CLINICAL FOCUS

Your guide to key clinical issues in primary care

Connective tissue disorders

Overall key points

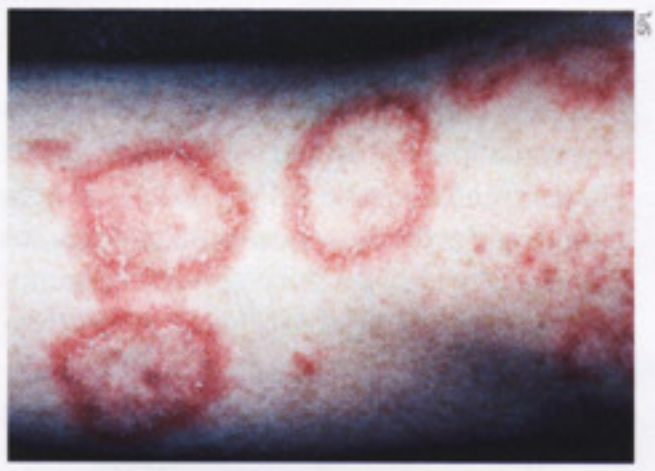
- Lupus is more common than multiple sclerosis and leukaemia.
- The antibody test for lupus is one of the most specific in medicine.
- Sjögren's syndrome is an under-diagnosed connective tissue disease.
- Hughes' syndrome causes many cases of thrombosis and miscarriage.
- Key features of scleroderma include Raynaud's phenomenon.

Part 1 Systemic lupus erythematosus

The autoimmune disorder systemic lupus erythematosus (SLE) has long been under-diagnosed, particularly in the UK. Prevalence is around one in 1,000, predominantly in women.[1] SLE is more common than MS and leukaemia.

Consider SLE in young women aged 15 to 45 years with unexplained prolonged illness. A simple, inexpensive blood test – antinuclear antibody (ANA) – can confirm diagnosis. New cases are unusual after the age of 45.

Fatigue is the cardinal feature of active SLE. Also look for joint pain (often without swelling), odd skin rashes that may be photosensitive and affect the hands, soles, elbows and face, and hair loss. Headaches may be migrainous and there may be adverse drug reactions – especially to sulphur-containing drugs. There may be a history of miscarriage; family history is common, as is a family history of arthritis, skin problems or autoimmune disease.



Atypical skin rashes may be photosensitive

When the neurological features of lupus predominate, the diagnosis may be missed. If in doubt, investigate at least with ANA (see box). American College of Rheumatology criteria are sometimes used in diagnosis. This is wrong: the criteria are for classification only.

SLE is a complex disease that mimics other conditions and fluctuates in severity. All patients should be referred, at least for initial assessment. The best care is collaborative. The London Lupus Centre has eight specialists providing diagnosis and treatment; patients come from all over the UK, but their day-to-day needs are still managed by local physicians.

Investigations for SLE

- FBC: leucopenia (absolute WBC of 2,000–3,000 usual; high WBC (<10,000) rare).
- Urinalysis: all lupus patients should use albumin self-testing strips (proteinuria is commonest early sign of renal involvement).
- ANA: best screening test for SLE (positive in >90 per cent of cases).
- DNA antibody: specific for lupus.
- Anticardiolipin: assesses thrombosis risk.

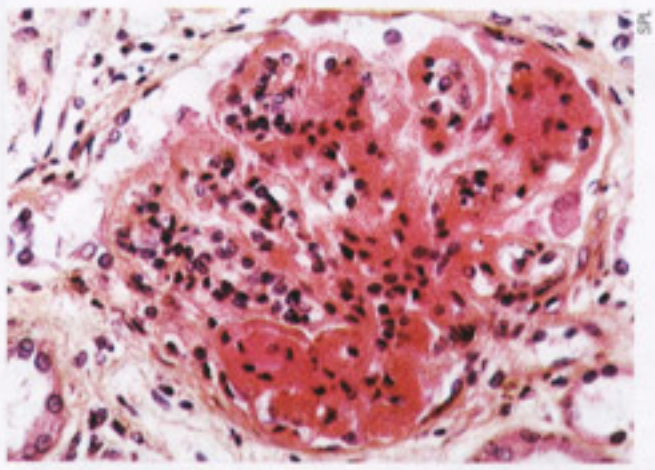
Part 2 Managing SLE

Three major advances in treating SLE are: wider use of antimalarials, a more conservative approach to steroids and immunosuppressives, and recognition of the associated clotting tendency requiring aspirin or anticoagulants in some people. SLE can be well controlled in most patients.

