# The differential diagnosis of neurogenic and referred leg pain

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## **Abstract**

## Background:

Neurogenic and referred leg pain are some of the most challenging clinical problems in spinal surgery due to the diversity of conditions that can act as aetiological factors.

#### Methods:

The literature was reviewed and combined with case studies to demonstrate different aetiological factors.

## Results:

At least 300 conditions were identified that might cause neurogenic and referred leg pain. An aetiological classification of neurogenic and referred leg pain is presented. The classification includes systemic conditions, conditions from the brain, spinal cord, cervical and thoracic spinal canal, lumbar spinal canal, lumbar nerve root canal, lumbar extraforaminal area, the pelvis and the lower extremity. Each one of these conditions can mimic a lumbar disc herniation accurately.

## Conclusion:

The aetiological classification can be used as a checklist when evaluating neurogenic and referred leg pain. Each condition deserves careful consideration and when overlooked might result in a missed diagnosis.

Key words: neurogenic, leg pain, nerve root

## Introduction

Leg pain is a common presenting symptom of lumbar disc herniation due to neurological compression. If conservative management fails, a large number of these patients might undergo lumbar spine surgery. Magnetic resonance imaging (MRI) is considered to be the cornerstone special investigation to confirm the diagnosis of a lumbar disc herniation. However, between 38% and 52% of asymptomatic individuals demonstrated significant lumbar disc bulging on MRI. Given the high prevalence of these findings and of back pain, the discovery by MRI of disc bulges may frequently be coincidental and the leg pain caused by an unrelated condition. It is therefore essential to consider all possible aetiological factors when evaluating leg pain.

Literature reviews combined with the author's personal experience in the examination of more than 15 000 patients with back pain were used to propose an aetiological classification of conditions to consider when evaluating leg pain.

## Conditions to consider when evaluating leg pain

## 1. Systemic conditions

## Metabolic neuropathy

Diabetes mellitus is the most common metabolic neuropathy. Its most common presentation is the distal symmetrical polyneuropathy with bilateral symmetrical pain in the lower extremities starting distally and moving proximally.<sup>3,4</sup> Other subtypes include proximal diabetes, truncal, cranial, median and ulnar neuropathies. Diabetic autonomic neuropathy affects each tissue, organ and system in the whole body and is strongly involved in the development of foot ulceration.<sup>5</sup>

A less common diabetes presentation is diabetic amyotrophy<sup>6</sup> which has most probably a vasculitis aetiology with ischaemia followed by axonal degeneration and demyelination. The main features are unilateral weakness, wasting and pain most commonly in the quadriceps. It spreads later to the contralateral side in an asymmetrical manner.

Other metabolic neuropathies to consider are *alcoholic* and *uraemic* neuropathies.<sup>7,8</sup>

## Vasculitic neuropathy

The primary pathology of vasculitic neuropathies is a vasculitis of the small and medium-sized vessels in the peripheral nervous system9 with an area of infarction in the nerve.10,11 The presenting symptoms are severe pain localised to the region of the infarction, motor deficit, numbness and paraesthesias. Vasculitic neuropathies are classified into primary and secondary vasculitides.10 Primary vasculitic neuropathy includes Churg-Strauss syndrome, microscopic polyangiitis, classic polyarteritis nodosa and Wegener granulomatosis. Secondary vasculitis occurs as a complication of connective tissue disease (systemic lupus erythematosus, rheumatoid arthritis and Sjögren syndrome), infection (hepatitis B and C, human immunodeficiency virus, Lyme disease, cytomegalovirus, Herpes zoster virus and various bacterial infections), medication (sulphonamides, other antibiotics and anti-viral agents) and malignancies representing a paraneoplastic vasculitis.11-15

## Paraneoplastic peripheral neuropathy

In addition to the paraneoplastic vasculitis and the local effect of the tumour, malignancies can also cause a paraneoplastic sensorimotor neuropathy which might even be more debilitating than the cancer itself. The detection of anti-neuronal antibodies and EMG changes help to identify the neuropathy as paraneoplastic. A paraneoplastic myopathy might also develop which can cause leg pain. 16,17



Figure 1. The coronal MRI demonstrated a lesion in the lung apex (bronchus carcinoma)

### Case 1

This 53-year-old female patient presented with severe acute onset unilateral pain in the L5 nerve root distribution. The MRI of the lumbar spine failed to demonstrate any neurological compression. The coronal images of the MRI thoracic spine demonstrated a lesion in the lung which was biopsied and turned out to be a bronchus carcinoma (*Figure 1*). The antineuronal antibodies and EMG confirmed a paraneoplastic neuropathy.

### Case 2

This 64-year-old male patient presented with severe unilateral pain in the L5 and S1 nerve root distribution 25 months after an uncomplicated L4 to S1 decompression and fusion procedure. The plain radiographs demonstrated an uncomplicated fusion and the MRI a wide decompression without neurological compression. The anti-neuronal antibodies demonstrated a positive anti-PNMA(Ma/Ta) which is associated with small cell bronchus carcinoma. This prompted a chest CT scan which demonstrated a small lesion in the apex of the right lung. A lung biopsy demonstrated a bronchus carcinoma.

## Vascular occlusion

Vascular occlusion can mimic neurogenic claudication. The peripheral pulses should therefore be palpated in every back pain examination.

# 2. Brain

Brain-related causes of leg pain include multiple sclerosis, 18,19 Parkinson's disease, 20 motor neurone disease, 21 post-stroke pain in lenticulo-capsular haemorrhages 22 and space-occupying lesions.

## Case 3

This 57-year-old male patient presented with spontaneous onset pain in the right lower extremity 12 years after an L4 to S1 fusion, neurological decompression and instrumentation. The plain radiographs failed to demonstrate any complications and no neurological compression could be demonstrated on the MRI lumbar spine. The history of the systemic diseases revealed resection of a melanoma behind the right scapula three years before. A CT scan of the brain demonstrated multiple melanoma metastases (Figure 2).

