PHARMACY & THERAPEUTICS
UPDATE

METHODIST

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Critical Drug Shortages

On-going shortages and strategies to minimize the impact to patient care for drugs with limited availability

Shortage:	*Lidocaine, Bupivacaine injection with epinephrine*
Action:	*alternative concentrations, sizes without epi*
Shortage:	*Protamine injection*
Action:	*conservative use, dosing of protamine/heparin*

In this Issue

If you have any questions or concerns, please contact the NMH Pharmacy Purchasing Department: 402-354-4337.

COVID Vaccine Induced Thrombotic Disorders

On April 13th, the FDA and CDC suggested pausing use of the Johnson & Johnson COVID vaccine to allow for investigation of rare cases of severe thrombosis associated with thrombocytopenia occurring post-vaccination, more commonly referred to as Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) or Thrombosis with Thrombocytopenia Syndrome (TTS). The syndrome has been characterized by venous or arterial thrombosis (often cerebral or abdominal), mild to severe thrombocytopenia, and a positive (+) platelet heparin dependent antibody (PF4) test.

After a review of reported events and a detailed risk/benefit analysis, on April 23rd the CDC voted to recommend the J&J COVID vaccine again be available under FDA's EUA, ensuring women <50yo are aware of risk prior to receiving and that other options are available.

Treatment recommendations are somewhat similar to severe heparin induced thrombocytopenia (HIT). In patients presenting with documented or suspected thrombosis, thrombocytopenia (platelet count <150k), are 4-30 days post-vaccination, and have a +/pending PF4 test, treatment should include the following:

1. IVIG 1 gram/kg daily X 2 days
2. Non-heparin AC, chosen based on the clinical status and organ function of the patient:
   - Parenteral direct thrombin inhibitor (argatroban or bivalirudin, provided the baseline PTT is normal)
   - Direct oral anticoagulants (DOACs)
   - Fondaparinux (Arixtra®)

   Low fibrinogen/bleeding are associated with VITT, and should not absolutely preclude anticoagulation, especially if platelets are >20k or rising following IVIG initiation.
3. Based on similarities to HIT, avoid platelet transfusions. However, risk/benefit assessment in individual patients with serious bleeding and/or need for surgical intervention may favor platelet transfusion, following initiation of IVIG, non-heparin anticoagulant, and fibrinogen replacement (if deficient).

While VITT is a rarely reported event, additional supply of argatroban and fondaparinux at Methodist have been secured. PF4 ELISA ASSAYS are be performed at Methodist once daily, 7 days a week. PF4 tests received in lab before 6:30 will be routinely tested and reported that same evening.

Adapted from: Hematology.org, accessed 5.10.21

Cerner Brand Name Deletions

A few common brand names will no longer be available in Powerchart due to a recent drug database update. These products can be ordered under their generic names:

- Kayexalate- search for sodium polystyrene sulfonate
- Romazicon- search for flumazenil
- Compazine- search for prochlorperazine
- Prelone- search for prednisolone
- Zometa-search for zoledronic acid

Heart Failure Staging Update

The 2017 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines classify heart failure (HF) based on both the evolution and progression of the disease. The authors of these guidelines identified 4 stages of HF.

- **Stage A:** patients at high risk of developing heart failure, but no structural disorder of the heart
- **Stage B:** patients with structural disorder of the heart, but have never had symptoms of HF
- **Stage C:** patients who have had or currently have symptoms of HF associated with underlying structural heart disease.
- **Stage D:** patients with end-stage disease who require special treatment such as, mechanical circulatory support, continuous inotropic infusions, cardiac transplantation or hospice care

These guidelines also refer to functional classification of HF, in which patients are assigned to 1 of 4 classes based on the degree of effort that is needed to provoke symptoms.

- **Class I**: patients that have symptoms at levels that would only limit normal individuals
- **Class II:** patients that exhibit symptoms upon normal exertion
- **Class III:** patients that experience symptoms on less-than-ordinary exertion
- **Class IV:** patients that have symptoms at rest

A recently published multi-society consensus statement, proposes a new universal definition of HF and revisions of the staging and classification system of HF. The proposed definition of HF is designed to be contemporary and simple, but conceptually comprehensive. The proposed definition: "[Heart failure] is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion."

The proposed revision to the staging of HF is relatively unchanged. However, the tweaks are meant to enhance the understanding and to address the changing role of biomarkers. The terminology is meant to avoid the stigma of HF before symptoms become apparent and to stress to patients and clinicians that there are therapies that can be used to prevent HF from progressing. ***The proposed changes to staging of HF include:***

- **At-risk for HF (stage A):** patients at risk for HF but without current or prior symptoms or signs and without structural or biomarker evidence of heart disease
- **Pre-HF (stage B):** patients without current or prior symptoms or signs of HF, but evidence of structural heart disease or abnormal cardiac function or elevated natriuretic peptide levels
- **HF (stage C):** patients with current or prior symptoms and/or signs of HF caused by structural and/or functional cardiac abnormality
- **Advanced HF (stage D):** patients with severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite guideline-directed management and therapy (GDMT), refractory or intolerant to GDMT, requiring advanced therapies such as consideration for transplant, mechanical circulatory support or palliative care

The document also recommends a revision to the classification system according to left ventricular ejection fraction (LVEF). Most clinicians agree on the classification of HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). However, the patients that fall in between these two are more of a grey area. The proposed change to the classification system based on ejection fraction include:

- **HF with reduced EF (HFrEF):** LVEF up to 40%
- **HF with mildly reduced EF (HFmrEF):** LVEF of 41-49%
- **HF with preserved EF (HFpEF):** LVEF ≥ 50%
- **HF with improved EF (HFimpEF):** HF with a baseline LVEF of ≤ 40%, an increase of at least 10 points from baseline and a second measurement of LVEF of ≥ 40%

References: 1. Yancy, CW et al. ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Card Fail. 2017 Aug;23(8):628-651. 2. Bozkurt B et al. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. J Card Fail. 2021 Mar 1:S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Epub ahead of print. PMID: 33663906

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