

### What are the extra-articular causes of knee pain?

Anatomical structures with sensory nerve supply include the patellar tendon, retinacular tissue, bursa, synovial tissue and the fat pads. Patellar and quadriceps tendinopathy may be caused by mechanical factors, overload or enthesitis. Inflammation in the infrapatellar fat pad (Hoffa's fat pad) presents with anterior knee pain below the pole of the patellar with exacerbation of the symptoms by knee extension.

A common cause for anteromedial pain is inflammation of the pes anserine bursa, which separates the medial collateral ligament and the medial hamstring tendons. Pain is worse on knee extension, resisted knee flexion and/or adduction of the legs.<sup>5</sup>

### What is the 'too many toes' sign?

The posterior tibial tendon is responsible for the suspension of the medial arch of the foot. Dysfunction of the tendon either from degenerative changes or inflammatory disorders results in an acquired flat foot with valgus hindfoot and forefoot abduction. If the foot is inspected from behind, more toes are visible lateral to the ankle than will be seen in a normal foot.<sup>6</sup>

### What are the risk factors for Achilles tendon rupture?

The three common sites of rupture are the hypovascular region of the tendon, which can be found 2 - 6 cm proximal to the insertion, the enthesial site and the musculotendinous junction. Enthesitis from inflammatory rheumatic diseases such as seronegative spondyloarthropathies, rheumatoid arthritis and gout predisposes the patient to tendon rupture. Other causes of rupture may include steroid treatment, particularly local administration of steroid, xanthomas and oral fluoroquinolones.<sup>6</sup>

### What are the soft-tissue causes of forefoot pain?

One of the most common soft-tissue masses of the foot are the ganglia, often located dorsal to the metatarsophalangeal joints and tendons. Bursitis may occur in the intermetatarsal areas or beneath the metatarsal heads secondary to repetitive trauma, infection or inflammatory disorders.

Sharp burning pain in the ball of the foot usually located between the 3rd and 4th metatarsal heads is most likely due to a Morton's neuroma. This is not a tumour but is related to peripheral fibrosis following compression of the interdigital nerves. Therapy includes changing footwear, orthotics and steroid infiltration.<sup>6</sup>

### Summary

- Lower limb pain is a common presenting complaint with numerous aetiological factors.

- Due consideration of mechanical, traumatic and repetitive strain disorders as well as a search for metabolic and inflammatory conditions will allow for early diagnosis and management.

References available at [www.cmej.org.za](http://www.cmej.org.za)

## The lungs in the rheumatic diseases

**ISMAIL S KALLA, MB BCH, FCP (SA), FCCP (USA), Cert Pulmonology (SA), Cert Critical Care (SA)**

*Pulmonologist/intensivist, Department of Pulmonology and Critical Care, University of the Witwatersrand, Johannesburg*

Correspondence to: I S Kalla ([isk786@telkomsa.net](mailto:isk786@telkomsa.net))

There are many different approaches to the evaluation of the lungs in patients with collagen vascular diseases. Many books have been published about the evaluation of the lungs in patients with rheumatic diseases (connective tissue diseases (CTDs) and rheumatoid arthritis (RA)). Unfortunately, it still remains a challenging task – even for a pulmonologist. As with all medical conditions, there is no substitute for a thorough history and careful examination of the patient. Although significant heterogeneity exists among the different collagen vascular diseases, they share one aspect that is common to their pathogenesis: circulating auto-antibodies and immune-mediated organ dysfunction.

There are several tools to evaluate the lungs of patients with a CTD. Currently none is as valuable as the chest radiograph as an initial screening tool to exclude major pathology. If pathology is identified, a high-resolution computerised tomography (HRCT) scan of the chest is performed to confirm the pathology and ascertain a possible aetiology.<sup>1-3</sup> The most important rheumatic diseases that affect the lungs include:

- RA
- systemic lupus erythematosus (SLE)
- systemic sclerosis
- Sjögren's syndrome
- polymyositis /dermatomyositis /anti-synthetase syndromes
- mixed CTDs
- primary vasculitic syndromes (e.g. Wegener's granulomatosis).

When evaluating the lungs of patients with a CTD several different aspects of the disease process need to be considered before the clinician can come up with an appropriate differential diagnosis. The most important questions the treating clinician (general practitioner, general physician, rheumatologist or pulmonologist) has to consider include:

- Has the patient's CTD been well characterised clinically, serologically and radiologically?
- Is the collagen vascular disease well established and is the patient on appropriate therapy?
- Is there a super-added infective aetiology (i.e. viral, fungal, bacterial or mycobacterium)?
- Is there a possibility of drug toxicity (i.e. methotrexate (MTX) lung toxicity, salazopyrine toxicity or disease related to biological agents)?
- Has the patient developed an unrelated separate pathology (i.e. hypersensitivity pneumonitis, a secondary malignancy or an aspiration pneumonitis)?<sup>4,5</sup>

With the above possibilities in mind, Table I highlights the most common disease-associated (CTD) pulmonary manifestations.

