Hi Clinical Problem Solvers! My name is Kaitlyn Thomas and I'm a third year medical student from Lake Erie College of Osteopathic Medicine here to walk you through an illness script for DRESS syndrome, also known as DiHS, something I've found challenging to recognize.

First, why do I say DRESS and DiHS? DRESS is an abbreviation for Drug Reaction with Eosinophilia and Systemic Symptoms. DiHS is an abbreviation for Drug-Induced Hypersensitivity syndrome. When this syndrome was classified it was thought to only be caused by drug reactions to anticonvulsants, and named DiHS. Later, DRESS was used to describe the syndrome based on new case reports from a variety of drugs that were causing an acute systemic illness with eosinophilia and the same systemic illness as DiHS. Today, DRESS is the primary name for the syndrome, but DiHS can be seen in previous literature.

It's important to understand the pathophysiology that leads to DRESS in order to identify it’s symptoms. This is a type IV hypersensitivity reaction, meaning it is cell-mediated by cytotoxic T cells. Typically, the reaction is delayed around 2-8 weeks after starting the medication.

The culprits follow a simple memory device, think about the four As. Antiepileptics, Allopurinol, Antipsychotics and Antibiotics.

Risk Factors include HLA haplotypes, especially HLA-B*1502, associated w/ carbamazepine reactions, and HLA-B*1508, associated with allopurinol.

Viral reactivation is another possible cause of DRESS syndrome in conjunction with one of the offending medications. Remember the 4 As! The proposed hypothesis is that a virus-drug interaction leads to proliferation of the T cells and the clinical manifestations of DRESS syndrome. The viruses believed to play a role include EBV, CMV and HHV6.

Research has shown there are several patterns of skin histopathology that will be present, including interface dermatitis, and lymphocytic infiltration. Interface dermatitis is the most common and is an erythema multiforme or lichenoid pattern. Apopotosis of keratinocytes is correlated with severity of the disease. Lymphocytic infiltration is linked to the severity of the liver injury and severity of eosinophilia. Yea, for real!

In a patient with DRESS, fever and malaise may be present, but probably won’t help us narrow our differential. Diffuse lymphadenopathy can be seen with some drugs, such as minocycline, but the rash is an important sign! It's usually described as erythematous, maculopapular, and confluent. Let's break each of those terms down! Erythematous is redness of the skin, and maculopapular describes flat discolorations on the skin with small raised bumps. Macules describe the flat lesions and papules describe the raised lesions. Confluent refers to the idea that the rash runs together and lesions merge; thus, they aren’t discrete entities.

50% or more of patients with DRESS may also have erythroderma, also known as exfoliative dermatitis. It is potentially life-threatening, involves a large skin surface area (>90%), and occurs acutely. Facial edema is present in about half of cases. It is typically symmetric with mucosal pain but without erosions.

Several organs may be affected. About 80% of patients have liver involvement with hepatitis or acute liver failure and a finding of hepatomegaly. The kidneys may develop acute interstitial nephritis, the lungs, pneumonitis and the heart may develop eosinophilic myocarditis or pericarditis. Who knew the 4As could affect so many different organs in this syndrome?

Elevated white blood cells and eosinophilia is present in about 70% of cases and may clinch the diagnosis. Atypical lymphocytosis may also be seen on blood smear. Liver function testing may show increased ALT or alkaline phosphatase. Creatinine may be elevated and urinalysis may show increased protein and white blood cells suggestive of AIN.

Remember the 4 As! Antiepileptics, Allopurinol, Antipsychotics and Antibiotics.
When you see one of these drugs in the patient's medication history, they have a confluent maculopapular rash and there are signs of inflammation with eosinophils on labs, DRESS syndrome should raise to the top of your differential.

When thinking about your differential, there are several other diagnoses to consider. Stevens Johnson Syndrome is life threatening. However, SJS is more likely to start in the trunk while DRESS begins in the extremities and face. SJS will also demonstrate necrotic centers in the skin lesions and a positive Nikolsky sign. Cutaneous Lymphoma, Hypereosinophilic syndrome and acute generalized exanthematous pustulosis should also be ruled out. Hypereosniophilic syndrome will have pulmonary infiltrates compared to the pneumonitis in DRESS, and thrombocytopenia; cutaneous lymphoma will appear over a much longer period of time and acute generalized exanthematous pustulosis will present w/in 2 weeks of medication initiation with primarily pustules and spontaneous resolution.

If you are suspicious for DRESS syndrome, the medication should be stopped immediately as prognosis is tied to how quickly the medication is stopped. Then depending on the severity of the condition, you may add topical or systemic steroids.

We hope you enjoyed this illness script!