

# On-Demand Clinical News

## Anticoagulation at End of Life

Joelle K. Potts, PharmD, CGP

Coagulation is the process by which a blood clot forms, and involves both platelets and coagulation factors that are part of the coagulation (or clotting) cascade. Although certainly we have each experienced the process of normal clot formation after cell wall damage due to a cut or injury, pathologic blood clots can sometimes form in intact vessels in the absence of trauma or injury, as a venous thromboembolism (VTE), deep vein thrombosis (DVT), pulmonary embolism (PE), or stroke. Virchow's Triad describes three situations that can increase one's risk of forming a pathologic blood clot, some of which are relatively common in the hospice population: hypercoagulable state (e.g. malignancy, sepsis), circulatory stasis (e.g. atrial fibrillation, left ventricular dysfunction, immobility), and vascular wall injury (e.g. heart valve disease or replacement, atherosclerosis, venepuncture).<sup>1</sup>

Ultimately,  
when to stop or  
switch an anticoagulant  
or antiplatelet therapy is  
a very patient-specific  
decision, especially  
in the hospice  
population.



There are a number of medications commonly used to treat and/or prevent pathologic clot formation, and they typically fall under two general categories: anticoagulant medications and antiplatelet medications. Anticoagulant medications typically work at various sites in the clotting cascade, while antiplatelet medications primarily affect the platelets.<sup>2</sup>

Continued on page 2

## Asymptomatic Bacteriuria

Kristin Braschler, PharmD, BCPS

How and when to manage asymptomatic bacteriuria (ASBU) can be unclear, as well as when to screen. As defined by the Infectious Diseases Society of America (IDSA), ASBU is urine containing  $\geq 10^5$  colony-forming units (cfu)/mL, that has been appropriately collected and transported from a patient without signs or symptoms of a urinary tract infection (UTI). Further, diagnosis is made in non-catheterized, non-pregnant women when the same bacterial strain is isolated on two consecutive specimens.<sup>1</sup> Diagnosis is made in men, in pregnant women, and in catheterized men/women when a bacterial strain is isolated from a single voided specimen.<sup>1,2</sup>

Absent in ASBU, the signs and symptoms of a UTI are typically easily identified by clinicians, and include flank pain, suprapubic pain, urgency, polyuria, incontinence, dysuria, hematuria and/or fever. In cases of catheterized patients, nonspecific symptoms such as cognitive/functional impairment and/or fever may be the only indications of infection.<sup>1</sup> In spinal cord injury patients, infection may be suspected if cloudy/malodorous urine, pyuria, or other nonspecific symptoms like increased spasticity, dysreflexia, or fever are present.<sup>1</sup> However, in the absence of these signs and symptoms in most other patients, cloudy or foul-smelling urine, the presence of white blood cells in the urine, mental status changes, and/or falls alone are NOT automatically an indication for treatment.<sup>1,3</sup>

ASBU has not demonstrated to be associated with death or other adverse events in elderly men.<sup>1</sup> In long term care residents, treatment of ASBU is associated with development of adverse events and organism resistance.<sup>1</sup> In other populations,<sup>1,4</sup> treatment of ASBU increased risk of recurrent UTIs and adverse effects, but did not reduce the risk of symptomatic infection or hospitalization.

Continued on page 4

Anticoagulant Medications	
Vitamin K Antagonist	PO: warfarin (Coumadin®, Jantoven®)
Direct Thrombin Inhibitors	PO: dabigatran etexilate (Pradaxa®); INJ: bivalirudin (Angiomax®), desirudin (Iprivask®), argatroban
Factor Xa Inhibitors	PO: apixaban (Eliquis®), rivaroxaban (Xarelto®), edoxaban (Savaysa®); INJ fondaparinux (Arixtra®)
Heparin	
Low Molecular Weight Heparins	INJ: enoxaparin (Lovenox®), dalteparin (Fragmin®), tinzaparin (Innohep®), nadroparin (Fraxiparine®, Fraxiparine Forte®)
Antithrombin	INJ (brand names): Atryn® (recombinant derived), Thrombate III® (plasma derived)

Antiplatelet Medications	
Miscellaneous	PO: dipyridamole (Persantine®), aspirin (immediate release)/dipyridamole (extended release) (Aggrenox®)
Salicylate/NSAID	PO: aspirin
Thienopyridines	PO: clopidogrel (Plavix®), prasugrel (Effient®)
Phosphodiesterase-3 Enzyme Inhibitors	PO: cilostazol (Pletal®), anagrelide (Agylin®)
Cyclopentyltriazolopyrimidine	PO: ticagrelor (Brilinta®)
Glycoprotein IIb/IIIa Inhibitors	INJ: abciximab (ReoPro®), eptifibatide (Integrilin®), tirofiban (Aggrastat®)
Protease-Activated Receptor-1 (PAR-1) Antagonist	PO: vorapaxar (Zontivity®)

The questions of when to discontinue anticoagulant and antiplatelet medications at end of life in a particular patient, or when it may be safe and appropriate to switch to a preferred/lower-cost option, can be challenging ones. Although these questions have not been studied extensively in the hospice population, a few articles discuss issues related to these decisions.