Although steroids are needed (and may even be life-saving) in most lupus patients, it is now recognised that the daily doses of 60mg prednisolone or more that were once used often did more harm than good. Most patients now end up on doses below 10mg daily, and more are being weaned off medication totally.

Hydroxychloroquine 200mg daily is safe and effective. Risk of ocular toxicity at low dose is minimal, even over five years. Patients with severe skin rash may benefit from a second antimalarial, mepacrine. A low dose (100mg) can be added on alternate days.

A move towards more conservative 'pulse' cyclophosphamide regimens in lupus nephritis has drastically reduced associated side-effects of ovarian failure and infection. New immunosuppressives (mycophenolate; rituximab) are finding an important place in treatment.



Renal involvement: control hypertension

Three aspects of general care are increasingly important: prevention and treatment of osteoporosis in patients on steroids; management of hypercholesterolaemia; and strict control of hypertension in those with renal involvement.

There are two special features of SLE in pregnancy – an increased chance of lupus flare in the puerperium and increased risk of miscarriage in patients with antiphospholipid antibodies.

Pharmacotherapy in SLE

- Steroids: most patients now receive below 10mg prednisolone daily.
- Antimalarials: hydroxychloroquine helps fatigue, skin rashes and arthralgia; mepacrine may be added for severe rash.
- Immunosuppressives: eg, cyclophosphamide; mycophenolate (successful in induction and maintenance of lupus nephritis); rituximab (promising in severe SLE).

Part 3 Sjögren's and Hughes' syndromes

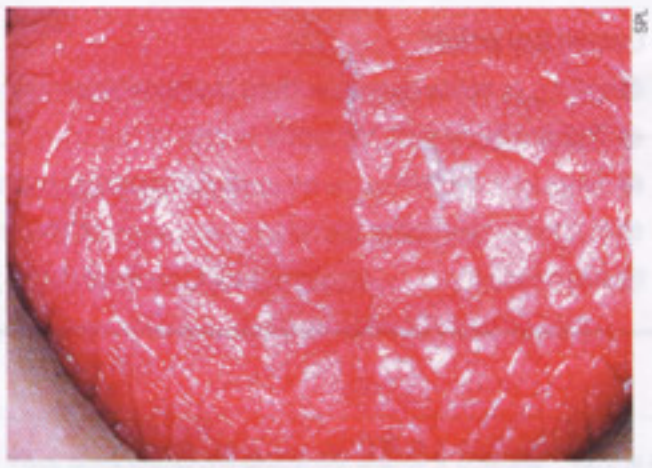
Sjögren's syndrome, one of the most underdiagnosed connective tissue diseases, should be regarded as the first cousin of lupus – less dramatic but with similar features associated with an oyeractive immune system. It is most commonly diagnosed in 50 to 60 year olds, and has a female to male ratio of 9:1.

Sjögren's syndrome should be considered in middle-aged women with aches and pains or chronic fatigue syndrome (CFS). Schirmer's test is vital in differential diagnosis, and the ANA blood test is usually positive.

The classically described dry eyes, mouth and tongue with arthritis only tell a fraction of the story. Fatigue, arthralgia and myalgia are common. Symptoms vary from mild aches to full-blown and sometimes acute rheumatoid arthritic-like synovitis; attacks can be episodic.

Dry mucous membranes are a hallmark but patients complain of gritty rather than dry eyes. Dryness may affect the mouth (making swallowing difficult), vagina (causing dyspareunia), and neck of the bladder (giving symptoms of interstitial cystitis).

Patients with Sjögren's suffer more allergies; allergy to Septrin is almost universal and some give clear histories of food allergy. Sjögren's is a genuine cause of joint pain that occurs after eating certain foods.



