The prevalence of each RegiSCAR category in this study is similar to that in other publications on DRESS.[3-5] This study differs as it recorded AEM. The results show that AEM appeared in DRESS as often as the established RegiSCAR criteria, including hepatic abnormalities and acute kidney injury. AEM was significantly more prevalent in patients with DRESS than in patients with other drug eruptions. The cause of AEM in DRESS is not known. This phenomenon may be due to disease involvement of the hematologic organ systems. Toxic eosinophilic granule proteins released during DRESS are thought to mediate organ damage and may affect the bone marrow, liver, and/or spleen and account for abnormalities seen in multiple blood cell lines.[1] Our study supports this theory by showing that patients with DRESS and AEM were more likely to have eosinophilia and hepatic involvement than were patients without AEM. Limitations of this study include small sample size at a single medical center. Larger multicenter studies are needed to determine whether this finding can be replicated elsewhere. The presence of AEM may aid in the diagnosis of DRESS and could be evaluated as a component of the diagnostic scoring system.

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Initiation of methotrexate with or without a test dose: A retrospective toxicity study

To the Editor: Many dermatologists initiate methotrexate with a small test dose (TD), followed by laboratory evaluation before the second dose. Intended to minimize the risk for early adverse events, this practice has been noted in guidelines,[1,2] though some have questioned its necessity.[3] Clinical trials utilizing methotrexate without a TD have reported a low incidence of serious adverse events.[4] We performed a retrospective study to compare the frequency of adverse events in patients initiating methotrexate with and without a TD.

Our electronic medical records were searched for patients with a new prescription for methotrexate from dermatology or rheumatology during 2010-2015. Patients were included if use of a TD, the initial dose, dose changes, date and reason of discontinuation, and baseline and follow-up laboratory values for a 4-month period after initiation of methotrexate were documented. TD was defined as an initial methotrexate dose of ≤10 mg and laboratory monitoring before the second weekly methotrexate dose. Laboratory values were graded according to standard terminology.[5]

The initial search identified 812 patients; 174 met inclusion criteria. Most dermatology patients received a TD, and most rheumatology patients did not (Table I). As expected, the initial methotrexate dose was lower in the TD group, but both groups had a mean initial dose <10 mg, with a range of 5-15 mg in the no-TD group (Table I). Patients receiving a TD had significantly more laboratory draws than those without a TD during the first 4 months of therapy (Table I). Initial doses were lower in dermatology patients (mean 5.9 mg) than rheumatology patients (mean 8.4 mg, $P < .001$).

There were no deaths or hospitalizations attributed to methotrexate toxicity. Laboratory values obtained 1 week after a TD showed no new grade 3 or 4 abnormalities and prompted only 1 management change, which was discontinuation of methotrexate in 1 patient with mild (grade 1) alanine

Table I. Characteristics and outcomes during first 4 months of therapy by test dose utilization

Characteristic	Test dose	No test dose	*P* value*
Specialty			
Dermatology	56	19	<.001
Rheumatology	2	94	
Age, y, mean (range)	45.3 (10-85)	51.3 (6-82)	.03
Sex			
Male	19	26	.20
Female	39	87	
Diagnosis			
Psoriasis	41	17	<.001
Rheumatoid arthritis	1	66	
Other	15	30	
Baseline creatinine >1.4 mg/dL			
Yes	0	1	1
No	58	112	
New grade 2 laboratory abnormality†			
Yes	2	2	.61
No	56	111	
New grade ≥3 laboratory abnormality†			
Yes	0	0	NA‡
No	58	113	
Discontinuation due to clinical toxicity§			
Yes	2	5	1
No	56	108	
Discontinuation due to laboratory toxicity			
Yes	1	1	1
No	57	112	
Discontinuation due to any clinical or laboratory toxicity			
Yes	3	6	1
No	55	107	
No. laboratory draws, mean (range)	3.5 (1-9)	2.5 (1-5)	<.001
Initial dose, mg, mean (range)	5.4 (5-10)	8.3 (5-15)	<.001
Dosage during first 4 months, mg/wk,¶ mean (range)	12.9 (0.3-19.1)	11.6 (2.1-19.1)	.08