The ILDs pose the greatest diagnostic challenge and therapeutic dilemma. There are various different histological sub-classifications of the ILDs, but the most important include:

- UIP = usual interstitial pneumonia (formerly called CFA= cryptogenic fibrosing alveolitis)
- NSIP = nonspecific interstitial pneumonitis
- OP = organising pneumonia (formerly called BOOP= bronchiolitis obliterans organising pneumonia)
- LIP = lymphocytic interstitial pneumonia.

NSIP is the most common histological pattern associated with a CTD. However, in RA a UIP pattern is more common, while in Sjögren's syndrome LIP is the predominant histological pattern. Furthermore, patients with scleroderma are particularly prone to developing pulmonary vascular hypertension.

**Table I. Major pulmonary manifestations of the rheumatic diseases**

	Systemic sclerosis	Rheumatoid arthritis	Sjögren's syndrome	Mixed CTDs	Polymyositis/ dermatomyositis	SLE
Airways	–	++	++	+	–	+
ILD	+++	++	++	++	+++	+
Pleural	–	++	+	+	–	+++
Vascular	+++	–	–	++	+	+
DAH	–	–	–	–	–	++

ILD = interstitial lung disease; DAH = diffuse alveolar haemorrhage.

This could be as a result of the vasculopathy associated with the scleroderma, vascular hyper-reactivity associated with Raynaud's phenomenon, hypoxia due to an ILD or pulmonary thrombo-embolic disease. Unfortunately, the pulmonary hypertension carries with it a grave prognosis for the patient and needs to be specifically evaluated for. Pulmonary thrombo-embolic disease (PTED) might also be a complicating feature of the anti-phospholipid syndrome.<sup>6</sup>

When a patient with a CTD-associated ILD is being evaluated, the following initial questions need to be answered before an accurate diagnosis can be made:

- Does the patient have a well-characterised CTD, and if so:
  - Does the ILD pattern fit with the CTD? Alternatively, is there a separate pathology, i.e. infection or drug toxicity?
- If the patient does not have a known CTD:
  - Are there extra-thoracic features of a CTD?
  - Is this the pulmonary manifestations of a *forme fruste* CTD?<sup>4,5</sup>

The aspects that are paramount to establishing a diagnosis of a rheumatic disease include:

- good skin examination
- good joint examination
- nailfold capillaroscopy
- ANA, RF, CPK, aldolase
- If ANA+, then do extractable nuclear Ag panel
- If ↑CPK/aldolase or ANA+ then do myositis-specific Ab panel including anti-Jo 1
- If +RF, then do anti-CCP as well as hand/foot X-rays.

Of note when evaluating CTD-associated ILD:

- The ILD may be the first or lone manifestation of a CTD.
- The extra-thoracic manifestations of an underlying CTD may be subtle and must be assessed for.
- ANA and RF are poor screening tests, especially when considering the anti-synthetase syndromes, Sjögren's syndrome and the mixed CTDs because the ANA/RF might be negative in these conditions.<sup>5</sup>

- P = Pleural space**  
Pleural effusion/pericardial effusions  
Pleural thickening
- A = Airways and alveolar spaces**  
Airways: large airways for airway hyper-reactivity or scarring from bronchiectasis, smaller airways for air-trapping and bronchiolitis obliterans  
Alveolar spaces: for consolidation identified by air bronchiograms implying an alveolar filling process by either blood, pus, fluid or cells
- I = Interstitium**  
The connective tissue network supporting the capillary bed is identified by reticular infiltrates and honey-comb changes. Particular attention needs to be paid to the zone of the lung involved, as ankylosing spondylitis has a preponderance to involve the apices and RA the bases  
Vascular bed involvement, including looking for pulmonary arterial or venous hypertension  
Nodular infiltrates for an active capillaritis or alveolitis
- N = Neuromuscular**  
Peripheral nerve disease identified by phrenic nerve involvement  
Muscular involvement identified by vanishing lung syndrome associated with small lung fields and diaphragmatic elevations
- T = Thoracic skeleton**  
Evidence of vertebral collapse, sternal head erosions and costochondritis

Once the diagnosis of a CTD-associated ILD has been established based on history and clinical examination, a useful approach to the plain radiograph is to use the following anatomic acronym when viewing the chest X-ray: PAIN T

When a diagnosis of a CTD-associated ILD is strongly suspected on the plain radiograph, a HRCT scan will provide the necessary clarification as to the particular anatomical regions involved. Important clues to the presence of a CTD-associated ILD include the presence of a dilated

oesophagus, pericardial thickening with effusion and presence of bilateral, bibasilar and predominantly peripheral changes. When evaluating the lung parenchyma, particular attention should be paid to the predominant pattern of lung involvement. Table II highlights the most common HRCT chest patterns associated with the rheumatic diseases.<sup>2,3</sup>

