Scleroderma spectrum diseases comprise Raynaud’s phenomenon, the clinically distinct subsets of scleroderma and localised scleroderma.

Accurate disease subsetting and staging of the disease within each subset are critical in initial assessment of patients with scleroderma.

Strong associations between autoantibody specificities and disease presentation and outcome support serological profiling as an essential tool in the assessment of scleroderma.

Screening for major complications facilitates early intervention and may improve disease outcome in diffuse cutaneous systemic sclerosis.

Current evidence supports targeted immunosuppression and advanced therapies for significant interstitial lung disease and pulmonary arterial hypertension.

Introduction

The various forms of systemic sclerosis (SSc) are the most important subgroups of a spectrum of disorders, which includes Raynaud’s phenomenon and localised scleroderma conditions, collectively referred to as ‘scleroderma’. In these conditions there is an important interplay between inflammatory, vascular and fibrotic features which may affect the skin and internal organs. There are several discrete subsets of SSc and these must be considered in diagnosis and management. An important group of cases shares clinical and laboratory features of other autoimmune rheumatic conditions, the SSc overlap syndromes. A working classification of scleroderma is outlined in Figure 1. It is important to highlight that while the localised and systemic forms of the condition are distinct and patients with localised scleroderma may be confidently reassured that they will not develop internal organ manifestations as a direct result of their condition, there is an increasing number of cases in which there is co-existence of localised and systemic forms of the disease. This is most clearly evident in cases of limited cutaneous systemic sclerosis ( lcSSc) that develop areas of localised scleroderma.
Differential diagnosis for the scleroderma spectrum

Although the hallmark of scleroderma is ‘hard skin’, or dermal fibrosis, this is only one aspect of the disease. It is important when considering a diagnosis within this spectrum first to assess the presence of cardinal features such as Raynaud’s phenomenon and skin involvement. The algorithm illustrated in Figure 2 offers a simple approach to discrimination of cases within the spectrum. It is also important to consider other causes of skin change that may mimic scleroderma. These are listed in Table 1 and some of these diseases could be considered as scleroderma variants and may provide important insight into common pathogenic mechanisms. Others are clinical mimics but likely to have a very different mechanism and require specific approaches to therapy. For example, in the case of metabolic diseases, these need to be managed systemically. Raynaud’s phenomenon provides the other main source for differential diagnosis. It is important to differentiate the various forms of Raynaud’s phenomenon from other causes of acrocyanosis or circulatory insufficiency. Some very important differential diagnoses, such as vasculitis, atrial myxoma or critical macrovascular disease, are uncommon but serious and will require urgent specific therapy. The mimics of Raynaud’s phenomenon are listed in Table 2.

Raynaud’s phenomenon

Raynaud’s phenomenon is a common symptom and most often is not associated with any underlying disease when it is designated primary Raynaud’s phenomenon. Such cases are mostly

- Primary Raynaud’s phenomenon
- Autoimmune Raynaud’s phenomenon

Internal organ disease

- Vasculopathy

Skin sclerosis

- Limited systemic sclerosis
- Limited cutaneous systemic sclerosis
- Diffuse cutaneous systemic sclerosis
- Systemic sclerosis sine scleroderma
- Scleroderma overlap syndromes

Localised

- Morphoea
  - Localised
  - Generalised
- Linear scleroderma
- Linear scleroderma en coup de sabre

**FIGURE 1.** The clinical spectrum of scleroderma: hallmark pathological processes of vasculopathy, inflammation, fibrosis.