NA, Not applicable.
*On the basis of 2-sample Student *t* tests for quantitative variables and Fisher's exact test for categorical variables.
†Tests included were hemoglobin concentration, white blood cell count, absolute neutrophil count, platelet count, and alanine aminotransferase concentration.
‡*P* value was undefined due to a failure to observe any grade 3 abnormalities.
§Includes clinical symptoms, such as nausea or hair loss.
¶Calculation of mean dose during the first 4 months can include doses of 0 when methotrexate was discontinued or disrupted.

aminotransferase elevation of uncertain etiology. There were no discontinuations due to hematologic toxicity in either group. Most discontinuations were secondary to nausea or other gastrointestinal symptoms. The incidence of methotrexate discontinuation (any cause) and of grade 2 laboratory abnormalities during the first 4 months of treatment did not significantly differ according to TD use or size of the initial dose (Tables I and II). Our study is limited by sample size and baseline differences between groups in diagnosis and treating specialty.

In conclusion, laboratory evaluation 1 week after a methotrexate TD rarely prompted management changes in our patients and can likely be safely omitted in most dermatology and rheumatology patients with normal renal function. We found no significant difference in the incidence of toxicity with initial doses ranging 5-10 mg, and data from clinical trials[4] suggest that initiation of methotrexate at doses of 15-17.5 mg/wk is associated with a low risk for serious adverse events. Greater caution in dosing and monitoring might be needed in patients who have renal disease or are otherwise at increased risk for methotrexate toxicity.

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Table II. Patients with grade 2 laboratory abnormalities or discontinuing methotrexate (any cause) during first 4 months of therapy by initial dose received

	Grade 2 abnormality*		Discontinued	
Category	**Yes**	**No**	**Yes**	**No**
Initial dose, mg				
5.0	2	57	2	57
7.5	2	72	4	70
10.0	0	33	3	30
12.5	0	3	0	3
15.0	0	2	0	2
Odds ratio†	0.73		1.11	
P value‡	.32		.48	

*Tests included were hemoglobin concentration, white blood cell count, absolute neutrophil count, platelet count, and alanine aminotransferase concentration.
†Odds ratio represents the odds of having a grade 2 abnormality or discontinuing methotrexate for each 1-mg increase in initial dose. Odds ratio was obtained from a logistic regression of having a grade 2 abnormality or discontinuing methotrexate on the initial dose of methotrexate.
‡*P* value for the odds ratio.

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Evaluating results of an interferon-γ release assay in patients with autoimmune disease who are taking hydroxychloroquine

To the Editor: New treatment options are emerging for patients with autoimmune diseases, and these treatments require careful evaluation before their initiation. Patients with autoimmune disease are already at an increased risk for reactivation of latent tuberculosis compared with the general population, and therefore great care must be exercised when starting immunosuppressive therapy.[1] Given these risks, standard of care requires screening for latent tuberculosis in this vulnerable population before initiating immunosuppressants. QuantiFERON-TB Gold (QFT-G) is a widely used interferon-γ release assay that is used to screen patients for tuberculosis. Briefly, patients' blood is incubated with *Mycobacterium tuberculosis* antigens; levels of interferon-γ released are then measured. Results, based on quantitative thresholds of interferon-γ detected, are reported as determinate—either clearly positive or clearly negative—or indeterminate.

Clinical studies on the efficacy of QFT-G demonstrate higher rates of indeterminate results among immunosuppressed populations compared with the general population.[1,2] This is clinically important, because indeterminate QFT-G results may preclude patients from starting certain therapies or enrolling in clinical trials. In addition, many patients with autoimmune disease are started on hydroxychloroquine before escalating therapy to immunosuppressive therapies, which require tuberculosis screening before their initiation.[3] Interestingly, hydroxychloroquine is proposed to reduce levels of interferon-γ and therefore may affect the results of a QFT-G test.[3,4] Taken together, this suggests that patients with autoimmune disease who are being treated with hydroxychloroquine may face barriers to accessing novel therapies when screened with QFT-G because of falsely indeterminate test results.

The medical records of 89 patients enrolled in prospective longitudinal databases for cutaneous lupus and dermatomyositis with QFT-G testing were reviewed. Patients were sorted into groups based on the presence or absence of