# 3. Spinal cord

Spinal cord conditions which should be excluded in the evaluation of leg pain are multiple sclerosis,<sup>18,19</sup> motor neurone disease,<sup>21</sup> transverse myelitis,<sup>22,23</sup> syringomyelia,<sup>24,25</sup> and any posterior (compression of substantia gelatinosa at the tip of the posterior column) or anterolateral (compression of lateral spino-thalamic tract)<sup>26</sup> situated space-occupying lesion, for example intervertebral disc herniation,<sup>27,28</sup> tumour, haematoma or abscess. An atypical Brown-Sequard lesion can also be produced, with loss of pain and thermal sensation on the contralateral side and leg pain on the ipsilateral side.<sup>27,29</sup>

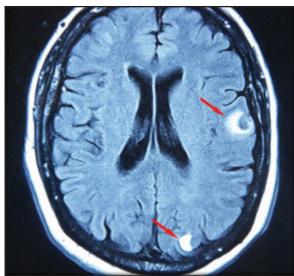


Figure 2. Brain CT scan with multiple melanoma metastases in a patient who presented with leg pain only

### Case 4

This 73-year-old female patient presented with excruciating pain in the L5 distribution of the right lower extremity and was booked for an emergency laminectomy.

An MRI thoracic spine demonstrated a posterior situated meningioma at T7



Figure 3 (a) Figure 3 (b)

Figure 3. A patient with leg pain only. Figure 3 (a) demonstrates a small disc bulging on the asymptomatic side on the lumbar spine MRI. Figure 3 (b) demonstrates a T7 meningioma responsible for the leg pain.

When the patient presented for a second opinion, the MRI of the lumbar spine demonstrated a small disc bulging on the asymptomatic side. An MRI thoracic spine was requested which demonstrated a posterior situated meningioma at T7 (*Figure 3*) which was removed and the L5 nerve root symptoms resolved completely.

# 4. Cervical and thoracic spinal canal

Any posterior or anterolateral situated space-occupying lesion in the cervical and thoracic spinal canal may cause compression on the lateral spino-thalamic tract and substantia gelatinosa at the tip of the posterior column of the spinal cord with resulting leg pain, for example haematoma, abscess, soft tissue or bone tumours, etc.<sup>26-29</sup>

## 5. Conus medullaris

At the conus medullaris the nerve roots are positioned lateral to the spinal cord (*Figure 4*). A parasagittal disc herniation or any other space-occupying lesion (for example intradural or extradural tumours, haematoma, abscess, primary bone tumours, metastases, etc.) can therefore cause compression of the nerve roots with leg pain without much compression on the spinal cord.

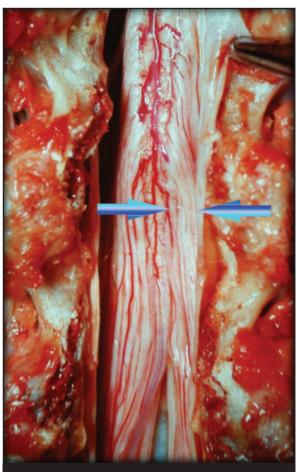


Figure 4. The conus medullaris. The nerve roots (between the arrows) are positioned lateral to the spinal cord.

### Case 5

This 58-year-old male patient presented with severe pain in the right lower extremity in the L4 nerve distribution seven years after a T12 to S1 fusion and pedicle instrumentation. The CT myelogram demonstrated intervertebral disc and gas sequestration in the right parasagittal position with severe compression on the nerve roots but only slight displacement of the conus medullaris (*Figure 5*). Removal of the gas and disc sequestration alleviated the L4 symptoms completely.

# 6. Lumbar spinal canal

As far back as 1933, Baastrup<sup>30</sup> reported on the *interspinous bursa* (kissing spines, Baastrup's disease) as a cause of leg pain<sup>31,32</sup> (*Figure 6*). The bursa can communicate with an epidural cyst with severe neurological compression.<sup>33</sup>

In *facet joint* syndrome, osteoarthrosis of the facet joint with a normal spinal canal and nerve root canal can give buttock and leg pain<sup>34,35</sup> (*Figure 7*). Hypertrophy of the facet joints gives spinal stenosis and leg pain (*Figure 8*).

A facet joint cyst can compress the nerve root with leg pain. With both superior or inferior rotational instability, the facet joints may rotate into the spinal canal with neurological compression and leg pain (*Figure 9*).

In *degenerative spondylolisthesis*, the vertebral body and inferior facet joints displace anteriorly. The inferior facet joints move forwards and compress the dural sac and nerve roots against the posterior aspect of the cranial vertebral body. If the flexion radiographs demonstrate superimposed instability with further anterior translation of the inferior facet joints in the flexed position, the compression on the dural sac is aggravated significantly. This dynamic compression on the dural sac is not demonstrated on the MRI and can only be appreciated on the stress radiographs (*Figures 10 and 11*).

Any *space-occupying lesion* in the lumbar spinal canal can give leg pain, for example intervertebral disc herniation or sequestration, soft tissue or bone tumours, haematoma, etc.

# 7. Lumbar nerve root canal

Inside the nerve root canal the facet joint might give leg pain with a combination of *loss of disc height* and posterior subluxation when the superior articular process moves upwards and forwards and might impinge the nerve root against the pedicle or the posterior aspect of the vertebral body, especially the inferior endplate (*Figure 12*).

In *spondylosis* osteophytes from the superior facet joint or posterior inferior vertebral endplate (*Figure 13*) may compress the nerve root.

Anterior subluxation of the vertebra in degenerative spondylolisthesis might be associated with hypertrophy of the superior facet joint with extension of the superior facet joint into the nerve root canal with compression of the nerve root and resulting leg pain.