**FIGURE 2.** Differential diagnosis within the scleroderma spectrum.

- Raynaud’s phenomenon
  - Antinuclear antibodies
  - Systemic sclerosis-specific reactivity
  - Abnormal nailfold capillaries
  - Trophic changes (pitting scars, pulp loss, ulcers)

- Isolated Raynaud’s phenomenon
  - Peripheral oedema
  - Gastro-oesophageal reflux
  - Heart, lung, kidney, bowel manifestations

- Overlap connective tissue diseases

- Systemic sclerosis

- Plaque or linear distribution
- Subcutaneous involvement
- Boggy texture
- Acral sparing
- Contractures

- Localised scleroderma

Skin sclerosis
seen in women and typically the symptoms start in teenage years of early adult life. The hallmarks of primary Raynaud’s phenomenon are early age of onset, family history of Raynaud’s phenomenon and absence of clinical features of an associated disease. It is very unusual to demonstrate trophic changes (e.g. finger-tip pulp atrophy or pitting scars), digital ulceration or gangrene in cases of primary Raynaud’s phenomenon. Secondary Raynaud’s phenomenon most often occurs in the context of a connective tissue disease (CTD) and although SSc is the most recognised association, SSc overlap syndromes and mixed or undifferentiated CTD are the other major conditions linked with Raynaud’s phenomenon. Only around 1% of Raynaud’s phenomenon cases are associated with a defined CTD. There is an important intermediate group of cases that demonstrates some of the serological features or microvascular abnormalities seen in Raynaud’s phenomenon. The latter can be seen at nailfold capillaroscopic assessment. Capillary drop-out and later haemorrhage or dilatation with structurally abnormal capillaries are cardinal features. The group of cases of Raynaud’s phenomenon with these abnormalities is important in that a significant proportion will eventually progress to develop a more defined CTD. These cases are therefore often designated pre-scleroderma (although many do not develop into full-blown SSc) or autoimmune Raynaud’s phenomenon. Our practice is to follow these cases on an intermittent basis although progression may only occur after 5–10 years of follow-up. It is important to appreciate that some patients with early SSc do not exhibit Raynaud’s phenomenon and that in particular in rapidly progressive diffuse cutaneous systemic sclerosis (dcSSc) the Raynaud’s phenomenon that is universal in established disease may develop some time after onset of skin or other manifestations. Absence of Raynaud’s phenomenon therefore cannot be taken as excluding SSc in new onset cases. Management of Raynaud’s phenomenon depends upon avoiding precipitants, smoking cessation and good patient education. A variety of supplements and vitamins are reported by patients to be helpful although formal evidence of benefit is sparse. The most severe cases may benefit from prescription vasodilator drugs. Calcium channel blockers are often tried first but other agents that have been found to be helpful include angiotensin II receptor blockers and in some cases selective serotonin reuptake antagonists, which appear to reduce vasospasm and may act through depletion of platelet serotonin levels.

### Localised scleroderma

The localised forms of scleroderma are classified according to the distribution, number and extent of lesions. In adults these forms of scleroderma are generally less severe than SSc although the most extensive cases of generalised morphea are severe and often require systemic therapy. Linear scleroderma may be associated with trophic changes and involvement of subcutaneous connective tissue. This is most dramatic in cases of parasagittal linear scleroderma of the scalp or face – en coup de sabre. Plaque morphea is the mildest form of localised scleroderma and may be treated topically or with phototherapy. Systemic treatment in childhood-onset localised scleroderma includes corticosteroid therapy and systemic immunosuppression with methotrexate. Other immunosuppressive therapies may be used in refractory cases. Extension of existing lesions or development of new lesions is generally taken as evidence of activity. Infrared thermography may provide a valuable adjunct to clinical assessment of disease activity although changes due to local atrophy in later disease may be misleading.

### Systemic sclerosis

The most important conditions within the scleroderma spectrum are the various forms of SSc. There has been a tremendous growth in understanding about the clinical features of SSc with more logical and systematic approaches to disease management. In particular the importance of standardised baseline assessment and longitudinal
follow-up has been recognised. These approaches have led to a significant improvement in outcome and recent published series suggest that 5-year survival for dcSSc has improved from 69% to 84% in the current era.\(^3\)

