

# **ASH Clinical Practice Guidelines** on Venous Thromboembolism (VTE):

## What You Should Know

The American Society of Hematology (ASH) has long recognized the need for a comprehensive set of guidelines for hematologists and other clinicians on venous thromboembolism (VTE), a common and serious blood clotting condition that includes both deep-vein thrombosis (DVT) and pulmonary embolism (PE).

In partnership with the McMaster University GRADE Centre, a world leader in guideline development and an authority on thrombosis, ASH brought together more than 100 experts including hematologists, clinicians, specialists, and patient representatives to synthesize the research and develop clinical practice guidelines for VTE.



# Prophylaxis for Hospitalized and Non-Hospitalized Medical Patients



What it covers



Why it matters



Who it affects



What are the highlights

- · Who should receive an intervention and what that intervention should be
- Interventions considered include blood thinning medications of different types and mechanical compression (e.g., pneumatic compression devices or graduated compression stockings).
- Medical inpatients, long-term care residents, persons with minor injuries, and longdistance travelers are at increased risk of VTE, which can be fatal (20-25% of all VTE instances occur in these groups).
- It is important to ensure that at-risk patients receive the appropriate measures to prevent VTE without excess bleeding side effects.
- The guidelines recommend the best approaches for preventing VTE in these populations while minimizing unnecessary or over-treatment.
- Medical inpatients (including those in intensive care units), long-term care residents, persons with minor injuries, and long-distance travelers (>4 hours by air)
- · Health care providers working in hospitals
- For patients who are hospitalized, risk assessment for VTE and bleeding help inform a
  decision on effective prophylactic measures.
- In medical inpatients at high bleeding risk who require prophylaxis, mechanical prophylaxis is preferred over blood-thinning medications.
- In medical inpatients at high VTE risk but acceptable bleeding risk, blood thinning medication is preferred over mechanical prophylaxis.
- In medical inpatients, when medication is used to prevent VTE, low-molecular-weight heparin is preferred over unfractionated heparin because it is only administered once a day and has fewer complications.
- In medical inpatients, when a medication is used to prevent VTE, low-molecular-weight heparin during the hospital stay is preferred over a direct oral anticoagulant administered in hospital or after discharge.
- The use of combined modalities in medical inpatients (e.g., compression devices plus a blood thinner) is not necessary.
- Long-distance air travelers who do not have an elevated risk of thrombosis do not need
  to wear compression socks or take a blood thinner like aspirin to prevent thrombosis.
  Air travelers at substantially increased risk may benefit from graduated compression
  stockings or low-molecular-weight heparin.

### Total number of panel recommendations: 21

#### REFERENCE

Schünemann, H. J., Cushman, M., Burnett, A. E., Kahn, S. R., Beyer-Westendorf, J., Spencer, F. A., Rezende, S. M., Zakai, N. A., Bauer, K. A., Dentali, F., Lansing, J., Balduzzi, S., Darzi, A., Morgano, G. P., Neumann, I., Nieuwlaat, R., Yepes-Nuñez, J. J., Zhang, Y., & Wiercioch, W. <u>American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. Blood Advances. 2018; 2:3198-3225</u>



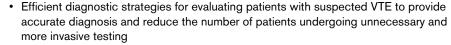
## **Diagnosis of VTE**



What it covers



Why it matters



- Accurate diagnosis of VTE is important due to the morbidity and mortality associated with missed diagnoses and the potential side effects, patient inconvenience, and resource implications of anticoagulant treatment given for VTE.
- · While a number of patients are initially suspected of having blood clots, many of them do not.
- · For patients at low likelihood of having VTE, it is important to rule out VTE without subjecting patients to unnecessary tests.