Robin R. Hill, et al. compared patients taking warfarin who were receiving hospice/palliative care services to those taking warfarin who were not on hospice/palliative care.<sup>3</sup> They found that hospice patients typically required more frequent INR monitoring, and were more likely to be above and below their target INR range, but their risks and incidences of warfarin-related adverse events were similar to those of the non-hospice population.

In their Center to Advance Palliative Care (CAPC) Fast Fact #278,<sup>4</sup> Janet Abraham, et al. discuss the use of warfarin in palliative care, and suggest that good times to stop warfarin include the following situations:

- If a patient insists on being ambulatory but is wobbly enough to fall – the risk of an intracranial hemorrhage is likely greater than the benefit of preventing an embolic stroke;
- When a patient’s dietary intake drops 50% or more from his/her usual balanced diet, if intake changes to favorites-only (e.g. ice cream) rather than vitamin K-rich foods, or when eating is highly erratic – the risk of bleeding escalates significantly if warfarin is continued;
- If a patient develops liver failure – as liver failure typically decreases the synthesis of coagulation factors;
- If a patient does not agree to checking INRs; or
- When there is frank bleeding.

According to the low molecular weight heparin monograph by Robert Twycross and Andrew Wilcock, indefinite anticoagulation and/or thromboprophylaxis with low molecular weight heparin is typically discontinued only if contraindications develop and/or when patients have a poor performance status in their last few weeks of life (i.e. when the patient reaches the stage when symptom relief alone is appropriate, including if a new VTE episode were to occur).<sup>5</sup>

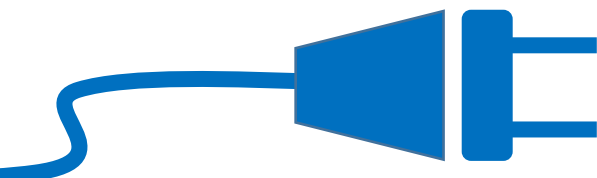
Jeffrey L. Spiess provides a thorough review of the limited studies available that evaluated the risks and benefits of discontinuing warfarin in patients with VTE and nonvalvular atrial fibrillation (afib), although he notes that most studies exclude patients with conditions often found at end of life.<sup>6</sup> He found that the annual recurrence rate of VTE was 3.2% to 10.9% in patients whose anticoagulation was discontinued after at least 3 months of therapy. For patients with nonvalvular afib, he recommends using the CHADS<sub>2</sub> Score, which estimates the stroke risk for patients with afib by assigning points for various risk factors (CHF, HTN, diabetes, age 75 or older, and history of stroke or TIA symptoms); the higher a patient's points, the higher their theoretical risk of stroke. The CHA<sub>2</sub>DS<sub>2</sub>-VASc Score includes additional risk factors in this calculation, and therefore may provide better risk stratification.<sup>7</sup>

Spiess also describes another tool that can be used to evaluate the risk vs. benefit of discontinuing warfarin at end of life: the Bleeding Risk Index.<sup>8</sup> It also assigns points for various risk factors (age 65 or older, prior stroke, prior GI bleed, as well as recent MI, hematocrit less than 30%, creatinine greater than 1.5mg/dL, or diabetes); again, the higher a patient's points, the higher his/her theoretical risk of having a significant bleeding event while taking warfarin. However, it is important to note that the Bleeding Risk Index was developed to evaluate the risks of bleeding in outpatients being started on warfarin, rather than when it's best to stop warfarin, and is not hospice-specific. In general, and based on these considerations, Spiess proposes that decisions on whether to use or continue warfarin in palliative care and hospice patients should be based on whether they have a high risk of rethrombosis or embolism, and whether they have a high bleeding risk.

Ultimately, when to stop or switch an anticoagulant or antiplatelet therapy is a very patient-specific decision, especially in the hospice population. These decisions involving anticoagulation at end of life should involve a case-by-case evaluation of the patient's history and risks vs. benefits, with consideration of goals of therapy (e.g. will it improve comfort or palliate symptoms), patient prognosis, and patient preferences.

