



Five Things Physicians and Patients Should Question

1

Don't repeat HbA1c testing in stable patients within 3 months of a previous result.

The lifespan of a HbA1c is approximately 90–120 days, and the full effects of a patient's change in behavior, diet, or newly adjusted medications will not be fully appreciated until all previous HbA1c in circulation are replaced (~90 days). Therefore, testing at time intervals earlier than 3 months may not allow enough time to pass to reach the expected target by the clinician. Testing at 6-month intervals may be considered when glycemic targets are consistently achieved.

2

Don't perform an extensive work-up in otherwise healthy neutropenic patients of African or Middle Eastern ancestry prior to Duffy-null phenotype testing.

Individuals, typically of African or Middle Eastern ancestry, may present with an ANC <1500 cells/ μ L with no signs of recurrent infections, immunocompromise, or malignancy. Frequently, the lower ANC is a normal variant associated with the red blood cell Duffy-null phenotype [Fy(a-b-)] that should be confirmed by Blood Bank phenotyping. Asymptomatic Duffy-null individuals do not require additional testing and should not be denied clinical trial participation or prescription of certain medications (including chemotherapy) based on ANC alone.

3

Don't order ANA and ENA unless the patient is suspected to have a connective tissue disease.

Testing for anti-nuclear antibody (ANA) and extractable nuclear antigen (ENA) should be avoided in the investigation of widespread pain or fatigue alone. Instead, testing should only be performed in patients suspected to have a diagnosis of a connective tissue disease (e.g., lupus, rheumatoid arthritis). ANA positivity can be as high as 20% in patients with non-rheumatic conditions and healthy individuals. For this reason, proper pre-test probability is important, and false positive results may lead to further unnecessary testing. Repeat testing is also not recommended unless the clinical picture changes significantly.

4

Do not measure the INR in patients who are taking an anti-Xa inhibitor.

Anti-Xa inhibitors (e.g., rivaroxaban [Xarelto[®]], apixaban [Eliquis[®]]) are commonly prescribed anticoagulants. Their indications include (but are not limited to): reducing the risk of stroke or systemic embolism in patients with nonvalvular atrial fibrillation; treating deep venous thromboembolism (DVT) and pulmonary embolism; and DVT prophylaxis. Bleeding is a common complication from anti-Xa inhibitor use that may require reversal with andexanet alfa, prothrombin complex concentrate, or plasma. While the INR is commonly used to measure the anticoagulation effect of vitamin K antagonists (e.g., warfarin), it is insensitive for anti-Xa inhibitors, potentially leading to inappropriate patient management decisions.

5

Don't employ a specific direct oral anticoagulant [DOAC] reversal agent without identifying the DOAC and estimating its plasma concentration.

In 2015, the US FDA approved idarucizumab as a reversal immunoglobulin specific for the direct thrombin inhibitor dabigatran. In 2018, andexanet alfa was approved as a factor Xa mimetic reversal agent for the direct anti-Xa oral anticoagulants rivaroxaban and apixaban.¹ Clinicians employ reversal agents to control major bleeding associated with presumed DOAC overdose when compression, blood product support, and antifibrinolytics are ineffective, often in preparation for an invasive procedure.² A reversal agent should be employed only when the clinician can identify the DOAC using, for instance, an anti-Xa assay* or dilute thrombin time [DTT] assay*, establish the likelihood that it is the bleeding source, and estimate its dose or plasma concentration.³ In addition to their documented risk of ischemic complications, reversal agents are maintained in collaborative inventory systems with controlled access, owing to scarcity and costs.⁴ Andexanet alfa, for instance, costs \$27,500 for a low dose regimen and \$49,500 for a high dose, and CMS reimbursement is limited to 50% of the low dose investment.⁵ A rapid urinary "dipstick" detection device* is a viable point-of-care alternative to the anti-Xa or DTT assays as the stick distinguishes dabigatran from the anti-Xa inhibitors.⁶ For those facilities that do not offer a rapid turnaround DOAC assay specific to the agent, clinicians must establish the DOAC identity and time of the most recent dosage by history before establishing treatment.⁷ Healthcare systems shall collaborate with the laboratory medicine service to develop strategies that ensure efficacy and stewardship of reversal agents.⁸

*Off-label or research use only.