Any *nerve root lesion*, for example a nerve root cyst or nerve root tumour, should be considered. The most common benign nerve root tumours are the schwannomas, neurofibromas<sup>36</sup> and less common haemangioblastomas<sup>37,38</sup> and non-Hodgkin lymphomas.<sup>39</sup> Nerve sheath tumours can originate from the intradural or extradural position.<sup>40</sup>

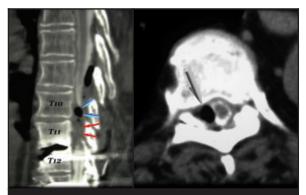


Figure 5 (a)

Figure 5 (b)

Figure 5. A patient with L4 leg pain. In Figure 5 (a) gas (blue arrows) and disc (red arrows) sequestrations are demonstrated. In Figure 5 (b) the gas sequestration (blue arrow) is positioned over the nerve roots lateral to the spinal cord with only slight displacement of the spinal cord



Figure 6. The interspinous bursas are demonstrated between the red arrows.

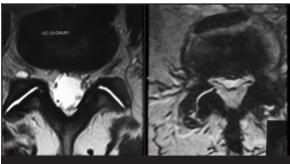
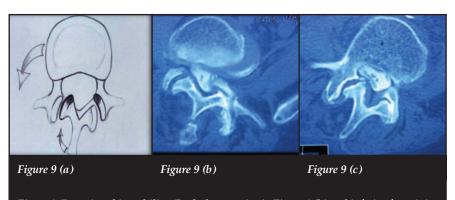


Figure 7

Figure 8

Facet joint disease. Facet joint osteoarthrosis in Figure 7 and facet joint hypertrophy with spinal stenosis in Figure 8.



A facet joint cyst can compress the nerve root with leg pain

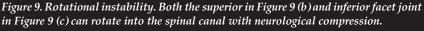




Figure 10 (a) Figure 10 (b)

Figure 10. Degenerative spondylolisthesis. The space available for the dural sac between the posterior aspect of the vertebral body and the anterior aspect of the inferior facet joints (between the red arrows) measured 15 mm with the back in extension with 4 mm anterior displacement [Figure 10 (a)] and decreases to only 4 mm in flexion when the anterior displacement increases to 16 mm with severe dural sac compression [Figure 10 (b)].

Figure 11 (a)

Figure 11 (b)

Figure 11. The MRI was done with 4 mm anterior displacement of L4 on L5 in Figure 11 (a) and (b). At 16 mm anterior displacement, as demonstrated on the stress radiographs in Figure 10, the inferior facet joints and lamina at the position of the white arrows in Figure 11 (b) will move forwards to the position of the red arrows with severe aggravation of the existing compression. The MRI fails to demonstrate the effect of this additional dynamic compression of instability which is well demonstrated on

Malignant peripheral nerve sheath tumours (MPNSTs) are grouped together by the World Health Organisation as MPNST and include previous terminology such as malignant neurilemmomas, neurogenic sarcoma and neurofibrosarcoma.<sup>41</sup>

In *isthmic spondylolisthesis* the nerve root canal is narrowed by the combination of disc bulging and pars interarticularis hypertrophy.

The *pedicle moves down* and might compress the nerve root in complete loss of disc height in combination with spondylolisthesis (*Figure 14*) and degenerative scoliosis.

*Intervertebral disc herniation* into the nerve root canal is the most common cause of nerve root canal narrowing and neurological compression.

A *nerve root anomaly* might easily be mistaken for a disc fragment with grave consequences. The most common anomaly is the conjoint nerve root with two nerve roots derived from a common dural sheath followed by two nerve roots in one foramina.<sup>42-44</sup>

# 8. Lumbar extraforaminal area

plain stress radiographs (Figure 10).

A *far lateral disc herniation* may compress the nerve root after it has left the nerve root canal (*Figure 15*).

The *corporotransverse ligament* extends from the vertebral body to the transverse process of the same vertebra.<sup>45</sup> It may entrap the nerve root in rotatory subluxation in combination with complete disc space narrowing.

*Psoas pathology,* for example abscess, haematoma, tumour or any other space-occupying lesion, may compress the nerve root in its course through the psoas.<sup>46</sup>

In *spondylolisthesis* with severe disc space narrowing, the L5 nerve root may be impinged between the L5 transverse process and the ala of the sacrum (*Figure 14*). This may also occur in degenerative scoliosis with tilting of L5 and depression of the concave L5 transverse process (*Figure 16*).



Figure 12. The superior facet joint moves upwards and forwards (red arrow) in loss of disc height with possible nerve root compression.



Figure 13. An osteophyte from the inferior vertebral endplate extends into the nerve root canal with nerve root compression.

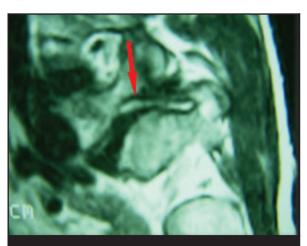


Figure 14. The pedicle moves down with nerve root compression.

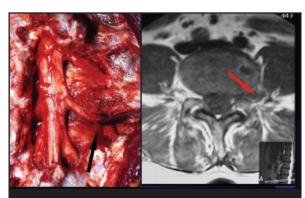


Figure 15. The position of a far lateral disc herniation is demonstrated on the cadaver dissection (black arrow) on the left side and the MRI (red arrow) on the right.

# 9. Pelvis

At the entrance to the pelvis, a large osteophyte from the *L5 transitional vertebra pseudoarthrosis* might compress the L5 nerve root (*Figure 17*).

