logarithmic but biphasic in nature. The biological half-life of the drug was shorter (24 h if estimated by visual inspection; 13 h if estimated by the method of residuals (1)) during the first two days, longer (52 h) for the following three days (Figure 1).

At therapeutic concentration in plasma, digoxin enters the elimination (β) phase from the distribution (α) phase within 7 to 12 h after an oral dose (2); the mean half-life for digoxin elimination is about 1.6 days (39 h) in individuals whose renal and hepatic function is normal (3). Dungan et al. (4) reported that the half-life of digoxin in children is similar to that found in adults with normal renal function (4).

We found four cases (Table 1) of suicidal or accidental digoxin poisoning in the literature in which sufficient serial determinations of serum digoxin concentrations were reported that we could assess the kinetics of elimination. Hobson and Zetter (5) reported that the half-life was longer (43 h) initially and shorter (15 h) during the following days in a 60-year-old woman who had a history of heart disease and was treated with digoxin (Case 1). They postulated that the early prolongation of serum digoxin half-life observed was the result of continued intestinal absorption of the ingested drug. From five serum digoxin values obtained during four days, Smith and Willerson (6) estimated the apparent half-lives of digoxin in the serum of a 51-year-old man being treated with digoxin to be 10 h on the first day, 21 h on the second day, and 32 h during the following two days (Case 2). Bertler et al. (7) estimated the half-lives of digoxin in serum of a 78-year-old man who was being treated with digoxin to be 24 h for the first two days and 60 h during the following six days (Case 3). Ahmark (8) estimated the half-lives of serum digoxin in a 45-year-old man with no history of heart disease to be 20 h during the first two days and 33 h during the following two days (Case 4).

Cardiac disease and increasing age are both associated with diminished creatinine clearance and with decreased renal and total clearance of digoxin (9). Serum creatinine or creatinine clearance was normal in Cases 1 and 4, and slightly above-normal in Case 3. Cardiac disease and previous treatment with digoxin were noted in Cases 1, 2, and 3. The patient in the present report is a teenager, with normal renal function and no history of cardiac disease. Nevertheless, the value of the half-life of the biphasic elimination phase in our case is quite similar to those in Cases 2, 3, and 4. It is not now known whether the early short half-life actually represents a prolonged distribution phase or some unique pharmacokinetics of the elimination phase provoked by digoxin overdose, such as an alteration in the volume of distribution or in clearance (or both) of the drug. More extensive studies are needed to explain this interesting observation.

Table 1. Elimination Half-Life of Serum Digoxin after a Massive Overdose

<table>
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<tr>
<th>Case</th>
<th>Patient's age, yr</th>
<th>History of heart disease</th>
<th>No. of digoxin detms.</th>
<th>t1/2, h</th>
<th>Initial</th>
<th>Final</th>
<th>Reference</th>
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<td>33</td>
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<tr>
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<td>no</td>
<td>12</td>
<td>24</td>
<td>52</td>
<td>This report</td>
<td>13%</td>
</tr>
</tbody>
</table>

*All except the first were men.

References

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William Stempsey
Bernard E. Statland

Effect of Light on 125I-Labeled Triiodothyronine in Different RIA Buffer Systems

To the Editor:

The buffers most commonly used in RIA systems for the measurement of thyroid hormones in human serum are Tris (1, 2), phosphate-buffered saline (PBS) (1, 2), and barbitral (3). Thimerosal (Methylolate), salicylate, and 8-anilino-1-naphthyl sulfonic acid (ANS) are frequently used to block the effects of thyroxin-binding globulin (1–3). Commercially available RIA kits usually contain ready-to-use tracer solutions prepared with these buffers. Because exposure to light is suspected to be responsible for erroneous assay results, we investigated the influence of light on the performance of 125I-labeled triiodothyronine (125I-T₃) in these different buffer systems.

Using the Chloramine T method (4, 5), we prepared 125I-T₃ with a specific activity of 3000 Ci/g (= 72.15 TBq/mmol). The tracer solutions contained about 60 000 cpm/mL in the following buffer systems: (a) barbitral (50 mmol/L, pH 8.6) and sodium salicylate (30 mmol/L); (b) Tris (50 mmol/L, pH 8.9) and thimerosal (7 mmol/L); and (c) phosphate (100 mmol/L, pH 7.6), sodium chloride (150 mmol/L) and ANS (6 mmol/L). The last is abbreviated PBS/ANS. We placed 100 mL of each solution in clear glass bottles, irradiated with ultraviolet light (254 nm; CAMAG, West Berlin, F.R.G.) at a distance of 5 cm for up to 66 h, and tested the irradiated solutions for use in a commercially available coated-tube RIA system (SPAC T3; Byk-Mallinkrodt, Dietzenbach, F.R.G.).

