Q&A column, 12/15

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Submit a Question

Q. How is haloperidol usually administered in a hospital? If blood is drawn within one to two hours after a dose, should the drug's concentration be in the therapeutic range?

A. Depending on the medical situation, haloperidol can be administered orally, intramuscularly, or intravenously in a hospital setting. Based on the drug's pharmacokinetics, if the drug is in the water-soluble form (e.g. lactate, hydrogen chloride), intramuscularly injected haloperidol should be circulating in the bloodstream within 20 minutes (time to peak concentration). Haloperidol has a half-life of 14 to 31 hours according to Baselt,[1] so blood concentrations are not going to decline quickly once absorption and distribution are complete. However, if the haloperidol is given intramuscularly in the form of an oily depot injection (e.g. decanoate), absorption will be much slower (six days to peak concentration and a half-life of three weeks).

There is no clearly established therapeutic range for haloperidol, and published therapeutic ranges are quite broad (5–17 ng/mL).[2].

1. Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*, 9th ed. Seal Beach, Calif.: Biomedical Publications; 2011.
2. Ulrich S, Neuhof S, Braun V, Meyer FP. Therapeutic window of serum haloperidol concentration in acute schizophrenia and schizoaffective disorder. *Pharmacopsychiatry*. 1998;31(5):163–169.

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The submitted question below and the first answer (by Alan H.B. Wu, PhD, of UCSF) were published in CAP TODAY in 2012. Recently, Dr. Wu and others concluded a study on laboratory results in transgender patients on hormone therapy, and we asked Dr. Wu to revisit the 2012 question by sharing the findings of their study. The second answer is his latest. –Editor

Q. Is there any protocol for reference ranges for transgender populations? We do not often encounter this problem because our physicians state either female or male. This time, though, the account ordered a prostate-specific antigen test and entered female. Our system is set to hold tests that normally would not be ordered. The doctor said this patient had a sex change and he wanted female on the report. We were able to "fix" this, but what about cases in which results are sex-dependent or a patient may be receiving hormone therapy?

A. This is a difficult question to answer because there are few studies on reference ranges among transgender patients. While it is well recognized that there are differences in reference ranges between males and females, it is not a simple matter of assigning normal ranges to the individual's original gender (at birth) or new one (after surgery). Some laboratory tests, such as for male and female hormones, are clearly altered by surgery. Others are dependent on differences in muscle mass between men and women (for example, creatinine) and might not be altered. Given this lack of data, there is no guidance for the laboratory as to correct reference range to accompany a laboratory result on a transgender patient. Since gender is usually self-reported, the best strategy is to use the appropriate reference range for that listing. The laboratory should accommodate a request by the attending physician to change the gender listed in the patient's demographic record because the attending is in the best position to evaluate the test result.

A. Subsequent to the 2012 publication of the preceding question and answer, we conducted a study at Emory University and the University of California, San Francisco, that examined reference ranges for 13 clinical laboratory tests in 55 male-to-female transgender patients on hormone replacement therapy (Roberts TK, et al. *Am J Med.* 2014;127:159–162). Results were compared against those of 20 healthy, cisgender males and females. We showed that for hemoglobin, hematocrit, and LDL cholesterol, these transwomen had reference ranges that resembled those of cisgender females, suggesting that their laboratory values changed in response to their transition therapy. For other tests such as alkaline phosphatase, potassium, and creatinine, the reference ranges remained similar to those of cisgender males. There was no difference between transgender and cisgender individuals for the other tests (ALP, AST, BUN, sodium, cholesterol, triglyceride, and HDL cholesterol). We concluded that it is not possible to predict the appropriate reference ranges for transgender subjects based on physiology or the effect of hormone replacement therapy.

Clinical laboratories should establish their own transgender reference ranges. As this may not be possible for most laboratories, establishing an individual's own homeostatic set-point may be the best approach for subsequent detection of an abnormality. There may be other steps clinical laboratories can take such as listing both sex (birth assignment) and gender (current assignment) where the two are not in agreement and possibly listing the reference ranges for both. With increasing attention toward gender assignment, the clinical laboratory issues unique to this population will become more apparent.

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Q. We are in the process of validating new hematology equipment. At one time, we were required to validate adequate mixing of the specimen on the analyzer. The current vendor says that a study performed by the vendor is sufficient and the study does not need to be replicated as part of the validation study on our newly purchased equipment. Is this true?

A. When bringing a new instrument into the laboratory, the laboratory is responsible for verifying claims provided

by the manufacturer. The laboratory must ensure that the instrument provides thorough mixing, especially that of a settled specimen. If studies were performed by the manufacturer, the laboratory should confirm that the study performed included settled specimens standing for different lengths of time and that not only fresh specimens were used. As stated in checklist requirement HEM.22000, some rocking platforms may be adequate to maintain even cellular distribution of previously well-mixed specimens, but are incapable of fully mixing a settled specimen. It is the responsibility of the laboratory to verify the manufacturer's claim. If the manufacturer's study did not include specific stability criteria that your laboratory is following, then you would need to perform your own mixing validation study.

College of American Pathologists. HEM.22000 Collection in anticoagulant. In: Hematology and Coagulation Checklist. July 28, 2015.

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Dr. Kiechle is medical director of clinical pathology, Memorial Healthcare, Hollywood, Fla. Use the reader service card to submit your inquiries, or address them to Sherrie Rice, CAP TODAY, 325 Waukegan Road, Northfield, IL 60093; srice@cap.org.*Those questions that are of general interest will be answered.*