# Persistence of High Serum Digoxin Concentrations

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## Case Description

An 86-year-old polymorbid man with a chronic myeloproliferative disease and thrombocythemia was admitted to the hospital with acute respiratory insufficiency and congestive heart failure. Laboratory results are shown in Table 1. Of note, there was an extremely high and persistent concentration of digoxin (more than 3 μg/L; therapeutic range: 0.50–1.20 μg/L), although administration of the drug was stopped on the first day of hospitalization.

**Table 1. Laboratory findings in patient's serum during hospitalization.**

| | Day after admission | | | | | | |
|---|---|---|---|---|---|---|---|
| Analyte | 0 | 1 | 3 | 4 | 7 | 9 | 11 |
| Digoxin, Architect i2000, Abbott, μg/L (TR: 0.50–1.20 μg/L) | 3.51 | 2.85 | 3.03 | 3.06 | 3.29 | 3.21 | 3.25 |
| Creatinine, μmol/L (mg/dL) (RI: 60–100 μmol/L [0.68–1.13 mg/dL]) | 214 (2.42) | 223 (2.52) | 223 (2.52) | 203 (2.3) | 287 (3.25) | 297 (3.36) | 259 (2.93) |
| eGFR, CKD-EPI, mL/min/1.73 $m^2$ (RI: > 60 mL/min/1.73 $m^2$) | 22.8 | 22.2 | 22.2 | 24.6 | 16.2 | 15.6 | 18.6 |
| NT-proBNP, ng/L (RI: <250 ng/L) | | | | | | | 7 720 |
| Digoxin, Cobas e601, Roche, μg/L | – | – | – | – | – | – | 0.57 |
| Digoxin, Access 2, Beckman Coulter, μg/L | – | – | – | – | – | – | 0.56 |
| Digoxin, LC-MS, μg/L | – | – | – | – | – | – | ND |

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; LC-MS, liquid chromatography–mass spectrometry; ND, not detected; RI, reference interval; TR, therapeutic range.

## Questions

1. How is digoxin eliminated?
2. Based on the data presented, what is the most likely cause of the persistently high serum digoxin concentrations?

## Discussion

Digoxin is eliminated primarily by the kidney. Despite impaired renal function in this patient, a gradual decrease in serum digoxin would be expected. The presence of heterophilic antibodies was excluded with heterophilic blocking tubes. Notably, an undetectable digoxin concentration by LC-MS would suggest the presence of digoxin-like immunoreactive substances. These substances are mostly endogenous and produced in volume expansion states (1–3) that can react with antidigoxin antibodies and thus interfere with some of the immunochemical determinations of digoxin (4).

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