Methemoglobin, myoglobin, and methemalbumin can cause abnormal dark color in patient samples. “Lipemia” was measured at 660- and 700-nm wavelengths (1); therefore any compounds that absorb light in this range will result in an increased lipemic index. In this patient, methemoglobin was always <7.5% (cooximetry), myoglobin was not detected (gel filtration chromatography and mass spectrometry), but an interference causing falsely increased results by immunoturbidimetry was observed. Haptoglobin was undetectable (nephelometry). Methemalbumin, formed when albumin binds excess heme (oxidized free heme), was markedly increased (multiwavelength spectrophotometry) (2, 3), consistent with intravascular hemolysis (4). Chemistry analyses were performed on both undiluted serum and serial dilutions to confirm acceptable analyte recovery and rule out potential interference (5).

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

References

Recent Trends in Designer Drug Abuse
Bridgit O. Crews†* and Matthew S. Petrie††

Designer drugs are compounds that are chemically synthesized and intended to mimic existing illegal drugs such as marijuana, cocaine, or methamphetamine. Although designer drugs have recently become a major focus for both the medical and law enforcement communities, their inception dates back nearly a century to the appearance of various morphine esters following the first international ban on opium.

A recent feature in Science highlights an alarming trend in modern designer drug abuse (1). Over the past few years the appearance of new synthetic designer drugs has grown exponentially and the current list is staggering.

“Bath salts” are one class of designer drug structurally related to the molecule cathinone. Cathinone is naturally found in the khat plant and has been used by people for hundreds of years for its mild stimulant properties. Structural permutations of the cathinone molecule result in compounds such as methylenedioxypyrovalerone (MDPV)2 and α-pyrrolidinopentiophenone (α-PVP) (Fig. 1). Cathinone and its designer drug analogs bind to monoamine transporters, producing effects similar to amphetamines or cocaine. Acute intoxication can result in psychosis, hallucinations, violent behavior, tachycardia, hypertension, hyperthermia, and death. In addition to MDPV and α-PVP, the cathinone molecule can be chemically substituted at 9 different positions, making structural possibilities for “bath salts” practically unlimited; however, there is little to no toxicological information on a majority of these compounds. Adding to the
expansive milieu of designer drugs are synthetic cannabinoids ("Spice"), which as a class contains over 1000 known structures. These compounds mimic the effects of Δ⁹-tetrahydrocannabinol by activating the endocannabinoid system in the brain but can exhibit much higher potencies and associated toxicities.

The rapid modification of compounds appearing on the market is a problem not only for drug enforcement agencies but also for the clinicians and scientists who strive to understand the effects of these drugs and treat overdosed patients. Many of the compounds that appear to be structurally similar do not necessarily produce similar effects. Small chemical changes can drastically affect potency, which puts users at greater risk of overdosing. Purity may also vary from batch to batch, and thus 2 packages with the same name do not necessarily contain the same compounds. Even less is known about the metabolites of many of these drugs, although many are extensively metabolized. This adds another layer of complexity because metabolites may exhibit pharmacological properties unique from those of the original compounds.

The evolving nature of designer drugs is a particularly challenging issue for clinical and forensic laboratorians attempting to detect drug abuse. In fact, eluding drug tests is a major motivation for many users. Immunodetection is not a feasible approach because a majority of these compounds do not appreciably cross-react with existing immunoassays at concentrations typically observed in blood or urine. Most laboratories striving to detect designer drugs utilize full-scan high-resolution mass spectrometry (HRMS). Full-scan HRMS approaches are especially useful for identifying emerging drugs because data can be retrospectively reanalyzed, although most often these approaches are validated for research use only. Clinically validated assays typically target only a handful of established (and already illegal) designer drugs and thus may lack sensitivity for the newest compounds on the market.

Drug enforcement agencies truly face a unique challenge. Just as one drug is identified and scheduled in one geographical location, a new drug appears somewhere else. It is difficult to know the best way to combat this problem, but the approach of using networks such as the National Drug Early Warning System and the American Association of Poison Control Centers has the potential to prevent local epidemics from spreading, which means that developing the capability to detect designer drug use in patients is an important priority.

**Author Contributions:** All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

**Authors’ Disclosures or Potential Conflicts of Interest:** No authors declared any potential conflicts of interest.

**Reference**