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You have a teenage patient sent in from the PCP for rash followed by scleral icterus that started 8 days ago. His PMHx only includes acne for which he started Bactrim 3 weeks ago. Around this same time, patient had a sore throat that was strep negative at the PCP, fevers with Tmax 101, and 1-2 episodes of emesis daily with overall decreased PO intake. Fevers and sore throat resolved 5 days ago. In the room, his vitals are normal for age, he is in NAD other than scratching at his head to toe rash, which is erythematous, peeling, papular coalescing into plaques, and sparing of the mucosa, palms and soles (see figure). You get fancy and notice it has a negative Nikolsky's sign. There is generalized lymphadenopathy. He also has impressive scleral icterus but no abdominal TTP or hepatosplenomegaly. Rashes are your least favorite chief complaint and that icterus looks bad, so you get some labs and find WBC 0.6, ANC 10, Hgb 13.5, normal smear, AST 251, ALT 492, ALKPPOS 829, GGT 2108, TBILI 21, DBILI 16, Lipase 540, and a UA with 2+ protein and 10RBCs, normal BUN/Cr, coags.

While trimethoprim-sulfamethoxazole (TMP-SMX) has long been used for UTI, GI, respiratory, and skin/soft tissue infections, as the incidence of MRSA has gone up, so too has the prescribing of TMP-SMX. Thus, there is an increased likelihood that you will see a patient who presents with an adverse drug reaction (ADR). The most common ADRs are GI and cutaneous side effects. Dermatologically, this ranges from **urticaria, a stereotypical morbilliform rash, fixed drug eruption, and much more rarely erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis**. It causes a transient decreased creatinine clearance and works to potentiate the effects of other drugs (warfarin, digoxin, phenytoin, increases hypoglycemia with sulfonylureas, induces hyperkalemia with K-sparing diuretics, etc.). **Neutropenia** followed by thrombocytopenia are the most common hematologic ADRs. **Hepatotoxicity** has also been shown with LFTs demonstrating hepatocellular or mixed pictures more frequently than cholestasis. Due to a preceding rash or eosinophilia prior to laboratory abnormalities, it has been hypothesized that hepatotoxicity is part of the drug hypersensitivity reaction, which brings us back to your patient...

Dermatology diagnoses the patient with DRESS, drug reaction with eosinophilia and systemic symptoms. The onset of **rash (2-6 weeks after starting the drug), fever, pharyngitis and lymphadenopathy** all fit. Interestingly, eosinophilia is not required and neutropenia, thrombocytopenia, and atypical lymphocytosis have been seen. **Nearly any organ can also be involved, with the liver** being the most frequent. In essence, DRESS is a tidy diagnosis for a patient presenting with multiple ADRs. For all cases of suspected ADR, the first step in management is to **stop the offending agent**. Other supportive treatments are based upon the constellation of symptoms, and the **use of systemic steroids is controversial**. Complete improvement is shown in the majority of cases, but depending on the extent of organ involvement, the course varies. The leading causes of death are “**liver failure, multiorgan failure, fulminant myocarditis, or hemophagocytosis**.”¹

Exanthematous (morbilliform) drug eruption



Numerous erythematous macules and papules are present in this patient with a morbilliform drug eruption.
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References // Further Reading:

- ¹Uptodate.com
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