The *lumbosacral ligament*<sup>47</sup> extends from the L5 vertebra to the ala of the sacrum and forms the roof of the lumbosacral tunnel through which the L5 nerve root passes. Ossification of the lumbosacral ligament in combination with osteophytes from the inferior L5 vertebral body endplate may impinge the L5 nerve root.<sup>47</sup>

A stress fracture of the sacrum can give back, buttock, groin and thigh pain.<sup>48</sup> It may also give direct compression or a neuropathy of the nerve root.<sup>49</sup> The most common associated stress fracture is that of the ipsilateral, contralateral or both pubic rami.<sup>50</sup> It may remain undetected on plain radiographs for months but readily demonstrated on the STIR and T2 weighted MRI images (*Figure 18*).<sup>51</sup> MRI alone identifies 99, 2% of stress fractures compared to 69% with the CT scan alone.<sup>51</sup> The MRI remains the investigation of choice in these cases.

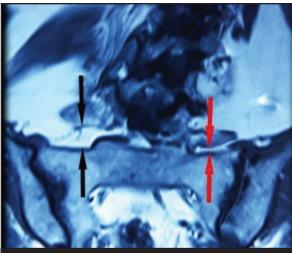


Figure 16. Tilting of L5 with dipping down of the left L5 transverse process (red arrows) and L5 nerve root compression

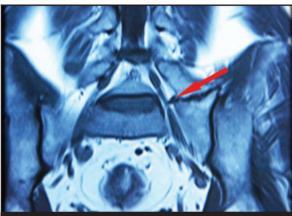


Figure 17. An osteophyte from the L5 transitional vertebra pseudoarthrosis extends medially with L5 nerve root compression.

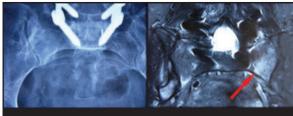


Figure 18 (a) Figure 18 (b)

Figure 18. The stress fracture of the sacrum is not visible on the plain radiographs in Figure 18 (a) but well demonstrated (red arrow) on the STIR sequences of the MRI in Figure 18 (b).

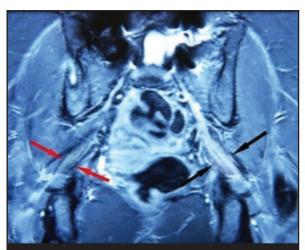


Figure 19. The MRI neurography demonstrates a neuropathy of the left ischiadic nerve (between black arrows) with enlargement, increased signal intensity, blurring of the perifascicular fat and loss of the normal fascicular appearance. A normal nerve is demonstrated between the red arrows.

Degenerative *sacroiliitis* can give buttock, groin and thigh pain.<sup>52</sup> An osteophyte from the sacroiliac joint extending anteriorly can compress a nerve root. Any type of infectious sacroiliitis (tuberculosis, brucellosis and piogenic)<sup>53</sup> and tumours of bone and the soft tissue in and around the sacroiliac joint can give pain in a similar distribution.<sup>54</sup> The sero-negative spondyloarthropathies (ankylosing spondylitis, psoriatic arthritis, reactive arthritis and Behcet's disease) should also be considered.<sup>55</sup>

A *lumbosacral radiculoplexus neuropathy* presents with asymmetrical lower limb pain, weakness, atrophy and paraesthesia. It can be caused by diabetic lumbosacral radiculoplexus neuropathy, non-diabetic lumbosacral radiculoplexus neuropathy, chronic inflammatory demyelinating polyneuropathy, connective tissue disease, Lyme disease, sarcoidosis, HIV and cytomegalovirus-related polyradiculopathy. The typical MRI neurography findings (*Figure 19*) are increased signal intensity and enlargement of the nerve and blurring of the perifascicular fat on the T2 weighted neurography sequences. (long echo times, radiofrequency saturation pulses to

suppress signals from adjacent vessels and frequency-selective fat suppression). <sup>60,61</sup> EMG, fasting blood glucose levels, sedimentation rate, rheumatoid factor, antinuclear antibodies, antineutrophil cytoplasmic antibodies, extractable nuclear antigen, HIV, <sup>56</sup> serum antibodies associated with neurological disorders (antineuronal, antiganglioside and anti-astrocyte antibodies) <sup>62</sup> and CSF evaluation are some of the special investigations of diagnostic value.

In the *piriformis muscle syndrome* hypertrophy, spasm, contracture or inflammation of the piriformis muscle may compress the ischiadic nerve with pain in any part of the ischiadic nerve distribution (*Figure 20*).

The diagnostic accuracy of a wide variety of clinical tests (tenderness on deep palpation over the piriformis, 63 Pace's sign, 64 Freiberg's sign, 65 FAIR test [flexion- adduction-internal rotation], 660 persistent piriformis position in external rotation) remain controversial. 67 The imaging diagnosis with an MRI of the pelvis is based on enlargement of the piriformis and MRI neurography. 59 Enlargement of the piriformis alone has a specificity of 66% and a sensitivity of 64%. If in addition the MRI neurography demonstrates an increased signal intensity and enlargement of the ischiadic nerve (*Figure 21*), the specificity increases to 93% and the sensitivity to 64%. 68

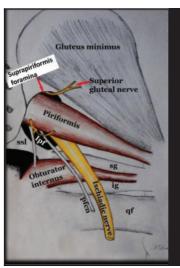


Figure 20. Posterior view of the right gluteal area. The ischiadic nerve emerges from underneath the piriformis and courses over the obturator internus. (Ipf: Infrapiriformis foramina; ssl: sacrospinalis ligament; sg: superior gemellis muscle; ig: inferior gemellis muscle; qf: quadratus femoris muscle; pfcn: posterior femoral cutaneous nerve)

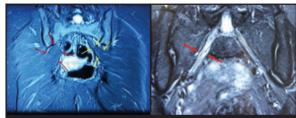


Figure 21 (a)

Figure 21 (b)

Figure 21. The piriformis syndrome. Figure 21 (a) demonstrates enlargement of the right piriformis muscle (between red arrows) and the normal size on the left side (yellow arrows). Figure 21 (b) demonstrates a neuropathy of the underlying ischiadic nerve with enlargement and increased signal intensity (between red arrows).

