References

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Can Quality-Control Sera Be Distinguished from Patients' Sera by Appearance?

To the Editor:
It is common practice in many laboratories to conduct studies in which unknown, or blind, specimens are interspersed among the workload of clinical specimens, and for this purpose it is convenient to use reconstituted lyophilized commercial control sera. However, it is also commonly supposed that analysts can recognize such specimens by their appearance, and so invalidate the blind nature of such studies. Indeed, when we have shown tubes of various control sera to experienced technologists and asked whether the specimens were patient or control sera, a rather uniform response has been that they were controls. But curiously, when they are asked "how do you know that this specimen is a control?" the answers have been vague: "It just looks like a control," or "It looks funny," or, more definitively, "It's coarsely turbid." The vagueness of these descriptions made it seem likely that even though control specimens might be recognizable as controls, some patients' specimens might also be thought to be controls. To gain an objective answer to the question of whether experienced analysts can recognize blind quality-control specimens by their appearance, we conducted the following experiment:

Forty-six patients' specimens were selected from about 500 specimens that had been received by the chemistry laboratory on a single day. They were selected to represent a variety of typical nonhemolyzed specimens; that is, the specimens had various degrees of lipemia and icterus, or "color." Two different control specimens were placed randomly among the patients' specimens. The rack of 48 specimens was presented to each of 12 experienced technologists and each was asked to "list the specimens that you think are control sera." Each technologist examined the specimens alone, and was unaware of the results of the others.

The results showed that the two control specimens were correctly identified 95.8% of the time (23 correct responses out of 24 total responses). However, patients' specimens were mistakenly identified as controls 12.1% of the time [67 incorrect responses out of 552 (46 specimens X 12 technologists) total responses]. Only one technologist correctly identified all of the patient specimens; the other scores ranged from 4.3% to 37% incorrect identification of patients' specimens. The scores were unrelated to the technologists' years of experience (which ranged from one year to more than 10 years, with an average of 4.6 years).

The misidentification of patients' specimens as controls was found to be related to specimen characteristics: clear, icteric, and lipemic specimens were misidentified with frequencies of 3%, 12%, and 54%, respectively. Two lipemic specimens were identified as controls nearly as frequently as the true controls.

Figure 1 shows the frequency with which the individual patients' specimens were identified as controls. Of the 46 specimens, 20 (43.5%) were called on one or more occasions, and the lipemic specimens accounted for more than half of the misidentifications.

This experiment was biased intentionally to favor the identification of the controls. The controls were similar to those used daily in our laboratory and so their appearances should have been familiar to the technologists. In addition these control specimens were both lipemic and icteric, which are apparently the principal cues used to "identify" control specimens.

These results confirm the common supposition that control specimens do have a distinctive appearance, but the
results also show that an appreciable number of patients' specimens have a similar appearance. The relatively high frequency of misidentification of patient specimens as controls suggests that the true controls were actually identified only as members of a group of similar specimens that, because of their lipemic and (or) icteric appearance, were thought to be control specimens.

One obvious conclusion of this study is that if anxious analysts seek to identify a few blind control specimens that are randomly interspersed among the daily workload of clinical specimens, their task will be onerous, for a significant number of the clinical specimens will be mistakenly believed to be controls.

A second conclusion is that there is still need for improvement in the technology of manufacture of commercial control specimens. Most clinical specimens are clear; thus commercial control specimens should also be clear. However, in our experience most such materials currently available have a peculiar opalescent turbidity that is similar to that of only a minority of clinical specimens.

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Noncorrelation between Serum Gold and Complement Concentrations

To the Editor:

In rheumatoid arthritis, low concentrations of complement components CH50, C3, and C4 are associated with severity. However, normal or above-normal concentrations may be observed in such patients (1). Therapy with gold salts (chrysotherapy) is commonly used and is effective in the treatment of rheumatoid arthritis; its mechanism of action is unknown. Gold is bound by proteins and is found in synovial fluids in concentrations comparable to those in serum or plasma (2).

We wish to report data on serum gold and complement concentrations in a patient who underwent chrysotherapy. The purpose of the study was to develop a new protocol for rapidly attaining therapeutic but nontoxic concentrations in chrysotherapy. Serum gold was determined by atomic absorption spectrophotometry (3). Complement CH50 and C4 were determined as previously described (4, 5), and C3 by radial immunodiffusion.

Table 1 gives the data. Serum gold ranged from 0.07 to 6.87 mg/liter, and C3 values from 0.91 to 1.91 g/liter. The initial slightly low C3 values are probably not significant, because C3 values did not change with large changes in serum gold. Serum CH50 ranged from 230 to greater than 300 hemolytic kilo-units per liter, while serum C4 values ranged from 286–1025 kilo-units/liter. Normal ranges for this laboratory are shown. Statistically, complement and serum gold concentrations correlated poorly.

At the end of the ninth dose in the course of chrysotherapy, the serum gold concentration was steady at 3.84 mg/liter. The half life ($t_{1/2}$) for gold elimination reportedly is 5.5 to 6.0 days (2). Because the patient was dosed every three days and the serum gold determined at three-day intervals, one would expect to reach a steady-state concentration at the end of five to six half-lives.

Our results suggest no correlation between serum complement and gold concentration.

References

Table 1. Serum Gold Concentration and Serum Complement CH50, C3, and C4 Values for a Patient with Rheumatoid Arthritis

<table>
<thead>
<tr>
<th>Date *</th>
<th>Gold, mg/liter</th>
<th>C3, g/liter</th>
<th>C4 kilo-units/liter</th>
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Normal range, this laboratory 1.78 ± 0.37 805 ± 213 210 ± 20

(±SD)

* Patient was given an initial intramuscular dose 10 mg of Myochrysine (Merck, Sharp & Dohme) on day one. The following doses were 50 mg every three days. Total gold (as Myochrinosum): 460 mg.


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Assay of N-Acetyl-β-D-glucosaminidase in Urine of Patients with Renal Transplants as an Indicator of Rejection

To the Editor:

We would like to comment on the Letter by Keyser et al. [Clin. Chem. 22, 925 (1976)] concerning the assay of urinary enzymes as an early indicator of rejection. We are pleased to note that their investigations confirm our previously published findings and that they are only disputing the timing of the earliest increase in urinary enzyme activity. There may be an explanation for this, since they use 24-h urine collections. We have found that random samples are adequate if urinary creatinine is measured in each to compensate for variations in urine flow (1). This also ensures...