**Epidemiology and classification**

SSc is uncommon rather than rare. Estimates of disease frequency suggest that approximately 1 in 10000 individuals are affected. This includes all subsets of the disease, and approximately one-fifth of cases demonstrate overlap features. There are new efforts to update the criteria for classification and diagnosis of SSc that will be more complete and represent recent changes in approach to assessment of SSc. The major subsets of SSc – dcSSc and lcSSc – are based upon the extent of skin involvement; patients classified as having dcSSc have proximal skin sclerosis. However, the subsets are much more diverse than this implies. The key characteristics of both subsets are listed in Table 3. With the exception of those who lack overt skin involvement but who harbour specific SSc antibodies against the hallmark antigens or who have SSc-associated capillaroscopic changes, whose disease may be described as ‘limited scleroderma’, all patients start with mild skin disease; those with lcSSc will, however, generally have a long preceding history of Raynaud’s phenomenon.

It is important to appreciate that while the frequency of individual internal organ complications differs between the major subsets, any complication can occur in either subset. The limitations of skin-based subsetting and the strong clinical association between individual scleroderma-associated auto-antibodies have suggested that classification based upon autoantibody profile may be more useful than the two skin-based subsets.\(^4\) It also transcends overlap cases that do not always fit easily within the major subsets. The individual associations for SSc-associated autoantibodies are listed in Table 4. There are emerging data that suggest that molecular correlates of the subgroups of SSc may be developed based upon gene expression signatures but as in other areas of molecular classification the advantages of such an approach have yet to be confirmed.\(^5\) Exciting possibilities in the future may depend upon studies that confirm likely efficacy for targeted therapies.

**Management of systemic sclerosis**

There has been a major shift in the general approach to management of patients with SSc. It is important to identify and treat organ-based disease at the earliest possible moment and therefore all cases should have comprehensive baseline assessment of cardiac, renal, pulmonary and gastrointestinal tract features of their disease.\(^6\) Subset classification and determining the stage of disease as

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**TABLE 2. Differential diagnosis of Raynaud’s phenomenon**

<table>
<thead>
<tr>
<th>Primary Raynaud’s phenomenon</th>
<th>Familial, onset in adolescence, female preponderance, no pulp tissue loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary Raynaud’s phenomenon</strong></td>
<td></td>
</tr>
<tr>
<td>Connective tissue disease-associated Raynaud’s phenomenon</td>
<td>SSc, SLE, polymyositis, MCTD, UCTD. Positive serology and abnormal nailfold capillaroscopy</td>
</tr>
<tr>
<td>Primary vasculitis</td>
<td>Typical rash, tissue loss and gangrene</td>
</tr>
<tr>
<td>Buerger’s disease</td>
<td>Smoking history, digital infarction, typical arteriographic features</td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome</td>
<td>Associated clinical context. Positive serology</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>Fixed insufficiency, predominant lower limb claudication</td>
</tr>
<tr>
<td>Embolic disease</td>
<td>Myxoma, infective endocarditis, macrovascular disease, PFO with paradoxical embolism</td>
</tr>
<tr>
<td>Cryoglobulinaemia</td>
<td>Serology, rash and associated haematological features</td>
</tr>
<tr>
<td>Paraproteinaemia</td>
<td>Hyperviscosity syndrome</td>
</tr>
</tbody>
</table>

**Other related conditions**

- Haematological – cold agglutinin disease
- Vibration white finger
- Thoracic outflow syndrome
early or late is important as those with early-stage dcSSc are particularly at risk of complications such as renal crisis and also show a higher frequency of severe lung fibrosis. Other complications such as pulmonary arterial hypertension (PAH) tend to occur later and emphasise the importance of ongoing regular assessment. Non-invasive testing performed at annual or semi-annual intervals has been adopted as a standard of care approach. Even in slowly progressive disease it is important to define the trend of organ dysfunction. As well as considering the life-threatening complications of SSc, it is critical that morbidity of the disease is also addressed. There are major complications that do not directly impact on survival but may pose tremendous practical problems. Issues related to dental care, calcinosis, sexual dysfunction and altered facial and general appearance may have a deleterious effect on quality of life in addition to emotional and psychological well-being.

