Systemic lupus erythematosus is a systemic autoimmune condition that can be associated with uveitis. The prevalence of SLE as a cause of uveitis varies in the literature. In 1990, Rosenbaum and Wernick\(^1\) reported on the use of routine antinuclear antibody (ANA) testing for patients with uveitis. Their Bayesian analysis required a pretest probability of SLE in patients with uveitis to establish the value of routine antinuclear antibody testing in patients with uveitis.

Rosenbaum and Wernick\(^1\) estimated that with a positive ANA test result in a patient with uveitis, the chance of the patient having SLE was less than 1%. They recommended against the routine screening of patients with uveitis with ANA testing in the absence of other features suggestive of SLE. A higher pretest probability resulted in a higher posttest probability.

Rodriguez et al\(^2\) described the etiology of uveitis in 1237 patients attending the Massachusetts Eye and Ear Infirmary, reporting the prevalence of SLE as 4.8%. Substituting this value for pretest probability into the Bayesian analysis performed by Rosenbaum and Wernick\(^1\) resulted in a 24% posttest probability of having SLE. Thus, the prevalence of SLE in uveitis determines the value of routine ANA testing.

The aim of this brief report was to provide an estimate of the prevalence of SLE as a cause of uveitis in patients attending specialist clinics based on worldwide reports of uveitis etiologies.

Methods

An extensive literature search using the Medline database was conducted from January 1, 1984, to March 20, 2015. Search terms included uveitis, etiology, patterns, epidemiology, and classification. Articles in English and pertaining to humans were included. The inclusion of studies was limited to those reporting on uveitis in adults and those that included sufficient data on etiology from which conclusions about SLE prevalence could be drawn.

In studies where all cases were assigned a diagnosis, the number of cases with SLE was recorded. In a number of studies, disease entities with low frequencies were grouped as other or miscellaneous. In these circumstances, certain assumptions were made to estimate SLE frequency. Such assumptions were designed to give the highest possible estimate of SLE frequency. For example, if a miscellaneous group with 16 patients and any 1 of a possible 6 diagnoses...
were found recorded in a table of etiologies and in the same
table, a diagnosis that appeared in 4 or more cases was men-
tioned specifically, then the assumption was made that no
more than 3 of the cases in the miscellaneous group
could be secondary to SLE. By using this method, a value
for the likely maximum of SLE prevalence in uveitis was
determined. We also calculated the prevalence by only
counting cases where a diagnosis of SLE was specifically
mentioned.

Results
In total, 63 studies were included that reported on the
etiology of uveitis in 53,315 patients (eReferences in the
Supplement). There was a range of 42 to 8759 patients
(median, 548 patients; mean, 833 patients). Five studies
reported exclusively on anterior uveitis, 2 reported on inter-
mediate uveitis only, and 1 reported only on posterior and
panuveitis combined. One study did not report on cases of
intermediate uveitis. All other studies included cases with
anterior uveitis, intermediate uveitis, posterior uveitis, and
panuveitis.

The mean SLE prevalence for all studies combined was
0.47% (95% CI, 0.41%-0.53%). If cases were only counted
where SLE was specifically mentioned, the prevalence esti-
mate was 0.31% (eTable in the Supplement).

The anatomical classification of uveitis associated
with SLE was presented in only 18 studies. In these 18
studies, there were 72 cases of anterior uveitis, 3 cases of
intermediate uveitis, 26 cases of posterior uveitis, and
4 cases of panuveitis.

Discussion
The overall prevalence of SLE in patients with uveitis seen
in specialist clinics was 0.47%. If we used this value as the
pretest probability in the Rosenbaum and Wernick analysis1
(specificity, 85%; sensitivity, 95%), we could derive values
for the positive and negative predictive values of positive
and negative ANA test results (Figure 1). The posttest prob-
ability of a patient with a positive ANA test result (ie, posi-
tive predictive value) was 2.9% (95% CI, 2.65%-3.19%).
Therefore, for every true-positive test result, there were 34
false-positive test results (Figure 2).

At a Glance
- 63 studies reporting on the etiology of uveitis
in 53,315 patients were reviewed to estimate the
prevalence of systemic lupus erythematosus as a
cause of uveitis.
- The estimated prevalence of systemic lupus erythematosus
in uveitis was 0.47% (95% CI, 0.41%-0.53%).
- The positive predictive value of routine antinuclear antibody
testing in uveitis was 2.9% (95% CI, 2.65%-3.19%).
- These data suggest routine antinuclear antibody testing in
uveitis should not be recommended but reserved for cases
where the pretest probability of systemic lupus erythematosus
is higher.

Figure 1. Bayesian Analysis of Routine Antinuclear Antibody Testing in Patients With Uveitis

- Positive predictive value = \( \frac{\text{number of true positives}}{\text{number of true and false positives}} \) = \( \frac{447}{447 + 14,929} \) = 0.029 = 2.9%
- Negative predictive value = \( \frac{\text{number of true negatives}}{\text{number of true and false negatives}} \) = \( \frac{84,601}{23 + 84,601} \) = 0.9997 = 99.97%
The specificity and sensitivity of ANA testing in diagnosing SLE varies in the literature. One series found the sensitivity to be only 70%.\(^3\) Other studies calculated the specificity and sensitivity of ANA testing in diagnosing SLE as 92% and 98%, respectively.\(^4\) Substituting these values into the calculations in the eTable in the Supplement gave a positive predictive value of 5.47% and negative predictive value of 99.99% (calculations not shown). Even with this improved sensitivity and specificity, for every true-positive ANA test result, there were 19 false-positive test results. False-positive test results may lead to anxiety for patients as well as costs in time and money in the referral for a rheumatology assessment.\(^5\)

Our estimated SLE prevalence in uveitis of 0.47% is a likely overestimate given the assumptions described earlier. If we use the lower estimated prevalence of 0.31%, the positive predictive value of a positive ANA test result is less than 2%.

### Conclusions

Our theoretical calculations for the positive predictive value of a positive ANA test result in uveitis were very close to those found in another study investigating patients who were referred to a tertiary rheumatology clinic for evaluation of a positive ANA test result. The authors confirmed the poor positive predictive value of a positive ANA test result for SLE was 2.1%. This low positive predictive value was largely due to unnecessary testing in patients with low pre-test probabilities of the disease.\(^6\) Our study reinforces this view and suggests that routine testing of ANA in patients with uveitis is not justified (an exception would be in patients with juvenile idiopathic arthritis and uveitis where a positive ANA test result may influence management and follow-up). A positive test result is much more likely to rep-
resent a false-positive test result than a true-positive test result. Patients with systemic features suggestive of SLE or in cases where the ocular phenotype is in keeping with SLE (eg, scleritis or retinal arteritis) will have a higher pretest probability. Our analysis suggests that ANA testing in these cases would be warranted.

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REFERENCES