Who it affects

- · Patients with suspected VTE
- · Clinicians and health care professionals



What are the highlights

- These recommendations confirm previous guidelines through a rigorous review of
- Unlike other VTE diagnosis guidelines, mathematical modelling was done to predict outcomes of various diagnostic pathways that have not been previously evaluated.
- Before considering a test, categorizing patients into the likelihood that they have VTE will help achieve an accurate diagnosis without exposing the patient to unnecessary testing.
- · A D-dimer test is the best first step to check for VTE in patients with low pre-test probability; if results are negative, no further testing is required.
- · When possible, clinicians should use a VQ scan, which exposes patients to lower radiation risk, versus a CT scan. Older individuals or those with preexisting lung disease are not ideal candidates for a VQ scan.

Total number of panel recommendations: 10

#### REFERENCE

Lim, W., Le Gal, G., Bates, S. M., Righini, M., Haramati, L. B., Lang, E., Kline, J. A., Chasteen, S., Snyder, M., Patel, P., Bhatt, M., Patel, P., Braun, C., Begum, H., Wiercioch, W., Schünemann, H. J., & Mustafa, R. A. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood Advances. 2018; 2:3226-3256.



# Optimal Management of Anticoagulation Therapy





What it covers



Why it matters



Who it affects



What are the highlights

- Optimal care management of anticoagulation therapy in patients who have previously experienced a clot
- Anticoagulant drugs must be used with skill in order to reduce risks of bleeding and developing another clot.
- Health care providers often have to make the difficult decision to continue or stop anticoagulation therapy following a major bleeding event.
- Patients who have already had a blood clot and need to take anticoagulant drugs
- · Pharmacists, clinicians, nurses, and health care policy makers
- Managing anticoagulation therapy is complex. Patients should receive care from specialized anticoagulation management service centers versus primary care physicians whenever possible.
- Most patients needing to interrupt warfarin for invasive procedures do not require a short-acting injectable anticoagulant administered during the peri-operative period, socalled bridge therapy.
- Management of life-threatening bleeding during anticoagulant therapy requires thoughtful use of anticoagulant reversal therapies.
- Many patients who survive major bleeding during anticoagulant therapy should resume taking anticoagulants.

Total number of panel recommendations: 25

#### REFERENCE

Witt, D. M., Nieuwlaat, R., Clark, N. P., Ansell, J., Holbrook, A., Skov, J., Shehab, N., Mock, J., Myers, T., Dentali, F., Crowther, M. A., Agarwal, A., Bhatt, M., Khatib, R., Riva, J. J., Zhang, Y., & Guyatt, G. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. Blood Advances. 2:3257-3291.



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## Heparin-Induced Thrombocytopenia





What it covers



Why it matters



Who it affects



What are the highlights

- A rare and serious adverse drug reaction that increases a patient's risk of developing venous or arterial thromboembolism, which may be limb- or life-threatening
- Suspected heparin-induced thrombocytopenia (HIT) cases in hospitalized patients is the most frequently requested hematologist consult by other physicians.
- HIT can lead to amputation or death for every day treatment is delayed, there is a ~6% risk of new thrombosis, amputation, and death.
- · HIT is frequently misdiagnosed and over diagnosed.
- 12 million U.S. patients receive heparin each year, up to 1% of whom will develop HIT.
- Surgical patients most commonly, especially those undergoing cardiac surgery
- · Hospitalists, surgeons, and cardiologists
- Using a clinical scoring system, the 4Ts score, rather than a gestalt approach will improve the accuracy of diagnosis and patient outcomes.
- Treatment options include not only conventional agents such as argatroban, bivalirudin, and danaparoid, but also newer agents such as fondaparinux and the direct oral anticoagulants.

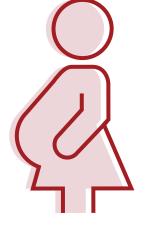
Total number of panel recommendations: 32

#### REFERENCE

Cuker, A., Arepally, G. M., Chong, B. H., Cines, D. B., Greinacher, A., Gruel, Y., Linkins, L. A., Rodner, S. B., Selleng, S., Warkentin, T. E., Wex, A., Mustafa, R. A., Morgan, R. L., & Santesso, N. (2018). American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. Blood Advances. 2:3360-3392.