A dry mouth and tongue are typical signs

Treatment involves artificial tears (hypromellose eye drops) and artificial saliva. Hydroxychloroquine 200mg daily can help fatigue and arthralgia. Low-dose steroids are occasionally used for flare-ups and immunosuppressives (eg, azathioprine or methotrexate) can be used in persistent cases.

In 1983 we reported a syndrome consisting of thrombosis (venous and arterial), recurrent miscarriage and other features, characterised by presence of antibodies against phospholipids, which also existed outside of lupus.[3] In 1995, I was honoured with the discovery, which was named Hughes' syndrome.

'Sticky blood', often used to describe the syndrome, refers to the risk of thrombosis and stroke in particular.[4] The anticardiolipin blood test confirms diagnosis; the lupus anticoagulant test is a clotting test.

Anticoagulants are required – most widely used is aspirin (75–150 mg daily); warfarin is vital in major thrombosis. Treatment can be dramatically effective. If 40 per cent of strokes in the under-40s are due to this treatable condition, there are enormous potential benefits for patients and the NHS.

Hughes' syndrome

Suspect a diagnosis in those with:

- Unexpected stroke or recurrent miscarriage.
- Recurrent DVT, any unexpected thrombosis, pulmonary embolism or atypical multiple sclerosis.
- Recurrent migraine, memory loss (from patchy cerebral ischaemia) and early, unexpected arterial disease can all be associated.

Part 4 Scleroderma

The two cardinal features of scleroderma are Raynaud's phenomenon and skin tightening. The disease takes many forms, ranging from localised (cutaneous) scleroderma to progressive, fatal systemic disease.

This rare condition, like most autoimmune conditions, affects females more than males. Aetiology is unknown though in some cases an environmental cause has been suspected.

Scleroderma usually begins with Raynaud's phenomenon. This is often severe and sometimes precedes other features by many years. There is then progressive tightening of the skin, with shininess and atrophy.

Fingers and hands are usually affected first. The skin around the eyes and mouth is often affected early on and tightening of the skin occurs in these situations. In progressive cases, skin of the entire body becomes thickened and atrophied, with underlying muscle wasting and weakness.

Involvement of the lungs leads to fibrosis with the patient complaining of dyspnoea. Crackles are heard on auscultation. In some cases fibrosis becomes so severe that there is respiratory failure or pulmonary hypertension.

Scleroderma affecting the GI tract most commonly presents with dysphagia from oesophageal involvement. If the whole length of the bowel is involved this can lead to other problems including malabsorbtion.

Renal involvement can lead to chronic renal failure, and can also present as significant hypertension.

As yet there is no specific treatment for scleroderma, other than managing the secondary phenomena.

Key points

- The two cardinal features are Raynaud's phenomenon and skin tightening.
- Aetiology is unknown but an environmental cause has been suspected in some cases.
- The disease usually begins with Raynaud's phenomenon, followed by progressive tightening of the skin.
- There is no specific treatment other than management of secondary phenomena.

Resources

- Hughes G. *The big three (Lupus, Sjögren's and Hughes' syndrome)*. Available from the Hughes' Syndrome Foundation: tel 020 7960 5561; www.hughes-syndrome.org
- Hughes G. *Hughes' syndrome: A guide for patients*. Springer Verlag. Also available from the Hughes' Syndrome Foundation.
- *Lupus: a patient's guide*. Available from St Thomas' Lupus Trust: tel 020 7188 3562; www.lupus.org.uk
- Khamashta M, editor. *Hughes' syndrome. Antiphospholipid syndrome*. Springer Verlag; 2006.

References

1. D'Cruz DP. Systemic lupus erythematosus. *BMJ* 2006;332:890-94.
2. Tincani A, et al. Pregnancy, lupus and antiphospholipid syndrome (Hughes syndrome). *Lupus* 2006;15:156-60.
3. Hughes GR. Thrombosis, abortion, cerebral disease and the lupus anticoagulant. *BMJ* 1983;287:1088-9.
4. Hughes GR. Migraine, memory loss and 'multiple sclerosis'. Neurological features of the antiphospholipid (Hughes') syndrome. *Postgrad Med J* 2003;79:81-83.

An archive of key articles is available at www.independentnurse.co.uk

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