Disease-modifying therapies for SSc are not available but all cases should be treated.7 Vascular manifestations such as Raynaud’s phenomenon and other complications can be addressed. Gastrointestinal tract symptoms can be ameliorated, especially gastro-oesophageal reflux. In patients with active dcSSc our practice is to recommend immunosuppressive treatment.8 Although formal clinical evidence for efficacy is lacking there is a wealth of experience that supports this approach and emerging data confirm the superiority over placebo of cyclophosphamide in treatment of lung involvement and of cyclophosphamide or methotrexate in management of skin sclerosis.9–11 Mycophenolate mofetil has been widely used, is well tolerated and may be considered. It is undergoing prospective evaluation as a treatment for SSc-associated lung fibrosis. So far there are no proven antifibrotic therapies but several agents are under evaluation including anticytokine strategies (e.g. anti-TGFβ1) and inhibitors of profibrotic cytokine signalling pathways such as imatinib mesylate. A scheme indicating general approaches to the management of SSc is summarised in Figure 3.

Management of specific organ-based complications

Pulmonary arterial hypertension

Pulmonary arterial hypertension (PAH), defined as an elevation in the mean pulmonary artery pressure

<table>
<thead>
<tr>
<th>TABLE 3. Hallmark features of the major subsets of systemic sclerosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited cutaneous disease</td>
</tr>
<tr>
<td>• Skin sclerosis confined to extremities and face but may extend to forearms</td>
</tr>
<tr>
<td>• Maximum skin score &lt;18 and skin shows indolent progression</td>
</tr>
<tr>
<td>• Prominent Raynaud’s phenomenon with long pre-existing history</td>
</tr>
<tr>
<td>• Lung fibrosis and PAH common</td>
</tr>
<tr>
<td>• Gastrointestinal tract disease universal</td>
</tr>
<tr>
<td>• Low risk of scleroderma renal crisis</td>
</tr>
<tr>
<td>• Classical cases with calcinosis, Raynaud’s phenomenon, oesophageal reflux, sclerodactyly and telangiectasia may be designated CREST syndrome but vigilance for other complications is essential</td>
</tr>
<tr>
<td>• ACA is the most frequently associated SSC-specific antibody</td>
</tr>
<tr>
<td>Diffuse cutaneous disease</td>
</tr>
<tr>
<td>• Proximal skin involvement on limbs, chest and abdominal wall</td>
</tr>
<tr>
<td>• Short pre-existing Raynaud’s phenomenon history</td>
</tr>
<tr>
<td>• Skin and joint symptoms may precede Raynaud’s phenomenon</td>
</tr>
<tr>
<td>• High risk of lung fibrosis and renal crisis</td>
</tr>
<tr>
<td>• Frequency of PAH and digital ulcers similar to lcSSc</td>
</tr>
<tr>
<td>• All organ-based complications may occur with greater frequency overall than in lcSSc</td>
</tr>
<tr>
<td>• Peak skin sclerosis score &gt;18 and correlates with outcome. Skin progression often rapid in first 18 months and usually plateaus or improves in second and subsequent years of disease</td>
</tr>
<tr>
<td>• Anti-topoisomerase and anti-RNA polymerase III antibodies are SSC-specific antibodies</td>
</tr>
</tbody>
</table>

ACA anticentromere antibody; dcSSc diffuse cutaneous systemic sclerosis; lcSSc limited cutaneous systemic sclerosis; PAH pulmonary arterial hypertension; RNA ribonucleic acid; SSc systemic sclerosis
>25 mmHg at rest, occurs in both limited and diffuse cutaneous forms of SSC, and is a leading cause of mortality. The outcome in SSC-associated PAH is considerably worse than that of idiopathic PAH. This may reflect co-morbidity or differences in underlying pathogenetic mechanisms. In SSC, PAH due to intrinsic fibroproliferative abnormalities in the pulmonary vasculature, pathologically indistinguishable from idiopathic PAH, is most common, with a prevalence of approximately 10–15%.