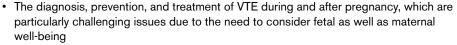


## **VTE in the Context of Pregnancy**





What it covers





Why it matters

- Pregnancy-associated VTE is a leading cause of maternal morbidity and mortality in Western countries.
- Factors such as prior VTE, inherited clotting disorders, increasing age, cesarean delivery, co-existent diseases (e.g., sickle cell disease, lupus), and obesity also increase risk.
- Pregnant women are more likely to be older, overweight, have additional medical conditions, and undergo a cesarean delivery than in the past.



Who it affects

- Pregnant women, especially those who have previously experienced a blood clot or have other risk factors for blood clots
- · Obstetrician-gynecologists, maternal fetal specialists, and internists



What are the highlights

- A conservative approach to prescribing prophylaxis, in which prophylaxis is given only
  to those patients for whom the available research suggests benefit, is key to minimize
  potential harm from over treatment.
- In the majority of cases, low-molecular-weight heparin is likely to be the best approach for managing superficial thrombosis.
- For treatment of pulmonary embolism and deep-vein thrombosis with low-molecularweight heparin, it is acceptable to do weight-based dosing instead of using regular blood tests to adjust the dose.
- A majority of pregnant women with newly diagnosed VTE at low risk of complications can be treated as outpatients, rather than admitted to hospital, as long as the right supports are in place.

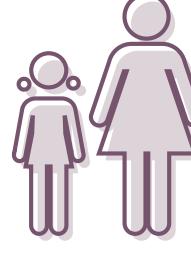
Total number of panel recommendations: 31

#### REFERENCE

Bates, S. M., Rajasekhar, A., Middeldorp, S., McLintock, C., Rodger, M. A., James, A. H., Vazquez, S. R., Greer, I. A., Riva, J. J., Bhatt, M., Schwab, N., Barrett, D., LaHaye, A., & Rochwerg, B. American Society of Hematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy. Blood Advances. 2:3317-3359.



### **Treatment of Pediatric VTE**





What it covers



Why it matters

- Treating VTE in pediatric patients
- The incidence of VTE in children at a population level is very low, but it is higher in hospitalized children (in fact, hospital acquired VTE is said to be the second most common cause of preventable harm in hospitalized children – behind infection).
- VTE treatment and complications are different for children spanning a wide age range.
- Children are one of the most challenging patient populations to treat because VTE always occurs in the context of another serious diagnosis that also must be treated.
- · Research in pediatric VTE is very limited.
- Much of the existing evidence is extrapolated from adult practice.



Who it affects

- Very ill children, newborns through 18 years of age; most common in small children and teenagers
- Pediatricians, pediatric hematologists, pediatric oncologists, pediatric intensivists, and neonatologists



What are the highlights

- Sometimes DVT causes symptoms, and sometimes it is found incidentally in an imaging study for something else. These guidelines inform how to treat these different situations. This distinction has not been addressed by guidelines in the past.
- · Central venous line-associated clots are the most common clots in children.
- If the central venous line is not working and the child is at the end of treatment, it should most likely be removed.
- Renal vein thrombosis, the most common spontaneous VTE in children, should all receive anticoagulation therapy.
- Due to the low level of existing evidence, additional research is required to develop more evidence-based care recommendations.

Total number of panel recommendations: 30

#### REFERENCE

Monagle, P., Cuello, C. A., Augustine, C., Bonduel, M., Brandão, L. R., Capman, T., Chan, A. K., Hanson, S., Male, C., Meerpohl, J., Newall, F., O'Brien, S. H., Raffini, L., van Ommen, H., Wiernikowski, J., Williams, S., Bhatt, M., Riva, J. J., Roldan, Y., Schwab, N., Mustafa, R. A., & Vesely, S. K. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. Blood Advances. 2:3292-3316.