How This List Was Created (1–4)

The American Society for Clinical Pathology (ASCP) list of recommendations was developed under the leadership of the ASCP Effective Test Utilization Steering Committee. This committee is chaired by an ASCP Past President and is comprised of subject matter and test utilization experts across the fields of pathology and laboratory medicine. The committee considered a list of possible recommendations compiled as the result of a survey administered to Society members serving on ASCP's many commissions, committees and councils. In addition, an announcement was made to ASCP's Advisory Board seeking suggestions for possible recommendations to promote member involvement. The laboratory tests targeted in our recommendations were selected because they are tests that are performed frequently; there is evidence that the test either offers no benefit or is harmful; use of the test is costly and it does not provide higher quality care; and eliminating it or changing to another test is within the control of the clinician. Implementation of these recommendations will result in higher quality care, lower costs and a more effective use of our laboratory resources and personnel.

How This List Was Created (5)

This recommendation was developed under the leadership of ASCLS's *Choosing Wisely* Committee and the ASCLS Board of Directors. The Committee examined numerous options based on evidence available. Subject matter experts from the ASCLS Scientific Assemblies reviewed, edited, and recommended approval of this recommendation, which was subsequently reviewed and approved by the ASCLS Board of Directors.

Sources

1. American Diabetes Association. Standards of medical care in diabetes—2007. *Diabetes Care*. 2007 Jan;30 Suppl 1:S4-S41. doi: 10.2337/dc07-S004. PMID: 17192377.
 2. Driskell OJ, Holland D, Waldron JL, Ford C, Scargill JJ, Heald A, Tran M, Hanna FW, Jones PW, Pemberton RJ, Fryer AA. Reduced testing frequency for glycosylated hemoglobin, HbA1c, is associated with deteriorating diabetes control. *Diabetes Care*. 2014 Oct;37(10):2731-7. doi: 10.2337/dc14-0297. PMID: 25249670.
 3. McCarter RJ, Hempte JM, Chalew SA. Mean blood glucose and biological variation have greater influence on HbA1c levels than glucose instability: an analysis of data from the Diabetes Control and Complications Trial. *Diabetes Care*. 2006 Feb;29(2):352-5. doi: 10.2337/diacare.29.02.06.dc05-1594. PMID: 16443886.
1. Merz LE, Achebe M. When non-Whiteness becomes a condition. *Blood*. 2021. 137(1):13-15.
1. Tozzoli R, Bizzaro N, Tonutti E, Villalta D, Bassetti D, Manoni F, Piazza A, Pradella M, Rizzotti P; Italian Society of Laboratory Medicine Study Group on the Diagnosis of Autoimmune Diseases. Guidelines for the laboratory use of autoantibody tests in the diagnosis and monitoring of autoimmune rheumatic diseases. *Am J Clin Pathol*. 2002 Feb;117(2):316-24. doi: 10.1309/Y5VF-C3DM-L8XV-U053. PMID: 11863229.
 2. Solomon DH, Kavanaugh AJ, Schur PH; American College of Rheumatology Ad Hoc Committee on Immunologic Testing Guidelines. Evidence-based guidelines for the use of immunologic tests: antinuclear antibody testing. *Arthritis Rheum*. 2002 Aug;47(4):434-44. doi: 10.1002/art.10561. PMID: 12209492.
 3. Ferrari R. Evaluation of the Canadian Rheumatology Association Choosing Wisely recommendation concerning anti-nuclear antibody (ANA) testing. *Clin Rheumatol*. 2015 Sep;34(9):1551-6. doi: 10.1007/s10067-015-2985-z. Epub 2015 Jun 2. PMID: 26032433.
1. Gosselin RC, Adcock DM, Bates SM, Douxfils J, Favaloro EJ, et al. International Council for Standardization in Haematology (ICSH) Recommendations for Laboratory Measurement of Direct Oral Anticoagulants. *Thromb Haemost*. 2018. 118(3):437-450. DOI: 10.1055/s-0038-1627480
 2. Milling Jr. TJ, Frontera JA. Exploring Indications for the Use of Direct Oral Anticoagulants and the Associated Risks of Major Bleeding. *Am J Manag Care*. 2017. 23(4 Suppl):S67- S80.
 3. Cuker A, Burnett A, Triller D, Crowther M, Ansell J, et al. Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum. *Am J Hematol*. 2019. 94(6):697-709. DOI: 10.1002/ajh.25475
1. Milling TJ, Pollack CV. A review of guidelines on anticoagulation reversal across different clinical scenarios—is there a general consensus? *Am J Emergency Med* 2020; 38: 1890–1903.
 2. Donnelly SJ, Crowther M, Eikelboom JW, et al. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. *NEJM* 2019; 380: 1326–35.
 3. Sobolewski KA, Brophy A, Choi S, Opsha Y. Real-world observational review of andexanet alfa prescribing and utilization outcomes at a community teaching hospital. *Crit Care Explorations*. 2021; 3: e0356. Published online 2021 Apr 2. doi: 10.1097/CCE.0000000000000356.
 4. Nederpelt CJ, Naar L, Sylvester KQ, et al. Evaluation of oral factor Xa inhibitor-associated extracranial bleeding reversal with andexanet alfa. *J Thromb Haemost*. 2020;18:2532–41.
 5. Cuker A, Burnett A, Triller D, et al. Reversal of direct oral anticoagulants. Guidance from the Anticoagulation Forum. *Am J Hematol* 2019; 94: 697–709.
 6. Harenberg J, Du S, Wehling M, et al. Measurement of dabigatran, rivaroxaban and apixaban in samples of plasma, serum and urine, under real life conditions. An international study. *Clin Chem Lab Med* 2016; 54: 275–83.
 7. Bhatt SH. Implementing effective protocols when using direct oral anticoagulant reversal agents: a review of updated guidelines and clinical data. *Pharmacy Time Continuing Education* 2020: 68–85.
 8. Nederpelt CJ, Naar L, Sylvester KW, et al. Evaluation of oral factor Xa inhibitor-association extracranial bleeding reversal with andexanet alfa. *J Thromb Haemost* 2020; 18: 2532–41.