The second pattern of pulmonary hypertension occurs in association with pulmonary fibrosis, and is driven by hypoxia as well as the destruction of the pulmonary vascular bed. PAH in SSC also occurs in the context of lung fibrosis, and typical histological changes of PAH may be found in lung biopsies from these patients. Indeed, it has been suggested that it is coexistent vasculopathy that determines outcome and survival in many cases of SSC-associated pulmonary fibrosis. PAH may remain asymptomatic until quite advanced. The initial symptoms include exertional breathlessness, and less often chest pain or syncope. In patients with SSC, it is typically detected during regular monitoring with pulmonary function tests (PFT), Doppler-echocardiography and electrocardiography (ECG) assessments. An isolated reduction in single-breath diffusion capacity (DLCO) with preservation of lung volumes is suggestive of PAH. Cardiac catheterisation is essential for diagnosis. Serum levels of the N-terminal pro-brain natriuretic peptide (BNP) may be helpful for screening and monitoring. The levels of serum BNP correlate with survival in patients with SSC-associated PAH. The current focus in the evaluation is on early identification and determination of severity. The World Health Organization/New York Heart Association (WHO/NYHA) functional classification is useful for assessment of severity of PAH and guidance for treatment decisions. Treatment options for functional class III PAH include oral endothelin-1 (ET-1) receptor blockade and 5'-phosphodiesterase inhibitor. Alternative therapies include inhaled and subcutaneous prostacyclin analogues. Intravenous agents are generally reserved for patients with severe or advancing PAH. Despite recent progress, the management of PAH remains a major challenge. This is a result of the poor outcome of SSC-associated PAH compared with idiopathic PAH, and the lack of high-quality evidence addressing issues such as combination therapy and the benefits of early intervention. Once the diagnosis of PAH is confirmed, the contribution of associated interstitial lung disease is considered. Patients with significant hypoxaemia benefit from supplemental oxygen. It is possible that lung fibrosis treatments such as immunosuppression may be appropriate (see below). In the absence of contraindication, supportive therapy with diuretics, oral anticoagulation and in some cases digoxin is considered. Patients in functional class III are eligible for advanced therapy. Our practice is to commence treatment with an oral ET-1 receptor antagonist when functional class III is reached; lack of response prompts

<table>
<thead>
<tr>
<th>Reactivity</th>
<th>Target antigen</th>
<th>Frequency</th>
<th>Clinical association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scl-70</td>
<td>Topoisomerase-1</td>
<td>30% dcSSc; 10% lcSSc</td>
<td>• Diffuse skin sclerosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Pulmonary fibrosis</td>
</tr>
<tr>
<td>RNAP</td>
<td>RNA polymerase III</td>
<td>25% dcSSc; 2% lcSSc</td>
<td>• Diffuse skin sclerosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Hypertensive renal crisis</td>
</tr>
<tr>
<td>Centromere</td>
<td>CENP-B protein</td>
<td>50% lcSSc; 2% dcSSc</td>
<td>• Limited skin sclerosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Severe gut disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Isolated PAH</td>
</tr>
<tr>
<td>nRNP</td>
<td>U1-RNP</td>
<td>15% Sc</td>
<td>• Overlap features of SLE, arthritis</td>
</tr>
<tr>
<td>PM-Scl</td>
<td>PM-Scl</td>
<td>5% Sc</td>
<td>• Myositis–systemic sclerosis overlap</td>
</tr>
<tr>
<td>Th/To</td>
<td>Ribonucleoprotein</td>
<td>5% Sc</td>
<td>• Associated with lung involvement in lcSSc including PAH</td>
</tr>
<tr>
<td>U3-RNP</td>
<td>Fibrillarin protein</td>
<td>5% Sc</td>
<td>• Isolated PAH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Cardiac involvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Myositis and poor outcome in dcSSc</td>
</tr>
</tbody>
</table>

dcSSc diffuse cutaneous systemic sclerosis; lcSSc limited cutaneous systemic sclerosis; PAH pulmonary arterial hypertension; SLE systemic lupus erythematosus
switching to a 5'-phosphodiesterase inhibitor, whereas partial response or transient response generally results in addition of 5'-phosphodiesterase inhibitor. Further deterioration can be managed by adding inhaled iloprost or parenteral prostacyclin. Recent recommendations have been published by several authoritative bodies.13