## **Prophylaxis for Surgical Patients**



What it covers



Why it matters



Who it affects



What are the highlights

- Evidence-based research that supports decision-making to prevent venous thromboembolism (VTE) – also known as blood clots in the veins – in patients undergoing several different kinds of major surgical procedures requiring hospitalization.
- Before prevention measures were put into place, VTE was a common cause of death in surgery and even with such measures, blood clots can be fatal.
- Prevention of VTE is used as an important factor in assessing and measuring the quality of surgical care delivered by hospitals.
- The guidelines focus on the outcomes that are most relevant and important to patients.
- Hematologists: Along with other consultants who may be tapped to provide counsel about prevention of VTE following different types of surgery.
- Surgeons: Those seeking the latest information on recommended types of prevention and the timing of prevention methods.
- Hospital Systems: VTE prevention is a common quality benchmark for the authoritative bodies who accredit hospitals.
- Patients: Patients undergoing major surgical procedures requiring hospitalization after surgery to understand the risk of developing clots and the various types of prevention methods recommended for specific kinds of surgery.
- Not all surgery requires measures to prevent blood clots, and the guidelines make recommendations for circumstances when the risks associated with potential bleeding may outweigh the benefits.
- The risks of blood clots associated with surgery depend on multiple factors including
  patient characteristics and the type of surgery. The panel made recommendations
  based on these factors. This includes when to consider prevention, and which type
  might be the most suitable mechanical or pharmacologic.

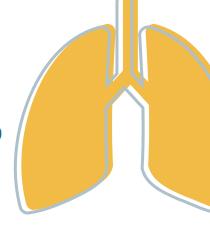
Total number of panel recommendations: 30

#### REFERENCE

Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv. 2019; 3(23):3898-3944.



## ASH Recommendations for Treatment of Deep Vein Thrombosis and Pulmonary Embolism





#### What it covers

 Evidence-based support for decision-making during each of the treatment phases of venous thromboembolism (VTE) and the recommended approach for the treatment in those phases

VTE treatment phases:

**Initial management:** from diagnosis until the first weeks of therapy

**Primary treatment:** typically a minimum of three months

Secondary prevention: extends for a prolonged, usually indefinite, period of time after the primary treatment phase



### Why it matters

- There is not a single approach to VTE treatment and prevention.
- There have been many recent clinical studies that inform/guide treatment at each
  of the various stages.



#### Who it affects

- Emergency department physicians and urgent care providers who make the initial management decisions for patients with acute deep-vein thrombosis (DVT) and pulmonary embolism (PE).
- · Vascular medicine and interventional specialists who treat patients with acute, severe VTE
- Thrombosis specialists and anticoagulation providers who implement and manage the antithrombotic therapies for patients with VTE
- Hematologists who consult about risks for recurrent thrombosis and hemorrhagic complications in patients on anticoagulant therapy
- All specialists and primary care providers who diagnose and manage the chronic complications that these patients can develop, including post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension



### What are the highlights

- The guidelines emphasize the need for VTE treatment decisions to be patient-centric and consider patients' perspectives that include the financial implications when choosing anti-coagulation therapy
- Strong recommendations from the panel include:

Use thrombolytic therapy to treat patients with pulmonary embolism who are hemodynamically compromised

Use anticoagulant therapy to treat patients in secondary prevention Use indefinite anticoagulation therapy to treat patients with recurring VTE

 The panel also made conditional recommendations expressing a preference for home treatment over hospital-based treatment of uncomplicated cases of DVT and PE. Home treatment is suggested when there is a low risk for complications as well as a preference for direct oral anticoagulants for primary treatment of VTE.

#### **Total number of panel recommendations: 28**

#### REFERENCE

Thomas L. Ortel, Ignacio Neumann, Walter Ageno, Rebecca Beyth, Nathan P. Clark, Adam Cuker, Barbara A. Hutten, Michael R. Jaff, Veena Manja, Sam Schulman, Caitlin Thurston, Suresh Vedantham, Peter Verhamme, Daniel M. Witt, Ivan D. Florez, Ariel Izcovich, Robby Nieuwlaat, Stephanie Ross, Holger J. Schünemann, Wojtek Wiercioch, Yuan Zhang, Yuqing Zhang; American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv 2020; 4 (19): 4693–4738. doi: https://doi.org/10.1182/bloodadvances.2020001830