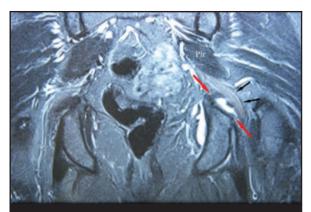


Figure 22. The ischiadic nerve (black arrows) is displaced posteriorly by the obturator internus muscle (between red arrows) with an area of increased signal intensity in the muscle.

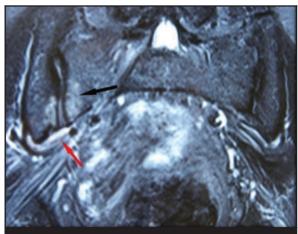


Figure 23. The MRI pelvis demonstrates a sacroiliitis on the right side (black arrow) with an effusion and area of high signal intensity around the joint. A neuropathy of the right superior gluteal nerve is demonstrated (red arrow) with enlargement and an increased signal intensity.

The ischiadic nerve passes underneath the piriformis and then over the obturator internus (*Figure 20*). Swelling and inflammation of the obturator internus might displace and irritate the ischiadic nerve with resultant leg pain (*Figure 22*). 69

Superior gluteal nerve entrapment syndrome is caused by any condition which narrows the suprapiriformis foramen (Figure 20), for example enlargement or spasm of the piriformis muscle, superior gluteal nerve perforating the piriformis, aneurysm or pseudoaneurysm of the superior gluteal artery, aneurysm or pseudoaneurysm of the superior gluteal artery, abscess and pelvic fracture. The clinical diagnosis is based on the triad of buttock pain, weakness of hip abduction and marked tenderness on deep palpation in the region just lateral to the greater schiadic notch.

### Case 6

This 55-year-old male patient presented with the clinical triad of superior gluteal nerve entrapment. The MRI pelvis demonstrated sacroiliitis on the right side with an effusion and a neuropathy of the superior gluteal nerve with enlargement and an increased signal intensity (*Figure 23*).

The *inferior gluteal nerve entrapment syndrome* is caused by any condition which narrows the infrapiriformis foramen, for example an aneurysm of the inferior gluteal artery, 63 pelvis fracture and abscess.<sup>76</sup>

In the *pudendal nerve entrapment syndrome* the pudendal nerve is compressed in the pudendal or Alcock's canal between the sacrospinous and sacrotuberous ligaments. The nerve might become ensheathed by ligamentous expansions that form a perineural compartment, by the falciform process of the sacrotuberous ligament or by duplication of the obturator fascia.<sup>77-79</sup> It causes chronic perineal pain typically presenting as pain in the penis, scrotum, labia, perineum, anorectal area and medial proximal thighs.<sup>77</sup>

There are special considerations in female patients regarding leg pain which deserve mentioning. Sciatica in pregnancy can be caused by direct compression of the gravid uterus on the lumbosacral plexus and blood vessels. 80,81 Incorrectly positioned leg stirrups on the obstetrical table can cause common peroneal nerve pain and weakness.  $^{\! 80,82}$ Obstetric neuropathy of the sciatic nerve during vaginal labour can be caused by continuous pressure of the foetus on the lumbosacral plexus as it crosses the pelvic brim during prolonged labour.83 Piriformis syndrome can be caused during labour following a piriformis haematoma after prolonged labour, and a piriformis abscess after epidural anaesthesia and forceps delivery.84 Sciatica secondary to pathological conditions  $^{\!80}$  include leiomyomas with lumbosacral plexus compression,85 endometriosis with infiltration or compression of the sciatic nerve86 and a large retroverted uterus with compression on the lumbosacral plexus.80 Sciatica secondary to iatrogenic trauma includes vaginal procedures which might be complicated by ischiadic neuropathy,87 superior gluteal artery aneurysm with superior gluteal nerve compression and the superior gluteal nerve neuropathy due to stretching of the superior gluteal nerve.

# Case 7

This 29-year-old female patient presented after two years of diligent conservative treatment for a small L5/S1 disc bulging with progressive deterioration of buttock and leg pain. The MRI pelvis demonstrated a large ovarian cyst which displaced a large uterus lateral and posterior with an underlying large piriformis muscle, and an increased signal intensity and enlargement of the ischiadic nerve (*Figure 24*).

Piriformis syndrome can be caused during prolonged labour, and a piriformis abscess after epidural anaesthesia and forceps delivery



Figure 24. The MRI pelvis demonstrates a large ovarian cyst, displacing a large uterus (a) against a large piriformis (b) with an underlying large ischiadic nerve with an increased signal intensity on MRI neurography (c).

# 10. Lower extremity

Greater trochanter bursitis and gluteus medius tendinitis remain some of the most common causes of leg pain in patients above 60 years of age.

A *stress fracture* of the femur neck, intertrochanteric area and the proximal femur presents with pain in the groin and anterior aspect of the proximal thigh. Plain radiographs may remain normal for a considerable time. An MRI and bone scan are useful in the early stages to confirm the diagnosis.

*Iliopsoas*<sup>88</sup> and *iliopectineal*<sup>89</sup> bursitis and synovitis present with pain in the groin and anterior aspect of the proximal thigh. They might also give femoral nerve palsy and pain.

