expressed as % S-cMg, the mean of which was 0.819 mmol/L. From this follows: % S-cMg<sup>com</sup> = [(0.9095 × 0.94)/0.819] × 100 = 10.4%.

Note that S-cMg<sup>com</sup>, measured by ISE, needs to be corrected for the water displacement effect by the serum proteins when it is related to S-cMg. Furthermore, our approach assumes, for example, that the added phosphate (1.09 mmol/L) complexes the same amount of magnesium as the phosphate already present (mean, 1.09 mmol/L). This is justified because the functions calculated from the theoretical complexation constants are quasi-linear in the range we investigated (8). In addition, complexation decreased proportionally when the concentrations of added complexants were only one-half of the concentrations of the original complexants.

On the other hand, when reliable values for S-cMg<sup>com</sup> and UF-cMg become available, we should be able to calculate S-cMg<sup>2+</sup> by subtracting S-cMg<sup>com</sup> and serum protein-bound magnesium (S-cMg<sup>pro</sup>) from S-cMg (Note: S-cMg<sup>pro</sup> = S-cMg – UF-cMg). If S-cMg<sup>2+</sup> correlates reasonably well with S-cMg, a practical standardization approach for S-cMg<sup>2+</sup>, based on S-cMg, should be possible. To investigate this, we measured the S-cMg and UF-cMg in 12 serum samples with an ion chromatography reference method (11); for S-cMg<sup>pro</sup>, we found a value of 31.5% (± 1.6%, 95% confidence interval), which is in good agreement with the 33.7% reported by Speich et al. (2) (Note: Like S-cMg<sup>com</sup>, UF-cMg must also be corrected). According to the above proposal, our data would yield a calculated value of 58.1% for S-cMg<sup>2+</sup>. We measured S-cMg<sup>2+</sup> with the AVL 988-4 and found an excellent correlation between S-cMg and pH-normalized S-cMg<sup>2+</sup> in a panel of 57 serum samples (r = 0.9223; P < 0.001; S-cMg range, 0.74–0.92 mmol/L).

From these preliminary results, we concluded that standardization of S-cMg<sup>2+</sup> on the basis of S-cMg is a realistic option. We will undertake additional experiments to substantiate our observation that, for serum samples from apparently healthy donors, S-cMg<sup>2+</sup> accounts for ~58% of S-cMg (the fraction is usually assumed to be 65%).

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An IgM Paraprotein Causing a Falsely Low Result in an Enzymatic Assay for Acetaminophen

To the Editor:

Since the development of enzymatic assays for acetaminophen in the early 1980s, their use has rapidly become widespread (1). Their advantages of speed and ready automation have ensured that >95% of laboratories submitting to a external quality assessment scheme now use this method (M.A. Thomas, personal communication). Given this fact and the absolute dependence on the laboratory result for clinical decision making, it is important to be aware of any possible discrepancies associated with this technique. I therefore report here a case of a man with an IgM monoclonal gammopathy who ingested acetaminophen and whose subsequent serum acetaminophen concentration was falsely low on enzymatic assay.

When we were investigating a 77-year-old man who was admitted after a cerebrovascular accident in 1990, we noted that he had an IgM<sub>M</sub> monoclonal component of 5 g/L. In the absence of any other clinical or laboratory evidence of a hematological dyscrasia, a diagnosis of monoclonal gammopathy of unknown significance (MGUS) was made. On a subsequent occasion, he was admitted to the Accident and Emergency Department after he ingested 100 tablets of acetaminophen 18 h previously. Samples were sent for acetaminophen analysis; however, in view of his history, N-acetylcysteine was administered before the results became available. Over succeeding days the patient’s alanine aminotransferase peaked at 2515 U/L, his bilirubin peaked at 40 μmol/L, and his international normalized ratio peaked at 1.3. The concentration of his IgM<sub>M</sub> monoclonal component was 7 g/L. His IgG was slightly low at 6.3 g/L (reference range, 7.0–19.0 g/L), but his IgA [1.53 g/L (reference range, 0.90–4.50 g/L)] and blood film were normal. After 6 days, he was discharged to a psychiatric ward.
and subsequently made a full recovery.

We assayed the serum acetylamino-
phen using a commercially available
zymatic kit (Cambridge Life Sci-
enes) that had been adapted for use
on a Cobas Fara II (Roche Diagnostic
Systems Ltd.) and determined that
his serum acetaminophen concentra-
tion was 53 mg/L. However, we
oted that the absorbance after the
first stage of the assay, which in-
volves addition of sample to re-
constituted enzyme reagent, was 0.145
absorbance units. This greatly ex-
cceeded the concentrations seen rou-
tinely with other sera (<0.01 absorb-
ance unit). Furthermore, the mea-
sured values did not change in a
linear fashion when the sample itself
was diluted. When a drop of serum
was added to water (the Sia water
(2), a flocculent precipitate
formed. The acetaminophen con-
centration determined by HPLC on a
Sephisorb column using an aqueous
solution of n-propanol was 86 mg/L.

In our automated enzymatic assay
for acetaminophen, samples are di-
luted with water and then mixed with
reconstituted enzyme reagent
(aryl acylamidase in Tris-HCl buffer,
pH 8.6). The absorbance at 615 nm is
then measured. After incubation, the
color reagent (o-cresol in ammoniacal
copper sulfate) is added, and a final
absorbance measurement is taken af-
after another 3 min. The acetamino-
phen concentration is calculated from
the difference between the two
absorbance readings. It appears that
addition of our patient’s serum to the
aqueous diluent or the enzyme re-
agent caused precipitation of his IgM
monoclonal paraprotein in a manner
akin to the Sia test. Because the Co-
bas Fara is configured in such a way
that dilution alone should not alter
the measured absorbance and be-
cause the final measured acetamino-
phen was actually lower than the
true value determined by HPLC, the
precipitate may well have partially
redissolved in the subsequent more
alkaline medium of the color reagent.

Several authors have recognized
that precipitation of paraproteins
may cause potentially unrecognized
interference in a range of different
assays. The interference in phosphate
(3) and calcium (4) determinations
has been attributed to precipitation
in an acid medium. In contrast, spu-
riously high hemoglobin values have
been reported when a monomeric
IgM paraprotein precipitated on ad-
dition of reagents.

Whether the presence of a parapro-
tein increases or decreases the mea-
sured results will depend on
whether a sample blank is included.
The latter eventuality, that of a spu-
riously low reading, is of particular
concern because potentially life-sav-
ing therapy with N-acetylcysteine
could be withheld on the basis of
erroneous laboratory findings.

If laboratories measure acetamino-
phen with an enzymatic assay, they
are advised to ensure that their
method can detect the increase in
absorbance that will occur if a para-
protein precipitates on dilution or
addition of reagents.

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