SydPath
ST VINCENT'S PATHOLOGY

www.sydpath.com.au

ANTI-NUCLEAR ANTIBODIES (ANA)

INFORMATION SHEET

INTRODUCTION

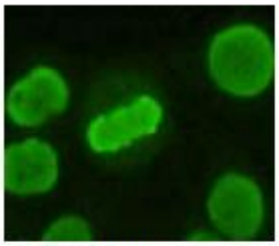
Anti-nuclear antibodies (ANA) are heterogeneous and are directed against various nuclear components. A positive ANA is sensitive, though not specific, for a variety of connective tissue disorders.

DETECTION OF ANA

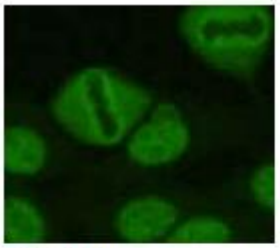
Anti-nuclear antibodies are detected in serum by an immunofluorescence assay in which diluted patient serum is allowed to react with isolated cells on a microscope slide. The result is expressed as a pattern and a titre.

EXAMPLES OF COMMON ANA PATTERNS AND THEIR DISEASE ASSOCIATIONS

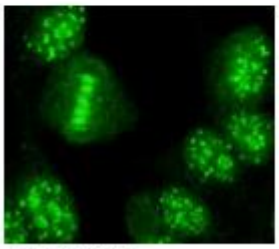
Different immunofluorescence patterns are loosely associated with different diseases and common patterns and diseases are identified below:



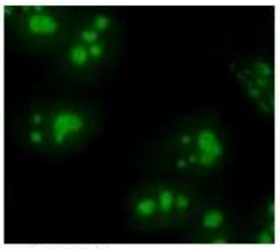
Homogenous
SLE
Drug-induced SLE
Rheumatoid arthritis



Speckled
Connective tissue diseases
Chronic inflammatory disorders



Centromere
Limited form of Scleroderma (CREST)



Nucleolar
Diffuse form of Scleroderma

INTERPRETATION OF ANA

The screening dilution used in SydPath is 1:80. In adults, an ANA titre > or = to 1/160 is of possible clinical significance. However, a positive ANA is clinically significant only in the presence of clinically relevant symptoms. This is because a high titre ANA can be present in up to 10-20% of normal individuals, particularly in women, in relatives of patients with auto-immune disease and with increasing age. ANA can also be seen with use of some drugs (e.g. procainamide, hydralazine, penicillamine, isoniazid, phenytoin, chlorpromazine,

sulfonamides, captopril). Those who have a high titre ANA but no relevant symptom, are thought to have a slightly increased lifetime risk of developing an autoimmune connective tissue disease and review may be required if disease symptoms develop. If the ANA is positive and considered to be of possible clinical significance, investigations outlined below may be helpful in diagnosis and assessment of disease activity.

ADDITIONAL INVESTIGATIONS IN A PATIENT WITH A POSITIVE ANA

1. Antibodies to double stranded DNA (dsDNA)

Highly specific for SLE, but usually only positive in severe aggressive disease and especially in the presence of nephritis. Absence of dsDNA does not exclude the diagnosis of SLE. Antibody levels alter quickly in response to changes in disease activity.

2. Antibodies to Extractable Nuclear Antigens (ENA)

- Sm: rarely seen but if detected, highly specific for SLE
- SSA: suggestive of Sjogren's syndrome, neonatal lupus or a subset of SLE
- SSB: suggestive of Sjogren's syndrome
- RNP: alone and in high levels is suggestive of mixed connective tissue disease.
- Jo-1: seen in some patients with polymyositis / dermatomyositis, and often signifies accompanying interstitial lung disease
- Scl-70: associated with diffuse form of scleroderma

3. Rheumatoid factor and Antibodies to cyclic citrullinated peptide (CCP) *(link)*:

Both antibodies are most frequently present in rheumatoid arthritis but are also seen in other situations, the most common of which is Sjogren's Syndrome (in the latter often in combination with positive ANA and anti-SSA and/or SSB ENAs).

4. Cardiolipin antibody, antibodies to B2GP1 and Lupus Anticoagulant *(link)*

These antibodies mark a group of patients at increased risk of developing arterial or venous thrombosis and recurrent miscarriages. Some of these patients have SLE, with a tendency to CNS involvement and thrombocytopaenia.

5. Complement components C3 and C4

Both tend to be reduced in active SLE because of consumption of components by immune complexes. Levels normalise with disease remission. As C3 and C4 are acute phase reactants, in inflammatory diseases other than SLE, their levels tend to be elevated.

6. Acute phase reactants (CRP, ESR, alpha-1-antitrypsin, fibrinogen, haptoglobin)

Elevated in active acute or chronic inflammatory diseases and fall with remission. Whilst patterns tend to be consistent, in some circumstances, serum levels of only selected proteins of this group are elevated in patients with inflammatory diseases. Very useful for monitoring disease activity.

7. EPG & immunoglobulin (IgG, A, M) levels:

A polyclonal increase in gamma globulins in EPG, or in Ig levels is suggestive of a chronic inflammatory process.