compression stockings, and surgery. In 10 RCTs involving 2,174 patients, LMWH given for 8 to 12 days significantly lowered the incidence of SVT extension and/or recurrence compared with placebo when using either prophylactic (OR 0.32; 95% CI, 0.16–0.65) or treatment doses (OR 0.33; 95% CI, 0.16–0.18). Although the incidence of VTE was lower initially in both the prophylactic (OR 0.25; 95% CI, 0.03–2.25) and therapeutic (OR 0.26; 95% CI, 0.03–2.34) treatment groups, the difference did not reach statistical significance.

Two RCTs (n=267) showed NSAIDs were more effective than placebo in reducing pain, inflammation, and recurrence/extension of SVT (OR 0.33; 95% CI, 0.16–0.68). There was no difference in the incidence of VTE. Two RCTs (n=274) evaluated NSAIDs versus LMWH. LMWH showed a statistically insignificant reduction of VTE (OR 0.93; 95% CI, 0.23–3.83) and SVT extension (OR 1.18; 95% CI, 0.53–2.60) relative to NSAIDs. These studies suffered from small sample sizes, making comparisons difficult.

Compression stockings plus LMWH appeared to be more effective at preventing VTE (OR 0.07; 95% CI, 0.00–1.32) or SVT extension/recurrence (OR 0.07; 95% CI, 0.01–0.52) when compared with compression stockings alone. However, the authors noted that the difference between compression stockings alone versus compression stockings plus LMWH for preventing VTE was not statistically significant.

The Cochrane review noted a comparison between LMWH and saphenofemoral disconnection in 1 unblinded RCT (n=60). This procedure did not significantly lower the risk of extension/recurrence compared with LMWH; however, the confidence interval was wide (OR 0.31; 95% CI, 0.03–3.17). Venous ligation in 592 patients showed a nonsignificant reduction in VTE (OR 0.32; 95% CI, 0.06–1.62) and SVT recurrence/extension (OR 0.42; 95% CI, 0.15–1.16). However, venous stripping with elastic stockings showed a significant decrease in SVT extension and recurrence (OR 0.07; 95% CI, 0.01–0.57) compared with elastic stockings alone.

The American College of Chest Physicians Guidelines advocates medical treatment over surgical intervention for SVT. Prophylactic-dose LMWH or intermediate doses of unfractionated heparin for at least 4 weeks are recommended. Alternatively, warfarin with a target INR of 2 to 3 (bridged for at least 5 days with LMWH) can be used. NSAIDs are recommended in patients with short-segment SVT or SVT that is distant from the saphenofemoral junction.

Michael M. Braun, DO
Madigan Army Medical Center
Joint Base Lewis-McChord, WA

Megan Belprez, MD
Womack FMR Clinic
Fort Bragg, NC

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department of the US Army at large.

What is the differential diagnosis for an elevated monocyte count in a patient with an acute febrile illness?

Evidence-Based Answer
Monocytosis can have many causes in a febrile patient with an acute illness. Etiologies can be broadly grouped into hematologic disorders, infections, inflammatory causes, and miscellaneous causes. The history and physical examination should guide the clinician in developing a differential diagnosis and planning further work-up. (SOR: C, based on expert opinion.)

Currently available information regarding the causes of monocytosis in a febrile patient is limited to narrative reviews and expert opinions from textbooks. Authors report that opinions are based on case reports and case series, many of which are decades old.

According to an authoritative text, the differential for an acute febrile illness with monocytosis can be broadly broken down into hematologic disorders, infections, inflammatory causes, and miscellaneous causes. Experts state that the differential diagnosis is broad but can usually be narrowed through careful history and examination.

According to a narrative review and general medical and authoritative texts, hematologic disorders causing monocytosis include various forms of leukemia, Hodgkin and non-Hodgkin lymphoma, and chronic or congenital neutropenia. Myelodysplastic disorders can exhibit monocytosis in up to 25%
of cases. Profound monocytosis is more likely to represent a hematologic disorder or malignancy than other causes. Nonhematologic malignancies can also cause monocytosis. The relative immunosuppression present with some malignancies can lead to infections, and hence a presentation with acute fever.

Although most general medical textbooks list infection as a cause of monocytosis, according to 1 authoritative text, infections do not typically cause isolated monocytosis. Both general medical and authoritative textbooks list various bacterial, viral, and protozoan causes of monocytosis. Bacterial infections that could cause monocytosis and fever include tuberculosis, syphilis, subacute bacterial endocarditis, ehrlichiosis/anaplasmosis, Rocky Mountain spotted fever, and brucellosis. The resolution of an acute bacterial infection such as pneumonia can also result in monocytosis. Viral causes of monocytosis and acute fever include dengue hemorrhagic fever, cytomegalovirus infection, and varicella-zoster infection. Malaria and leishmaniasis are protozoan illnesses that can also result in monocytosis.

Inflammatory and rheumatologic causes of monocytosis and fever include subacute lupus erythematosus, rheumatoid arthritis, temporal arteritis, sarcoidosis, and inflammatory bowel disease. A narrative review also supports these associations. Williams Hematology is the only text to include celiac disease as a possible cause of monocytosis.

Miscellaneous causes of fever and monocytosis include Kawasaki disease, postsplenectomy state, and drug reactions.

---

**Can medication prevent a transfusion reaction in someone with a history of febrile transfusion reactions?**

**Evidence-Based Answer**

No. Medication administration prior to transfusions does not reduce the incidence of febrile, nonhemolytic transfusion reactions (FNHTR), even in patients with a history of FNHTR. (SOR: B, based on a systematic review of low quality studies.)

A Cochrane review assessed the clinical effects and safety of pharmacologic interventions for the prevention of allergic and FNHTR in patients with and without a history of transfusion reactions. Criteria for considering studies for review included both published and unpublished RCTs with patients requiring a blood transfusion including cancer, hematologic malignancy, and chronic transfusions.

Of the 3 double-blind RCTs evaluated in the Cochrane review, 1 included patients with a history of either allergic or FNHTR, 1 excluded patients with a history of FNHTR, and 1 included only patients with a history of FNHTR. Due to heterogeneous study designs, a meta-analysis could not be performed.

The study that included patients with either allergic or FNHTR was a double-blind prospective RCT evaluating the efficacy of acetaminophen 650 mg p.o. plus diphenhydramine 25 mg IV versus placebo during leukocyte-reduced platelet transfusions. Information on timing of the premedication was not provided.

Of the 15 patients reporting a history of FNHTR, 4 reactions were reported in 14 transfusions in patients receiving premedications compared with 3 reactions reported in 13 transfusions in patients receiving placebo.

The other applicable study in the Cochrane review was a double-blind crossover RCT evaluating 73 patients with history of FNHTR. Participants on hematology or gastrointestinal wards were serially randomized to hydrocortisone 50 mg IV, diphenhydramine 50 mg IV, both, or placebo. Each medication was infused 30 minutes prior to transfusions. Blood products used were not described.

The Cochrane review mentioned “prevention of FNHTR” in 47 patients receiving both treatments, 16 patients receiving hydrocortisone alone, 6 receiving diphenhydramine alone (odds ratio favoring hydrocortisone of 2.38; 95% CI, 1.07–5.27), and