Q&A column

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.

Q. Can you provide a current reference for the various modifications of transfused red blood cells—for example, irradiation and white cell depletion—and their indications?

A. May 2020—Transfusion-associated graft-versus-host disease (TA-GVHD) is an uncommon complication of transfusing cellular products, including red blood cells, platelets, and granulocytes, and it has a high mortality rate. In cases of TA-GVHD, the recipient's immune system cannot destroy the viable lymphocytes that are present in donor blood because the donor and recipient share a common human leukocyte antigen (HLA) haplotype. This is why receiving blood from a first-degree relative puts the recipient at risk for developing TA-GVHD. Immunosuppressed patients are also at risk. The only way to prevent TA-GVHD is by irradiating cellular blood products prior to transfusion. The data on at-risk groups largely come from surveys conducted by the AABB and CAP. The U.S. government does not provide national guidelines on the use of irradiated blood components. In some institutions, universal irradiation of all cellular blood products is performed to make it easier to mitigate the risk of TA-GVHD for at-risk patients. An article by Pritchard AE, et al., provides a more complete list of patients who would be considered at risk for TA-GVHD and indicates where there is consensus on the medical indications for irradiation.[1]

Blood products in which white blood cells are removed through filtration are referred to as leukoreduced. Leukoreduction is performed on red blood cell and platelet products. It may be performed shortly after donation at the blood center, referred to as prestorage leukoreduction, or at the bedside during transfusion of red blood cells or platelets. Leukoreduced blood components are known to prevent febrile transfusion reactions, HLA alloimmunization, and transfusion-transmitted cytomegalovirus (TT-CMV). Among the potential benefits of prestorage leukoreduction are prevention of transfusion-associated immunomodulation, postoperative infection, and transmission of other bacterial and viral infections, such as human T-lymphotropic virus, variant Creutzfeldt-Jakob disease, and leishmaniasis. However, these benefits are not as well substantiated in the literature. Preference is often given to prestorage leukoreduced blood products over bedside-filtered leukoreduced blood products due to improved quality control conditions and because stored white blood cells release cytokines, which may contribute to febrile and cytokine-related transfusion reactions. The main controversy with leukoreduced blood products is whether it is necessary to give CMV seronegative blood in addition to leukoreduced blood. Prestorage leukoreduced blood is considered "CMV safe" by current standards. However, there is a lack of high-quality data for definitive practice guidelines, although a supplemental questionnaire accompanying a 2015 CAP transfusion medicine Survey suggests that leukoreduction is the primary TT-CMV mitigation strategy at CAP member institutions.[2]

1. Pritchard AE, Shaz BH. Survey of irradiation practice for the prevention of transfusion-associated graft-versus-host disease. Arch Pathol Lab Med. 2016;140(10):1092–1097.
2. Weisberg SP, Staley EM, Williams LA 3rd, et al. Survey on transfusion-transmitted cytomegalovirus and cytomegalovirus disease mitigation.

Arch Pathol Lab Med. 2017;141(12):1705–1711.

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Q. Please address allowable error relative to the immature platelet fraction test. Is the analytical measurement range applicable to the IPF?

A. Allowable error and analytical measurement range (AMR) for the immature platelet fraction (IPF) are neither defined by the manufacturer nor determined by our laboratory at this time. Allowable error and AMR may differ based on the clinical scenario, so additional experience with IPF is likely needed before they may be defined.

IPF is a relatively new parameter on modern complete blood count analyzers. Analogous to the immature granulocyte fraction for white blood cells and reticulocyte count and reticulocyte hemoglobin content for red blood cells, IPF helps determine the causes of thrombocytopenia. Elevated IPF is highly suggestive of peripheral destruction and sequestration of platelets (immune thrombocytopenia purpura), and nonelevated IPF is compatible with decreased megakaryopoiesis and other impairment of bone marrow platelet production (post-chemotherapy and post-stem cell transplantation).

To calculate the IPF, platelet size, determined by light forward scatter properties, is plotted versus platelet nucleic acid content (RNA), measured by proprietary platelet staining plus fluorescence. Large size and high RNA content are features of platelet immaturity and show a proportional (linear) relationship. The platelets with the highest three percent fluorescence content are identified, and mature and immature platelets are distinguished through complex flow cytometric and computer-based methods to determine the IPF, which is then expressed as a percent of platelets.

Importantly, though, as with any assay, the number of measurements informs the coefficient of variation. The CV of the automated IPF is decreased in the setting of marked thrombocytopenia.

Briggs C, Kunka S, Hart D, Oguni S, Machin SJ. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia. *Br J Haematol.* 2004;126(1):93–99.

Immature platelets—clinical use: differential diagnosis of thrombocytopenia. Sysmex Europe white paper. www.sysmex-europe.com/fileadmin/media/f100/White_Paper/Haematology/Sysmex_White_Paper_Differential_diagnosis_of_thrombocytopenia.pdf. Published 2017.

Kickler TS, Oguni S, Borowitz MJ. A clinical evaluation of high fluorescent platelet fraction percentage in thrombocytopenia. *Am J Clin Pathol.* 2006;125(2):282–287.

The value-driven laboratory: the role of the immature platelet fraction (IPF) in the differential diagnosis of thrombocytopenia. Sysmex America white paper. www.sysmex.com/us/en/Brochures/The%20Value%20Driven%20Laboratory_IPF_Final.pdf. Published 2014.

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Q. What is the normal random plasma glucose value?

A. Because blood glucose concentrations are in a constant dynamic flux to maintain physiologic homeostasis, there is no “normal” random blood glucose range or value. This concept also applies to the pathophysiologic states of diabetes or prediabetes, in which the overall average glucose concentrations are higher. This is explained in the American Diabetes Association’s “Standards of Medical Care in Diabetes” (*Diabetes Care.* 2019;42[suppl 1]:S13–S28) and guidelines from the World Health Organization.

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