*Non-traumatic focal mononeuropathies* may present with symptoms indistinguishable from a lumbar disc herniation and include the following conditions:

- Compression neuropathies: Acute, chronic and hereditary.<sup>90</sup>
- 2. Infectious neuropathies: *Herpes zoster*, Lyme disease, acquired immunodeficiency syndrome (AIDS), leprosy mononeuropathy, hepatitis B and C, cytomegalovirus, Epstein-Barr virus, various bacterial infections. <sup>11-15</sup>
- Inflammatory/vasculitic neuropathies: Churg-Strauss syndrome, microscopic polyangiitis, classic polyarteritis nodosa, Wegener granulomatosis, systemic lupus erythematosus, rheumatoid arthritis, Sjögren syndrome.
- 4. Drug-related neuropathies: Sulphonamides, other antibiotics, anti-viral agents.<sup>11-15</sup>
- Metabolic neuropathies: Diabetic amyotrophy, alcoholic and uraemic.<sup>68</sup>
- 6. Paraneoplastic neuropathies: Paraneoplastic vasculitis, paraneoplastic sensorimotor neuropathy. 16,17
- 7. Radiation neuropathy.90
- 8. Nerve and nerve sheath tumours.90
- 9. Hereditary: Familial amyloid polyneuropathy,<sup>91</sup> hereditary compression neuropathy.<sup>90</sup>

The *nerve entrapment syndromes* of the lower extremity include the following conditions:

The *iliohypogastric* (T12, L1), *ilioinguinal* (T12, L1) and *genitofemoral* (L1, 2) entrapment syndromes usually occur after lower abdominal surgery.<sup>92</sup>

Entrapment of the *lateral femoral cutaneous nerve* (L2-4) is also known as meralgia paraesthetica. Symptoms include anterior and lateral thigh burning, tingling and numbness.<sup>32</sup>

The femoral nerve (L2-4) is usually entrapped below the inguinal ligament where it lies in close proximity to the femoral head, the tendon insertion of the vastus intermedius, the psoas tendon, and the hip joint and hip joint capsule, all of which can cause entrapment. Other causes of entrapment include methylmethacrylate heat during total hip arthroplasty, pelvic procedures requiring acutely flexed, abducted and externally rotated positioning, compression by a foetus in difficult childbirth, pelvic fractures and radiation.

The *saphenous nerve* (L3,4) is the terminal and longest branch of the femoral nerve. It can become entrapped as it pierces the roof of the adductor canal, by femoral vessels, pes anserine bursitis, varicose vein operations and medial knee surgery. 92,93

Common peroneal neuropathy is the most common mononeuropathy of the lower extremity. It is most commonly entrapped as it courses along the lateral aspect of the fibula neck through a fibro-osseous tunnel by tight plaster casts, knee surgery, osteophytes, synovial cysts or ganglions and sitting in a prolonged crossed leg position. 93-96 Repetitive exercises involving inversion and pronation (for example runners and cyclists) stretch the common peroneal nerve against the fibula neck and fibrous arch of the peroneal tunnel. 93 Many cases are idiopathic in origin. 97

The *deep peroneal nerve* travels in the anterior compartment of the leg between the extensor digitorum longus and the extensor hallucis longus tendon until it reaches the ankle where it courses under the extensor retinaculum to enter the anterior tarsal tunnel where most of the entrapment occurs, referred to as the anterior tarsal tunnel syndrome with symptoms referring to the dorsum of the foot.<sup>98,99</sup> The entrapment is usually sport related.<sup>93</sup>

The *superficial peroneal nerve* courses through the anterolateral compartment of the leg until it pierces the deep fascia of the lateral compartment approximately 10 to 15 cm above the ankle where it may become entrapped. This is commonly seen in dancers in whom the nerve may become stretched during inversion or plantar flexion injuries.<sup>99,100</sup>

Proximal tibial entrapment neuropathy is uncommon, owing to the deep location of the nerve and abundant surrounding muscle tissue. Entrapment is usually related to space-occupying lesions in the popliteal fossa such as tumours, popliteal cyst, popliteal artery aneurysm and ganglia.<sup>99</sup>

Distal tibial entrapment usually occurs in the tarsal tunnel causing tarsal tunnel syndrome. Entrapment follows trauma (fracture, surgery and scarring), space-occupying lesion (tumour, ganglia, varicosities and an anomalous muscle) and foot deformities.<sup>99,101</sup>

The *sural nerve* runs distally between the two heads of the gastrocnemius beneath the crural fascia until it pierces the fascia between the middle and distal thirds of the calf. Compression of the nerve by mass lesion, scar tissue, ganglion, surgical trauma and thrombophlebitis has been reported. Extrinsic compression can occur from tight ski boots or casts. The crural fascia may act as a compression or fixation point in athletes with stretching of the nerve. 92,102-104

At the distal branches of the tibial nerve, *medial plantar nerve neuropathy* (Jogger's foot) can develop owing to repetitive trauma to the nerve while running with increased heel valgus and foot pronation. 99,105

Entrapment of the *inferior calcaneal nerve*, the first branch of the lateral plantar nerve, often manifests as heel pain (Baxter neuropathy).<sup>99</sup>

Interdigital neuropathy (Morton neuroma) is caused by a fibrotic nodule of the interdigital nerve most commonly at the second and third intermetatarsal spaces. The patients present with web space pain, tingling, numbness and paraesthesias. 99,106

Medial plantar proper digital neuropathy (Joplin's neuroma) is an entrapment neuropathy of the plantar proper digital nerve which is particularly susceptible to repetitive trauma. 99,107,108

The diagnosis of an entrapment neuropathy is based on a good clinical examination, typical EMG findings, MRI of the nerves and muscle, and blood investigations as mentioned under lumbosacral radiculoplexus neuropathy. The MRI includes signs of nerve entrapment, increased signal intensity, enlargement of the nerve, loss of the normal fascicular appearance or blurring of perifascicular fat.<sup>57</sup> The indirect signs of nerve injury are seen in the muscles supplied by the nerve with an increased signal intensity followed by atrophy and fat placement of the muscle.<sup>59,99</sup>

Leg pain may also be caused by *myositis or myopathy*. Palpation of the muscle may reveal local tenderness which is more pronounced than what would be expected of neurological compression, swelling and oedema, atrophy or hypertrophy and overlying skin changes.

