from Baxter Healthcare (Miami, FL) and included glucose 236 mmol/L, lactate 35 mmol/L, NaCl 132 mmol/L, MgCl₂ 0.75 mmol/L, and CaCl₂ 1.75 mmol/L. To prepare comparable solutions, we obtained reagent-grade glucose, CaCl₂, pyruvate (Sigma Chemical Co., St. Louis, MO), acetone, and lactate (Wako, Osaka, Japan).

We measured creatinine with a Hitachi 7450 automated analyzer (Hitachi, Tokyo, Japan), using alkaline picrate reagents (Latron Laboratory, Tokyo, Japan). The analyzer settings for this measurement were, according to the manufacturer’s guidelines: reagent 1 (NaOH 105 mmol/L, 280 μL), reagent 2 (picric acid 38 mmol/L) 70 μL, and sample volume 14 μL. The kinetic measurement of optical absorbance was determined between points 30 and 35 (360–420 s after the addition of reagents), with a main wavelength of 505 nm and secondary wavelength of 600 nm.

All analytes were measured on the same day. The between-run quality control data (CVs, n = 4) were 6.06% and 1.87%, respectively, for Wako control serum I (mean creatinine 117 μmol/L) and control serum II (mean 567 μmol/L).

Measurements of the constituents of the peritoneal dialysate solution and of their combinations revealed that no single constituent other than glucose interfered directly with the measurement. However, calcium enhanced the interference caused by glucose. In the presence of 1.75 mmol/L calcium, the spurious creatinine measurement caused by