**Pulmonary fibrosis**
The commonest forms of interstitial lung disease in SSc are histologically classified as non-specific interstitial pneumonia and usual interstitial pneumonia. Investigation and assessment of interstitial lung disease in SSc focuses on early detection, severity assessment and determination of progression that is best performed by regular PFTs. High resolution computerised tomography (HRCT) imaging remains the most valuable tool for detection of early lung fibrosis. Interstitial lung disease develops insidiously and generally progresses to fibrosis. Mildly symptomatic SSc patients often have normal chest radiographs despite interstitial lung disease, and PFTs are more discriminatory in this respect. DLCO is abnormal in over 70% of patients with dcSSc, including asymptomatic patients with normal chest radiograph. A reduction in DLCO is the earliest detected abnormality in SSc patients who go on to develop interstitial lung disease. The combination of normal lung volumes but reduced gas transfer in the face of normal chest imaging is suggestive of pulmonary vascular disease. The earliest detectable HRCT abnormality is a narrow, often ill-defined, subpleural crescent of increased density in the posterior segments of the lower lobes. It is important to perform HRCT in both prone and supine positions, particularly in patients with early SSc, in order to exclude the contribution of gravity to the radiographic appearances from vascular and interstitial pooling in the dependent areas. In addition to identifying early disease, HRCT can be used to quantify the extent and delineate the pattern of lung abnormality. A simple staging system has been developed that separates cases into mild or extensive disease that can be observed carefully or those requiring treatment with immunosuppression.14 There is now good evidence showing that some cases respond to cyclophosphamide15 but the limited treatment effect must be balanced against the well-known toxicity of this agent.

**Cardiac disease**
The frequency of significant cardiac involvement in SSc has been difficult to ascertain, although it is believed to be relatively frequent and can have a major impact on survival. A potential consequence of myocardial involvement is reduction in the ability to cope well with intercurrent haemodynamic cardiac stress such as that due to electrolyte disturbance, fluid shift or acidosis. Both the pericardium...
and the myocardium are frequently affected. In contrast to myocardial involvement, abnormalities of the pericardium are relatively easy to detect by virtue of the formation of a pericardial effusion. Up to 35% of SSc patients are found to have haemodynamically insignificant effusions.

**Gastrointestinal tract complications**

The gastrointestinal tract is the most commonly involved internal organ system in both diffuse and limited cutaneous subsets of SSc, and almost any part may be affected. Oesophageal involvement is frequent with dysmotility and lower oesophageal sphincter dysfunction. In patients with frank dysphagia, oesophagoscopy may be required to identify structural changes such as hiatus hernia, oesophageal strictures or Barrett’s metaplasia. The stomach is frequently involved, with delayed gastric emptying that can lead to postprandial bloating and vomiting. Gastrointestinal haemorrhage from gastric antral vascular ectasia may result in chronic iron-deficiency anaemia and these may be amenable to laser photocoagulation therapy. Severe involvement of the small intestine typically occurs in patients with established SSc, and can be a major cause of morbidity and mortality. At its most severe, small intestinal involvement leads to recurrent episodes of intestinal pseudo-obstruction due to ileus with dilated small bowel loops. Although clinical suspicion is raised by features of pseudo-obstruction, there are also characteristic abnormalities on diagnostic imaging. Contrast studies may show the characteristic ‘stack of coins’ sign. Small bowel bacterial overgrowth complicating hypomotility results in recurrent diarrhoea and bloating, and in more severe cases leads to malabsorption, weight loss, malnutrition and cachexia. The classic symptoms are change in bowel pattern, with frequent loose, floating, foul-smelling stools, and abdominal distension. Management of advanced bowel disease includes cyclical antibiotics, stimulation of intestinal motility with prokinetic agents such as erythromycin or domperidone, and supplemental alimentation. In the short term, nocturnal feeding to maintain nutrition and a nasogastric or nasojejunal feeding tube may be effective. Longer-term nutritional supplementation requires percutaneous jejunostomy, or gastroscopy if stomach emptying is not delayed. Pancreatic insufficiency may also contribute to diarrhoea and pancreatic enzyme supplementation should be considered for those individuals in whom antibiotic therapy has not been successful. Large bowel involvement is commonly manifested by constipation, which may be complicated by sigmoid volvulus. Anorectal incontinence is a frequent manifestation. Investigations include anal manometry and imaging to assess the integrity of the internal and external anal sphincter. A trial of biofeedback can be used although treatment response is often unsatisfactory. Sacral nerve stimulators with electrodes placed through the sacral foramen may be helpful in selected cases of severe faecal incontinence.