One of four basic patterns of abnormality may be present on the MRI, namely muscle oedema with an increased signal intensity, muscle atrophy with an increased fat content, mass within a muscle or an accessory muscle.109 The aetiology of muscle oedema is inflammatory myopathy (dermatomyositis, polymyositis and inclusion body myositis), polymyositis, myositis in collagen vascular disease (rheumatoid arthritis, systemic lupus erythematosus, mixed connective tissue disease and Sjögren syndrome), radiation myositis, Graves' disease, drug-induced myositis (lipid-lowering statins, antiretroviral medication), HIV myositis, myositis due to infection (high risk patients include diabetes, immuno-compromised patients, penetrating wounds), polymyositis, necrotising fasciitis and sarcoidosis. The denervation phases include a normal MRI in the acute phase, mixed oedema and paradoxical hypertrophy in the early subacute phase, mixed oedema and atrophy in the late subacute phase and atrophy in the chronic phase.109

Sport-related leg pain<sup>110</sup> includes tibial and fibular stress fractures,<sup>111</sup> medial tibial stress syndrome,<sup>112</sup> chronic exertional compartment syndrome,<sup>113</sup> tendinopathies,<sup>114,115</sup> nerve entrapment syndromes,<sup>116</sup> vascular syndromes<sup>117,118</sup> and myopathies.<sup>119</sup>

Finally, leg pain may be associated with three poorly understood *neurological conditions*, namely complex regional pain syndrome, <sup>120,121</sup> restless leg syndrome<sup>122</sup> and painful legs and moving toes syndrome. <sup>123</sup>

## Discussion

At least 300 conditions were identified that might cause neurogenic and referred leg pain. *Table I* is presented as an aetiological classification for neurogenic and referred leg pain and can serve as a checklist to ascertain that all appropriate conditions are evaluated. Each one of these conditions deserves careful consideration and if overlooked might result in a missed diagnosis or even the disaster of the creation of yet another failed back. Our treatment can only be as good as our diagnosis. If the diagnosis is missed, the treatment will obviously fail.

Each one of these conditions deserves careful consideration and if overlooked might result in a missed diagnosis

## Table I: Aetiological classification of neurogenic and referred leg pain

	1. Systemic	diseases	
Metabolic neuropathies	Diabetic polyneuropathy		
	Diabetic amyotrophy		
	Alcoholic neuropathy		
	Uraemic neuropathy		
Vasculitic neuropathies	Primary vasculitides	Churg-Strauss syndrome	
1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		Microscopic polyangiitis	
		Classic polyarteritis nadosa	
	Secondary vesculitides	Connective tissue disease:	
		<ul> <li>Systemic lupus erythematosus</li> </ul>	
		Rheumatoid arthritis	
		Sjögren syndrome	
		Infection:	
		Hepatitis B and C	

		HIV     Lyme disease     Cytomegalovirus     Herpes zaster virus     Other bacterial infections Medication:
		Sulfonamides     Antiviral agents
		Malignancy
		Paraneoplastic vasculitis
Paraneoplastic nerve and muscle	Sensorimotor neuropathy	
disease	Myopathy	
Vascular occlusion		

	2. Brain	
Multiple sclerosis		
Parkinson's disease		
Motor neurone disease		
Lenticulo-capsular haemorrhages		
Space-occupying lesions		

	3. Spinal cord	
Multiple sclerosis		
Motor neurone disease		
Syringomyelia		
Transverse myelitis		
Posterior or anterolateral situated	Tumour	
space- occupying lesion	Abscess	
	Haematoma	

4. Cervical and thoracic spinal canal		
L		
1 ''	Abscess, haematoma, tumour, etc	
space-occupying lesion		

5. Conus medullaris		
Parasagital space-occupying lesion	Disc pathology	
	Gas sequestration	
	Tumours	Soft tissue
		Intradural
		Extradural
		Bone
		metastasis

	6. Lumbar spir	nal canal	
Spinous process	Interspinous bursa		
Facet joint	Osteoarthrosis alone		$\neg$
	Hypertrophy		$\neg$
	Cyst		
	Rotational instability		$\neg \neg$
Anterior subluxation	Degenerative spondylolisthesis		$\neg \neg$
Posterior subluxation	Retrolisthesis		
Space-occupying lesion	Disc pathology		
	Haematoma		
	Tumours	Bone, soft tissue, metastasis	

	7. Lumbar nerve ro	ot canai
Loss of disc height with posterior	Superior articular process impingement	
subluxation		
Spondylosis	Osteophyte	Superior facet joint
		Inferior endplate
Lateral facet joint cyst		12 20 12 20
Anterior subluxation	Degenerative spondylolisthesis	Hypertrophy superior facet joint into nerve root canal
	Isthmic spondylolisthesis	Disc bulging
		Pars interarticularis hypertrophy
Merve root lesions	Cyst	
	Benign temours	Schwannomas
		Neurofibromas
		Haemangioblastomas
		Non-Hodgkin's lymphomos
	Malignant tumours	Malinant peripheral nerve sheath tumours
Disc herniation		
Pedicle compresses nerve root	Pedicle moves down	Loss of disc height with:
8		a) Spondylolisthesis
		b) Degenerative scoliosis
Nerve root anomaly	Conjoint nerve root	
	Two nerve roots in one canal	

	8. Lumbar extraforam	inal area
Far lateral disc herniation		Sec.
Corporo-transverse ligament	Ligament descends	a) Rotational subluxation
13) 37		b) Disc space narrowing
Psoas pathology	Abscess, haematoma, tumour, any space occupying lesion	
Transverse process moves down with complete disc space narrowing	Spondylolisthesis, degenerative scoliosis	L5 nerve root impinged between transverse process and ala of sacrum

