Connective Tissue Diseases (CTD)

Five diseases:

- Systemic lupus erythematosus (SLE)
- Scleroderma
- Polymyositis/dermatomyositis
- Sjögren’s syndrome
- Mixed connective tissue disease

Some clinical features, e.g. Raynaud’s phenomenon, arthralgia/arthritis may be present in all, but it is the production of non-organ specific antinuclear antibodies (ANAs) that characterises these diseases. Antibodies to specific nuclear antigens, e.g. anti-double stranded DNA, anti-RO or anti-LA are seen in each disease (see below). Patients occasionally exhibit clinical and serological features of more than one disease, e.g. scleroderma/polymyositis overlap.

The vasculitides are often grouped with the connective tissue diseases. This is primarily because the target organ (blood vessels) is a connective tissue. Vasculitis may be a feature of the ANA-associated CTDs. Some of the vasculitides are associated with the production of antineutrophil cytoplasmic antibodies (ANCAs), but many patients with vasculitis produce no autoantibodies.

Autoantibodies: A Synopsis

Antinuclear Antibody

- A simple screening test for connective tissue disease found in:
  - SLE (5% ANA negative), scleroderma, polymyositis, Sjögren’s syndrome, mixed connective tissue disease
  - rheumatoid arthritis (RA)
  - autoimmune hepatitis (chronic active hepatitis or primary biliary cirrhosis)
  - also seen with chronic infection and in low titres in normal population
  - titre – the higher the more significant, e.g. > 1 : 160 +
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- If ANA positive in a titre of $\geq 1: 160$, look for antibodies to DS DNA and extractable nuclear antigens (ENA). Among the ENAs are anti-RO, anti-LA, RNP and anti-Sm antibodies.

**Anti-double-stranded-DNA antibody (DSDNA)**
- Elevated in SLE – 70% of patients
- Also RA, chronic active hepatitis, chronic infections, all in low titre
- Titre can act as a guide to disease activity in SLE

**Antibodies to Other Nuclear Antigens**
- Anti-Ro
  - 75% primary Sjögren’s
  - 30% SLE
- Anti-La – less common
  - 50% Sjögren’s
  - 10% SLE
- Anti-Sm (Smith) – SLE
- Anti-RNP – mixed connective tissue disease
- Anti-Jo-1 – polymyositis
- Anti-Scl-70 – diffuse scleroderma
- Anti-centromere antibody – limited scleroderma

**Antineutrophil Cytoplasmic Antibody**
- C-ANCA (cytoplasmic) in Wegener’s (high specificity)
- P-ANCA (perinuclear) in microscopic polyarteritis but also present in many inflammatory diseases e.g. inflammatory bowel disease
- The protein recognised by C-ANCA is proteinase 3, by P-ANCA myeloperoxidase.

**Anti-phospholipid Antibodies**
- see Anti-phospholipid Syndrome (page 75)

**Rheumatoid Factor**
- Positive in approximately 70% with RA
- Also seen in many chronic diseases, other anti-immune diseases, neoplasia. Present in approximately 4% of normal population

**Cryoglobulins**
- Immunoglobulins which precipitate and form a gel in the cold. Soluble at body temperature (37°C)
- Must be transported to laboratory at 37°C