After the disease process has been assessed anatomically with the HRCT scan, the impact of the disease on the patient's health has to be physiologically quantified. This is achieved by means of a full lung function test. The important parameters measured include the lung volumes (vital capacity (VC) and total lung capacity (TLC) and the diffusion co-efficient (DLCO).<sup>5</sup>

The lung volumes are:

Increased (obstructive lung functions) with pathologies that lead to air trapping, i.e. airway hyper-reactivity (asthma), bronchiectasis and bronchiolitis obliterans or reduced (restrictive lung function) with pathologies that involve the lung parenchyma (ILD), the pleura or the thoracic cage.

The DLCO is decreased with pathologies that involve the lung parenchyma (ILD) or increased with pulmonary haemorrhage syndromes (Table III).

An additional important, yet simple and non-invasive, tool for monitoring CTD-associated ILD and the response to therapy is the determination of the 6-minute walk test, which is an objective assessment of effort tolerance. A slightly more invasive tool that also provides a wealth of information

**Table II. The most common HRCT chest patterns associated with the rheumatic diseases**

Nodular involvement
Infection
Alveolitis
Capillaritis
Granulomatous infiltrates
Interstitial
Atypical infections
Viral pneumonitis
Drug reaction
Idiopathic interstitial pneumonia (UIP v. NSIP)
Cystic
Lymphocytic interstitial pneumonias
Pneumocystis pneumonia
Necrotising infection
Ground glass
Active alveolitis
Diffuse air trapping with bronchiolitis
Variable perfusion with PTED
Air bronchiograms
Infection
BOOP

UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; PTED = pulmonary thrombo-embolic disease; BOOP = bronchiolitis obliterans organising pneumonia.

**Table III. The pulmonary function test abnormalities commonly encountered in CTD**

	<b>Lung volumes</b>	<b>DLCO</b>
Increased	Asthma, emphysema, bronchiectasis and bronchiolitis obliterans	Pulmonary haemorrhage syndromes, polycythaemia
Decreased	Interstitial pneumonia (ILD) BOOP Pleural and thoracic cage disease	Interstitial pneumonia (ILD) PTED

is bronchoscopy and bronchiolar lavage. It has the potential to exclude infection and ascertain the cellular nature of the alveolar filling process (i.e. blood, pus, fluid or cells). Furthermore, if there are no contraindications a transbronchial biopsy may be done to obtain a histological diagnosis.

In conclusion, a few words on methotrexate pneumonitis as it is the perennial question faced by all physicians treating rheumatic disease patients on methotrexate:

- occurs a few days to weeks after initiation of therapy
- not dose dependent
- major symptoms include dyspnoea, non-productive cough, fever
- eosinophilia present in >50% of patients
- CXR features include
  - diffuse alveolar infiltrate
  - hilar adenopathy
  - pleural effusions (10 - 15%)
- form of hypersensitivity pneumonitis with weakly formed granulomas
- can re-challenge patients if the response to drug withdrawal is good.<sup>7</sup>

### Summary

- The lungs are often affected by all the rheumatic diseases.
- The pathology in the lungs is multifactorial and involves different parts of the lung parenchyma.
- The main differential diagnosis includes disease progression, infection and drug toxicities.
- Special investigations such as a HRCT scan of the chest are often needed to determine the possible aetiology.
- Using an algorithm-based approach to the interpretation of the chest X-ray assists in narrowing the differential diagnosis.
- Lung function tests often aid in excluding the interstitial process from predominant airway diseases.
- A thorough musculoskeletal examination including particular attention to nail-fold capillaroscopy and the skin for specific rashes is invaluable.
- A multidisciplinary approach to total patient care improves patient outcomes.

References available at [www.cmej.org.za](http://www.cmej.org.za)

## SINGLE SUTURE

### Sexual superbug

An untreatable strain of the sexually transmitted disease gonorrhoea, resistant to all existing antibiotics, has been identified in Japan.

The news follows warnings recently from the US Centers for Disease Control (CDC) that it is only a matter of time before invincible strains of *Neisseria gonorrhoea* emerge in the US.

The Japanese superbug, called H041, was isolated by Magnus Unemo at the Örebro University Hospital in Sweden and reported this week in the International Society for Sexually Transmitted Disease Research meeting in Quebec, Canada.

Unemo, who found the bug in strains from Kyoto, says that it could go global in 10 - 20 years.

The CDC reports that some gonorrhoea strains in the US can now only be killed with one class of antibiotics – the cephalosporins.

New Scientist, 16 July 2011, p.5.