	9. Pelvis	
LS transitional vertebra	Pseudoarthrosis	L5 nerve root compression
	Osteophyte	
umbosacral ligament	Lumbosocral tunnel	L5 nerve root compression
tress fracture socrum	Leg pain	
	Neuropathy	
	Direct nerve compression	
acroiliac joint	Degenerative	
	Piogenic infection	÷
	Tuberculosis	
	Tumours	Bone, soft tissue
	Seronegative spondylarthropathies	Ankylosing spondylitis
		psoriasis arthritis
		reactive arthritis
		Behcet's disease
umbosacral radiculoplexus	Diabetic LRPN	
europathy (LRPN)	Non-diabetic LRPN	
8 63% 6	Chronic inflammatory demyelinating	3
	polyneuropathy	
	Connective tissue disease	
	Lyme disease	
	Sarcaidasis	1
	Cytomegalovirus	
iriformis syndrome	Hypertrophy, spasm, contracture, inflammation	Compression ischiadic nerve
uperior gluteal nerve entrapment	Narrowing of supropiriformis foromen	Spasm of piriformis
yndrome		Nerve perforating piriformis
		Aneurysm or pseudoaneurysm of superior gluteal
		Hip surgery
		Percutaneus iliasacral screws
		Abscess
		Pelvis fracture
ferior gluteal nerve entrapment	Narrowing of infrapiriformis foramen	Aneurysm of inferior gluteal artery
yndrome		Pelvis fracture
		Abscess
udendal nerve entrapment	Compression in pudendal canal	Between sacrospinous and sacrotuberous ligaments
yndrome	N 8	Falciform pracess
		Duplication of obturator fascia
pecial considerations in female	Sciatica in pregnancy	Uterus compresses nerves
atients	Obstetric table	Stirrups compress common peroneal nerve
	Obstetric neuropathy	Sciatic nerve compressed during vaginal delivery
	Piriformis syndrome during labour	Haematoma of piriformis
		Piriformis abscess after forceps delivery
	Leiomyomas	Lumbosacral plexus compression
	Endometriosis	Infiltration or compression of sciatic nerve
	Vaginal procedures	Superior gluteal artery aneurysm and nerve
		compression
		Sciatic and superior gluteal nerve neuropathy due to stretching
		pireiching

	10. Lower	extremity
Bursitis	Greater trochanter	
	Iliopsoas	
	Iliopectineal	
Tendinitis	Gluteus medius	
Stress fracture	Intertrochanteric	
	Proximal femur	
	Tibia	
	Fibula	
	Metatarsal	

Non-traumatic focal	Compression neuropathies	Acute, chronic, hereditary
mononeuropathies	Infectious neuropathies	Herpes zoster, Lyme disease
	114.1	HIV, leprosy, hepatitis B and C, bacterial infections,
		cyto-megalo- and Epstein-Barr virus
	Inflammatory/vasculitic neuropathies	Churg-Strauss syndrome, microscopic polyangiitis,
	initialination y/ vasconine neoropaintes	classic polyarteritis nodosa, Wegener granulomatosis
		systemic lupus erythematosis rheumatoid arthritis,
		Sjögren syndrome
	Drug-related neuropathies	Sulfanamides, antiviral agents
	Metabolic neuropathies	Diabetic amyotrophy
		Alcoholic
		Urgemic
	Paraneoplastic neuropathies	Vesculitis, sensorimeter neuropathy
	Radiation neuropathy	Testamo, sensenment morepany
	Nerve and nerve sheath tumuors	
	Hereditary	Familial amyloid polyneuropathy
		Heriditary compression neuropathy
Nerve entrapment syndromes	Iliohypogastric	
	Ilioinguinal	2
	Genitofemoral	A company of the control of the cont
	Lateral femoral cutaneous nerve	Meralgia paraesthetica
	Femoral nerve	Pelvis
		Hip joint
		Hip joint capsule
	1	Tendons of psoas and vastus intermedius
	1	Methylmethocrylate heat
	1	Pelvic procedures with acute flexion, abduction and
		external rotation
		Pelvic fractures
	Saphenous nerve	Roof of adductor conal
	Supricine Site in the	Femoral vessels
		Pes ansirinus bursitis
		Maria Caracter Caracter Control Contro
		Varicose vein operations
	S. Nat	Medial knee operations
	Common peroneal nerve	Lateral to fibula neck by tight plaster casts, knee
	68	surgery, osteophytes, synovial cysts, ganglions, sitting
		in crossed leg position, runners, cyclists
	Deep peroneal nerve	Anterior torsal tunnel syndrome
	Superficial peroneal nerve	Dancers: inversion and plantar flexion injuries
	Proximal tibial nerve	Popliteal fossa: popliteal cyst, popliteal artery
		aneurism, ganglia
	Distal tibial nerve	Tarsal tunnel syndrome: trouma, surgery, tumor,
		ganglia, varicosities, anomalous muscle, foot
		deformities
	Sural nerve	Mass lesion, scar fissue, ganglia, surgery,
		trombophlebitis, ski boots, athletes
	Medial plantar nerve	Jogger's foot
	Inferior calcaneal nerve	Baxter neuropathy
	The same of the sa	
	Interdigital nerve	Morton neuroma
	Medial plantar proper digital nerve	Joplins neuroma
Ayopathies/myositis	Inflammatory myopathy	Dermatomyositis
		Polymyositis
		Inclusion body myositis
	Myositis in collagen vascular disease	Rheumatoid arthritis
	myssan in temper razena assess	Systemic lupus erythematosis
		Mixed connective tissue disease
		Sjögren syndrome
	Radiation myositis	
	Grave's disease	
	Drug-induced myositis	Lipid-lowering statins
		Antiretroviral medication
	HIV myositis	
	Myositis due to infection	
	Polymyositis	1
		+
	Necrotising fasciitis	
	Sarcoidosis	
Sport-related leg pain	Stress fractures	
	Medial tibial stress syndrome	
	Tendinopathies	
	Nerve entrapment syndromes	
Nouvalanien   ean differen	Nerve entrapment syndromes Vascular syndromes	
Neurological conditions	Nerve entrapment syndromes Vascular syndromes Complex regional pain syndrome	
Neurological conditions	Nerve entrapment syndromes Vascular syndromes	

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