**Scleroderma renal crisis**

Scleroderma renal crisis typically causes accelerated hypertension and acute renal failure. Until the advent of angiotensin converting enzyme (ACE) inhibitors, scleroderma renal crisis was associated with a very high mortality. Over recent decades, mortality at 1 year fell from 85% to 24%. Other patterns of renal involvement in SSc include chronic vasculopathy with reduced glomerular filtration rate. Patients with overlap SSc may develop inflammatory glomerular disease including glomerulonephritis or vasculitis, typically associated with serological features of these diseases. Scleroderma renal crisis occurs in 10–15% of patients with dcSSc and only very rarely (1–2%) in lcSSc. Anti-RNA polymerase III antibodies are strongly predictive for renal crisis. Corticosteroids, along with ciclosporin, have been implicated as precipitants of scleroderma renal crisis. Microangiopathic haemolytic anaemia is common, and disseminated intravascular coagulation may develop. Approximately two-thirds of cases of scleroderma renal crisis require renal replacement therapy. Of these half eventually recover sufficiently to discontinue dialysis. This can occur for up to 24 months, and so decisions about renal transplantation should be postponed until that time. The possibility for delayed renal recovery distinguishes scleroderma renal crisis from other causes of end-stage renal failure. Improved outcomes are achieved with the use of ACE inhibitors as routine therapy for renal crisis. The efficacy of ACE inhibitors precludes future placebo-controlled studies in treating established scleroderma renal crisis. Nonetheless, the outcome of scleroderma renal crisis remains poor, with early mortality approaching 10%. It is likely that alternative vascular protective strategies such as prostacyclin supplementation and ET-1 receptor blockade may offer additional benefit in renal crisis but, unlike ACE inhibitors, these therapies will need to be formally assessed in future clinical trials.
Future perspectives

There has been much progress in management of SSc over the past decade and this has been associated with improvements in overall outcome. However, it remains a major challenge for clinicians and a diagnosis that needs to be made promptly so that appropriate specialist services can be accessed. There are emerging novel therapies and recommendations for management of specific complications with an appreciation of the importance of holistic approaches to cases and the central role of a multidisciplinary team. Through positive clinical trials and greater research collaboration and international co-operation there are now many more reasons to be positive about scleroderma and it is likely that outcomes and management will improve further over the next few years. In its worst forms it remains one of the most devastating and challenging of the autoimmune rheumatic diseases.

References

This is a public awareness campaign developed by the Rheumatology Futures Project Group (RFPG) and endorsed and supported by Arthritis Research UK, the Royal College of General Practitioners and the Primary Care Rheumatology Society.

The RFPG are also hoping for Department of Health backing for this campaign, which was one of the key recommendations in the National Audit Office Report published in July 2009.

Please download the poster (via www.arthritisresearchuk.org) and display it in your outpatients department, consulting rooms or any public areas of your hospital, or contact us (enquiries@arthritisresearchuk.org) and we will send you some.
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