

May 2017

Daratumumab interference with blood bank testing

Daratumumab (DARA), anti-CD38 immunoglobulin, is a novel FDA approved therapy for multiple myeloma which has increased survival for refractory patients. However, DARA has been found to interfere with blood compatibility testing. DARA binds to CD38 present on RBCs agglutinating all test cells present in antibody identification panel, indirect antiglobulin tests, and antihuman globulin crossmatches in all testing methods. This gives a picture similar to presence of RBC autoantibody and masks or interferes with identification of underlying alloantibodies. DARA does not interfere with ABORH tests.

Blood banks have developed several methods to overcome this interference and provide safe transfusions to patients on DARA. These include treating RBCs with dithiothreitol (DTT) or trypsin, neutralizing the antibody, and antigen matching by either serological phenotyping or genotyping. DTT has been described to inhibit DARA interference by denaturing cell surface CD38 on RBCs. Underlying unknown alloantibody (if present) can then be identified with traditional testing methods (gel, tube or solid phase).

It is very important for the clinical team to notify blood bank when a patient is started on DARA or blood is ordered on a patient who has received DARA. It is recommended that a baseline type and screen be performed before patients begin treatment. If a patient will be requiring continued transfusion support, RBC antigen genotyping may be ordered to facilitate interpretation of future testing results.

DARA also interferes with other laboratory testing, including protein electrophoresis (abnormal band patterns) and flow cytometry (identification of plasma cells).

FDA Warning Regarding Blood Lead Level Testing

According to CDC, at least 4 million households have children living in them, who are exposed to high levels of lead. Infants and young children are particularly prone to lead poisoning due to possible increased GI absorption compared to adults which adversely impacts developing brain and nervous system. Lead poisoning in young children typically results from drinking water from corroded plumbing, and/or inhaling/ingesting dust from deteriorating lead-based paint. Lead can also be transmitted through breast milk. Scientifically, there is no accepted safe blood lead level.

In contrast, adults may be exposed to lead through jobs such as paint manufacturing, and construction and police officers exposed to materials containing lead. A pregnant or lactating mother poses a special problem of not only causing health problems for the mother but also to the developing infant. U.S. Occupational Safety and Health Administration outlines lead monitoring procedures including frequency of blood testing for exposed workers.

Last fall, the FDA issued a warning regarding measurement of blood lead levels using Magellan LeadCare test system. The LeadCare system is based on electrochemistry, where the potential applied by the instrument allows lead present in the whole blood to accumulate near the measuring sensor. The lead levels are reported in ug/dL of blood. Subsequently, the manufacturers issued a mandate to include a 4-hour incubation step before specimen analysis to mitigate the potential interference believed to originate from rubber caps of EDTA vacutainer collections tubes..

Recently, the FDA escalated the warning to discontinue the use of Magellan LeadCare test system for determination of blood levels on venous blood due to persistent concerns of falsely low results. Due to lack of evidence, capillary blood

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samples are considered appropriate and can be analyzed using Magellan LeadCare system.

Following the FDA recommendations, Saint Luke's Hospital is sending all venous specimens requiring lead level determination to a reference laboratory that uses alternate methods including mass spectrometry or atomic absorption. Saint Luke's Hospital will continue to analyze capillary blood samples in-house.

Urine Toxicology Screening

Effective in May 2017, Saint Luke's Health System Laboratories will institute a new urine toxicology screen test, Alere iScreen. The new assay includes all previous drugs and additionally provides results for methadone and allows differentiation of amphetamine from methamphetamine. Of note, oxycodone, previously available only as a separate order, is now included in the screen as well, at a comparable detection level.

Screening assays for drug of abuse are designed to detect urine drug levels above a predetermined cutoff concentration. The threshold concentration above which each drug class will be detected is summarized in the following table.

Drug Class	Threshold
Amphetamines	1000 ng/mL
Methamphetamines	500 ng/mL
Barbiturates	300 ng/mL
Benzodiazepines	300 ng/mL
Cocaine	300 ng/mL
Methadone	300 ng/mL
Opiates	300 ng/mL
Phencyclidine	25 ng/mL
Oxycodone	100 ng/mL
THC (Cannabinoids)	50 ng/mL
TCA (Tricyclic antidepressants)	1000 ng/mL

Sample requirement is 40 ml random urine in a plastic urine container. Drug confirmations are not performed on Emergency Department patients unless specifically requested by the physician. For all other patients drug confirmations will be performed at a referral laboratory for all positive drugs except tricyclic antidepressants.

Haemophilus Influenzae in Review

Saint Luke's Microbiology has isolated Haemophilus influenzae from sterile body site samples of several patients in the last few weeks. H. influenzae is a small non-motile gram negative bacillus most commonly found in the upper respiratory tract. Its shape on Gram stain can vary from coccobacilli to filamentous rods. The name Haemophilus translates as 'blood-loving' and is derived from the organism's growth requirement for both hemin and NAD (also known as X and V factor) that are acquired from red blood cells. Colonization of the upper respiratory tract with H. influenzae occurs in early childhood.

Pathogenic Haemophilus influenzae strains are frequently mucoid & encapsulated, and can be typed as one of six serotypes (a-f) based on the polysaccharide capsule. Serious invasive infections in young children due to serotype b have been largely eliminated due to use of conjugate Hib vaccine. Other strains of H. influenzae, termed 'nontypeable' due to lack of a polysaccharide capsule, have emerged as major pathogens in recent years. Unlike type b strains, which enter the blood stream, nontypeable strains cause disease by local invasion of mucosal surfaces. Hence, these strains are most frequently associated with conjunctivitis, otitis media, exacerbations of COPD, community-acquired pneumonia and sinusitis. Neonatal and maternal sepsis occur less commonly but have an overall mortality rate of 50%. The causative nontypeable strain of these infections (biotype IV) is also associated with tubo-ovarian abscess and salpingitis. Nontypeable H. flu strains are less frequently isolated in other invasive adult infections including bacteremia and meningitis. Haemophilus influenzae isolated in Microbiology recently have represented a variety of encapsulated & nontypeable strains.

Overall, approximately 30% of Haemophilus influenzae strains produce beta-lactamase, so physicians treating patients empirically should consider using anti-microbials which maintain activity in the presence of this enzyme. All H. influenzae reported by Microbiology include a beta-lactamase result, and strains causing invasive infections have full susceptibility testing performed.

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