#### References:

1. Virchow's Triad: <http://www.dvtanswers.com/Images/virchow-triad%20-diagram.jpg> [accessed 4/11/2015]
2. Pharmacologic categories of medications: Drug monographs. Lexi-Drugs [database online]. Lexi-Comp, Inc. [accessed March–July, 2015]
3. Hill RR, Martinez KD, Delate T, Witt DM. A descriptive evaluation of warfarin use in patients receiving hospice or palliative care services. *J Thromb Thrombolysis*. 27, 2009. 334-339.
4. Abraham J, von Gunten CF, Weissman DE. Fast Fact #278: Warfarin and Palliative Care. Center to Advance Palliative Care. [www.capc.org/fast-facts/278-warfarin-and-palliative-care/](http://www.capc.org/fast-facts/278-warfarin-and-palliative-care/) [accessed 3/29/2015]
5. Twycross R, Wilcock A, Editors-in-Chief. *Hospice and Palliative Care Formulary USA*, Second Edition. palliatedrugs.com Ltd., Nottingham, UK. 2008. Low molecular weight heparin (LMWH); 56-65.
6. Spiess JL. Can I stop the warfarin? A review of the risks and benefits of discontinuing anticoagulation. *Journal of Palliative Medicine*. 12(1), 2009. 83-87.
7. CHADS<sub>2</sub> Score Calculator, with a link to CHA<sub>2</sub>DS<sub>2</sub>-VASc Score calculator, available at: <http://www.mdcalc.com/chads2-score-for-atrial-fibrillation-stroke-risk/> [accessed 5/10/2015]
8. Bleeding Risk Index for Warfarin Therapy Calculator, available at: <http://reference.medscape.com/calculator/bleeding-risk-index-warfarin> [accessed 5/24/2015]



**Connect with us on Facebook & Twitter!**

**(@PHCpharmacy)**

Don't miss important updates!

Join over 200 followers and keep up with PHC's Lunch & Learn, Conferences, Contests, Clinical News, & more.

Patients with indwelling Foley catheters very commonly present with bacteriuria. Treating ASBU (or even funguria) in this population usually does not provide benefit, and can encourage organism resistance.<sup>1</sup> If a patient has had a urinary catheter indwelling for more than two weeks and has symptoms suspicious for a UTI, some experts opt for a catheter change before sample collection,<sup>5</sup> as the risk of bacteremia developing from a urinary catheter change is considered low, and IDSA guidelines do not currently recommend prophylactic antibiotics for this procedure.<sup>1</sup>

Thus, in most patient populations, including those with indwelling urinary catheters, demonstration of benefits from treatment of ASBU is lacking.

However, there are certain populations for which treatment of ASBU has demonstrated benefit. In pregnant women, treatment of ASBU is recommended and appears to reduce risks of pyelonephritis, premature birth, and low birth weight.<sup>1</sup> One study suggests that in women with ASBU continuing 48 hours after catheter removal, treatment reduces progression to symptomatic infection.<sup>1</sup> Also, treatment of ASBU is recommended in patients undergoing certain urinary tract procedures that can injure mucosa, as ASBU in these cases can lead to sepsis.<sup>1</sup> Specifically, antibiotics are recommended in men with indwelling urinary catheters after a TURP procedure, until catheter removal.<sup>1</sup>

Screening for ASBU (i.e. a urine culture) is recommended for patients that are not typically encountered in hospice: pregnant women and patients undergoing a urinary procedure that may cause mucosal bleeding.<sup>1</sup>

#### Conclusion:

Screening for and treating ASBU lacks benefit for most patients. In elderly patients with new-onset or increased confusion and bacteriuria, consider other potentiators such as diuretics, dehydration, anticholinergics or other causes. Patient assessment is encouraged over reaching in reaction for antibiotics that may often be unnecessary, potentially harmful, and add to costs and pill burden.

#### References

1. Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005;40:643-54.
2. Allen VM, Yudin MH, Bouchard C, et al. Management of group B streptococcal bacteriuria in pregnancy. *J Obstet Gynaecol Can* 2012;34:482-6.
3. Rowe T, Towle V, Van Ness PH, Juthani-Mehta M. Lack of positive association between falls and bacteriuria plus pyuria in older nursing home residents. *J Am Geriatr Soc* 2013;61:653-4.
4. Cai T, Mazzoli S, Mondaini N, et al. The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat? *Clin Infect Dis* 2012;55:771-7.
5. Association for Professionals in Infection Control and Epidemiology. APIC implementation guide. Guide to preventing catheter-associated urinary tract infections. April 2014. [http://apic.org/Resource\\_/EliminationGuideForm/Off6ae59-0a3a-4640-97b5-eee38b8bed5b/File/CAUTI\\_06.pdf](http://apic.org/Resource_/EliminationGuideForm/Off6ae59-0a3a-4640-97b5-eee38b8bed5b/File/CAUTI_06.pdf). [accessed 3/9/2015]

## Upcoming Lunch & Learn Presentations

### **September: "Antipsychotics for Dementia: Under Control or Over Prescribed?"**

Tuesday, September 8, 2015 at 3:00pm ET; Wednesday, September 9, 2015 at 12:00pm ET

### **October: Topic to be determined**

Tuesday, October 13, 2015 at 3:00pm ET; Wednesday, October 14, 2015 at 12:00pm ET

ProCare HospiceCare welcomes all suggestions and comments. If you would like additional information about our services, have ideas for articles, or wish to submit a comment, email us at [resources@procarerx.com](mailto:resources@procarerx.com).

*The information provided within this newsletter is proprietary to ProCare Rx. Any reprint or reuse of this information must be approved via written consent.*

Copyright 2015, ProCare Rx



ProCare **HospiceCare**

1267 Professional Pkwy., Gainesville, GA 30507  
800.377.1037

Executive Editor: Dr. Meri Madison, PharmD, CGP