About the ABIM Foundation

The mission of the ABIM Foundation is to advance medical professionalism to improve the health care system. We achieve this by collaborating with physicians and physician leaders, medical trainees, health care delivery systems, payers, policymakers, consumer organizations and patients to foster a shared understanding of professionalism and how they can adopt the tenets of professionalism in practice.

To learn more about the ABIM Foundation, visit www.abimfoundation.org.



About the American Society for Clinical Pathology

Founded in 1922 in Chicago, ASCP is the world's largest professional membership organization for pathologists and laboratory professionals. ASCP provides excellence in education, certification, and advocacy on behalf of patients, anatomic and clinical pathologists, and medical laboratory professionals.

To learn more about ASCP, visit www.ascp.org.



STRONGERTOGETHER

About the American Society for Clinical Laboratory Science

The American Society for Clinical Laboratory Science (ASCLS) and its 9,000 clinical laboratory professional, student, and educator members in more than 50 state and regional constituent societies work to advance the expertise of clinical laboratory professionals who, as integral members of interprofessional healthcare teams, deliver quality, consumer-focused, outcomes-oriented clinical laboratory services through all phases of the testing process to prevent, diagnose, monitor and treat disease. The Society promotes high standards of practice by holding the profession accountable to a Code of Ethics, through dissemination of knowledge at educational programs and through publications; maintains a supportive community to advocate on behalf of current and future laboratory professionals; and provides laboratory professionals a voice to legislators and regulators through collective, grassroots efforts.

To learn more about ASCLS, visit <https://ascls.org/>



ASCLS
The American Society for
Clinical Laboratory Science