

## **Quality Improvement Project: Utility of Repeat Reflex Extractable Nuclear Antigen (ENA) Testing in Patients with a Positive Antinuclear Antibody (ANA) Test at the Minneapolis Veterans Affairs (VA) Health Care Center**

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**Background**– Serum antinuclear antibody (ANA) testing is commonly used as a screening tool for autoimmune disorders. In cases where there is a significant concern for an autoimmune disorder, more targeted antibody testing using an extractable nuclear antigen (ENA) panel may be conducted. In the Minneapolis VA system, the ENA panel is performed as a reflex to positive ANA titer that is greater than 1:80. In the past year (7/2023-7/2024), the total cost of ENA tests performed amounted to a cost of greater than \$47,000 with each test costing approximately \$70.

**Purpose**- The purpose of this study was to analyze the clinical utility of repeat (duplicate) ENA testing in the Minneapolis veteran population. This study will specifically analyze diagnosis related to assays, changes to ANA and ENA results, and rationale for ordering repeat testing. The findings may help inform lab testing protocols, reducing unnecessary tests while maintaining diagnostic accuracy.

**Methods** - As this project is intended to improve the Minneapolis VA Health Care System processes and not to expand the knowledge base of a scientific discipline, IRB approval was not required. Data was obtained through a local program analyst by searching lab test records for patients who have had one or more ANA and reflex ENA tests performed, between July 1, 2023 and July 1, 2024. The search was narrowed to patients who had repeat testing within this time period. 34 patients were identified with repeat tests on different calendar days. Tests repeated on the same day were thought to represent ordering error, and were excluded from analysis. Presumed Diagnosis for positive ANA, changes to ANA results, changes to ENA results, and reasons for repeat testing were extracted for analysis.

**Results**- Between July 1, 2023, and July 1, 2024, 99 repeat ENA tests were completed in 47 patients; 70 of which were tested on different days in 34 patients. Three patients had 3 tests performed.. There was an average of 113.7 days between repeat tests. All patients had a positive ANA with a titer greater than 1:80 as this was a requirement for inclusion. Autoimmune diagnoses associated with positive ANA included rheumatoid arthritis (n=1), antineutrophil cytoplasmic antibodies (ANCA) vasculitis (n=2), dermatomyositis/polymyositis (n=4), discoid lupus Erythematosus (DLE) (n=1), scleroderma (n=1), and mixed connective tissue disorder (n=1). The most common non-autoimmune diagnosis associated with positive ANA was malignancy (n=9). Ten patients had no associated diagnosis explaining their positive ANA.

Repeat ANA testing changed in 19 patients; ANA titer changed in 15 patients, ANA changed from negative to positive in 3 patients, and from positive to negative in 1 patient. None of the 34 patients had clinically meaningful change in repeat ENA tests. Zero of 37 repeat ENA tests demonstrated change in serologies. Two of the 37 repeat (5.4%) ENA tests demonstrated changes in titers that were not clinically significant. Reasons for repeat ANA and reflex ENA testing included five patients with clinical symptom change, in whom none had change in their ENA result. Six patients had repeat testing for serologic monitoring, with no ENA changes noted. There was no discernable reason for repeat testing in 23 (67.6%) patients.

### **Conclusion**–

Among 34 veteran patients with repeat ENA testing on separate days within one year (7/1/2023-7/1/2024), there were no changes in ENA serology. Based on this limited data set, repeat ENA testing in patients would not be recommended within a year unless a substantial clinical change occurred. This is congruent with prior studies that

state that repeating ENA serologies rarely changes or results in a new diagnosis of an ANA-associated rheumatic disease (AARD)(1,2). Further investigation would need to be completed to determine if there is any utility for repeat ENA testing over longer follow-up intervals.

1. Yeo AL, Leech M, Ojaimi S, Morand E. Utility of repeat extractable nuclear antigen antibody testing: a retrospective audit. *Rheumatol Oxf Engl*. 2023 Mar 1;62(3):1248–53.
2. Raissi TC, Hewson C, Pope JE. Repeat Testing of Antibodies and Complements in Systemic Lupus Erythematosus: When Is It Enough? *J Rheumatol*. 2018 Jun;45(6):827–34.