Figure 1 shows that zero binding decreases with increasing duration of ultraviolet irradiation, an effect most pronounced in the Tris buffer system, where binding decreases by 5% after only 1 h of irradiation and by more than 25% after 24 h. With the barbitral buffer system the decrease is smaller (4% after 2 h, 15% after 66 h of ultraviolet light). In the PBS/ANS system, zero binding of 125I-T₃ remains virtually constant. Similar observations were made in the discrimination difference (D) of the standard curve, i.e., zero binding minus the binding of the standard containing the highest concentration of T₃. The PBS/ANS system showed no change in discrimination, but the barbitral system had a decrease of 13%. We made no further measure-
ments in the Tris buffer system after 24 h of irradiation, because standards of higher concentration showed sometimes higher binding than zero or preceding standards.

The control values were in the expected range in the PBS/ANS system and also—in spite of the deterioration in zero binding and discrimination—in the barbital buffer system, over the whole range of irradiation.

Results were similar when we incubated the assay mixture for 2 h in bright sunlight: the Tris buffer system yielded erroneous results but the other systems performed well. After five weeks of storage of the tracers in the cold room, zero binding of $^{125}$I-T$_3$ in the Tris buffer system decreased by 10% if exposed to light but remained constant if the tracer was protected from light.

Using chromatographic methods, we detected no sizable amount of $^{125}$I or any other radioactive compound except $^{125}$I-T$_3$ in the irradiated samples. The cause for the deterioration of zero binding, discrimination, and consequently of assay results, especially in the Tris buffer system, remains to be clarified.

We conclude that the use of $^{125}$I-T$_3$ in PBS/ANS is not sensitive to light. $^{125}$I-T$_3$ in barbital/sodium salicylate is somewhat sensitive to light, but assay results are still acceptable. $^{125}$I-T$_3$ in Tris/thimerosal is very sensitive to light, and ultraviolet or bright sunlight should be excluded during the assay procedure.

References


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A Source of Error in Determination of Blood Gases

To the Editor:
The use of pre-heparinized plastic disposable syringes for the measurement of blood gases, although convenient, may lead to errors. We recently investigated the occurrence of occasional discrepancies between the actual bicarbonate values calculated in blood-gas analyses and total CO$_2$ as measured in the ASTRA 8, using venous plasma obtained with lithium heparin as the anticoagulant. Duplicate results on two blood gas analyzers (Corning Model 175 and Corning Model 178) showed no significant differences in pH, pCO$_2$, or pO$_2$. Hematocrit determinations on blood-gas samples showed much lower values when compared with hematology results from samples collected at the same time.

Example 1
Arterial sample
pH 7.46
pCO$_2$ 2.93 kPa (22 mmHg)
Calculated bicarbonate 16 mmol/L
Hematocrit 27%
Venous sample
Measured total CO$_2$ 25 mmol/L
Hematocrit 41%

Example 2
Arterial sample
pH 7.46
pCO$_2$ 3.20 kPa (24 mmHg)
Calculated bicarbonate 17 mmol/L
Hematocrit 33%
Venous sample
Measured total CO$_2$ 24 mmol/L
Hematocrit 42%

The disparity was traced to dilution of the blood-gas samples by the 0.8 mL of heparin solution in the disposable syringe; even after expulsion prior to the arterial puncture, about 0.2 mL remained in the dead space, enough to produce an appreciable dilution error if the 3.0-mL syringe was not completely filled.

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Interference by Metrizamide with the Du Pont aca Method for Cerebrospinal Fluid Protein

To the Editor:
Recently we measured protein in a clear, non-xanthochromic specimen of cerebrospinal fluid (CSF) from a 13-year-old boy who had undergone computerized axial tomography scanning. The radiographic contrast medium used was metrizamide (Amipaque*, Winthrop Labs, New York, NY 10016), a water-soluble material first introduced in the U.S. for myelography in 1978. The protein value as measured with the discrete analyzer (aca; Du Pont Co., Wilmington, DE 19891) was 2400 mg/L (reference interval 150–450 mg/L). In this method, the decrease in light transmission due to light scattering by the protein precipitate formed after trichloroacetic acid treatment is measured at 340 and 540 nm (1). A precipitate can be seen in a reagent pack if the CSF protein concentration exceeds the reference interval.

Because no precipitate was visible in the spent pack from the assay of this undiluted specimen, we suspected interference. We then measured protein in this specimen by another trichloroacetic acid precipitation method in which absorbance is measured at 450 nm (2), and found a protein value of 100 mg/L. When this same specimen was assayed for protein with a Coomassie Brilliant Blue dye-binding method (Bio-Science Labs, Great Neck, NY 11022), a value of 140 mg/L was obtained.

We believe the source of the interference was the radiographic contrast material metrizamide, which for many radiographic procedures is injected directly into the lumbar space. The absorption spectrum of a diluted specimen of the patient's spinal fluid was similar to that of a metrizamide solu-