The Hip and the Neuromuscular Physician
From EDX to Coxa Saltans

Faculty

Timothy Carey, MD, FRCS(C)
Associate Professor
University of Western Ontario
London, Ontario, Canada
Dr. Carey is a graduate of the University of Ottawa school of medicine and also completed his orthopaedic residency there after a year internship at the Toronto East General hospital. Two years of fellowship training in paediatric orthopaedic surgery followed at the Children's Hospital of Eastern Ontario and the Shriners Hospital, Tampa Unit. Dr. Carey has been on staff at the London Health Sciences Centre since 1995 and is currently an associate professor at the University of Western Ontario (UWO), program director of the orthopaedic residency training program UWO, and chief of paediatric orthopaedics division. His clinical interests include spinal deformity, cerebral palsy, and limb lengthening.

Timothy J. Doherty, MD, PhD, FRCP(C)
Associate Professor
Departments of Clinical Neurological Sciences and Rehabilitation Medicine
The Schulich School of Medicine and Dentistry
University of Western Ontario
London, Ontario, Canada
Dr. Doherty is an associate professor in the Departments of Clinical Neurological Sciences and Physical Medicine and Rehabilitation at the University of Western Ontario in London, Ontario. In 2005, he was named Canada Research Chair in Neuromuscular Function in Health, Aging, and Disease. He is a consultant physiatrist and clinical neurophysiologist at London Health Sciences Centre. Dr. Doherty is the author of over 60 peer-reviewed papers. His research focuses on the examination of the motor system and motor units in health, aging, and disease. Additionally, his research is aimed at understanding the physiological basis of impairment in the motor system and rehabilitation interventions to limit disability.

Thomas A. Miller, BSc, MD, FRCP(C)
Associate Professor
Schulich School of Medicine and Dentistry
Department of Physical Medicine & Rehabilitation
University of Western Ontario
St. Joseph's Health Care/Mount Hope
London, Ontario, Canada
Dr. Miller is a graduate of Queen's University and trained in physical medicine and rehabilitation at the University of Ottawa. He then performed a fellowship in clinical neurophysiology at the University of New South Wales, Australia. He is the medical director of the musculoskeletal rehabilitation program, director of the electrodiagnostic laboratory, the consultant physiatrist with the Hand and Upper Limb Centre, and co-director of the Peripheral Nerve Clinic, St. Joseph's Health Centre, London, Canada. Tom is an associate professor in the Schulich School of Medicine and Dentistry at the University of Western Ontario. Dr Miller is currently the president of the Canadian Association of Physical Medicine and Rehabilitation.

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Course Chair: David Bryan Shuster, MD

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Douglas C Ross, MD, MEd, FRCS(C)

Chair, Division of Plastic Surgery
Co-Director, Peripheral Nerve Clinic
Schulich School of Medicine and Dentistry
University of Western Ontario
London, Ontario, Canada

Dr. Ross is a graduate of the University of British Columbia (BSc, MD). He also holds a Masters of Education from the Ontario Institute for Studies in Education at the University of Toronto. He completed his plastic surgery training at the University of Toronto followed by two years of fellowship training in hand and microsurgery at Toronto, and hand surgery in Louisville, Kentucky. He has been a faculty member at the University of Western Ontario (UWO) since 1992. Dr. Ross is chair of the Division of Plastic Surgery at UWO, a staff member at the Hand & Upper Limb Centre at St. Joseph’s Health Centre, and co-director of the Peripheral Nerve Clinic in London. He serves as secretary of the Canadian Society for Surgery of the Hand and is a member of the American Society for Surgery of the Hand, the American Society for Peripheral Nerve, and the American Society for Reconstructive Microsurgery. His clinical interests include upper extremity surgery, reconstructive microsurgery and peripheral nerve surgery. He also has a strong interest in surgical education.

Keith Sequeira, MD, FRCP(C)

Associate Director
Regional Spinal Cord and Brain Injury Rehabilitation
Parkwood Hospital
London, Ontario, Canada

Dr. Sequeira is a graduate of the University of Toronto and completed his residency at the Albany Medical Center in New York where he was chief resident during his final year. He completed a fellowship in electrodiagnostic and sports medicine at Michigan State University. Dr. Sequeira is currently the associate director of the Regional Spinal Cord and Brain Injury Rehabilitation Programs at Parkwood Hospital in London, Ontario. He holds an appointment at the University of Western Ontario as an associate professor and residency program director in the Department of Physical Medicine & Rehabilitation. He is the director of the undergraduate musculoskeletal curriculum at the Schulich School of Medicine at the University of Western Ontario. He runs a spasticity clinic at Parkwood Hospital and is actively involved in spinal cord and brain injury research, medical school education and has been in active practice for over 10 years.
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OBJECTIVES
After attending this session, participants will be able to (1) distinguish and contrast presentations of musculoskeletal hip and pelvic pain for the clinical EDX physician, (2) summarize the myth and facts about piriformis syndrome, (3) develop a clinical and EDX approach to lumbosacral plexopathy, (4) demonstrate and recognize orthopedic treatment options for the hip, pelvis, and lower limb in neuromuscular disease, and (5) appreciate the surgical treatment options in nerve injury including “neurotization” for lower-limb nerve injuries.

PREREQUISITE
This course is designed as an educational opportunity for physicians.

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INTRODUCTION

Hip and groin injuries only account for 2-4% of all adult athletic injuries, but are a significant cause of morbidity. The complexity of the anatomy and the numerous structures (e.g., muscles, abdominal contents, nerves, cartilage) often make it a challenge to confirm diagnosis; in approximately 30% of cases, it remains unclear. The differential diagnoses include: muscle strain, tendonitis, apophysitis, fracture (stress, avulsion, trauma related), bursitis (trochanteric, ischial), iliotibial band syndrome, labral tear, femoroacetabular impingement, snapping hip syndrome, osteitis pubis, degenerative disease, peripheral nerve injury, and sports hernia.

This manuscript focuses on three important non-neurological causes of groin and buttock pain in young patients. It discusses the clinical features, diagnosis, treatment, and prognosis for femoroacetabular impingement (FAI), sports hernia (SH), and trochanteric bursitis (Table 1).

FEMOROACETABULAR IMPINGEMENT

Anatomy

The ball and socket hip joint consists of the femoral head and acetabulum. The articular surface of the acetabulum is a dense cartilage (type II collagen) that also covers most of the femoral head. The acetabular labrum is a fibrocartilaginous structure similar to that in the shoulder. The labrum is attached to the bony edge of the acetabulum and outlines the periphery. It ends at the inferior part of the acetabulum and is innervated by numerous sensory nerve endings mediating deep sensation, pressure, and pain. The labrum serves many functions. It deepens the socket, increases surface area, distributes load, and reduces articular stress. Its most important role is to improve stability of the joint by distributing pressure, especially during motion. The labrum also helps to seal the joint, maintaining fluid and hydrostatic pressure within it. It reduces the forces that would otherwise be applied to the articular cartilage of the joint. Because the labrum is deeply innervated, a tear can result in pain as well as early joint deterioration (osteoarthritis) and destabilization.

Description

FAI is a hip disorder characterized by impaired joint clearance between the femoral head/neck and acetabulum. Two types have been described: femoral cause (CAM) and acetabular cause (pincer) impingement. CAM impingement is caused by an abnormality of the anterolateral femoral head-neck junction that manifests as
labrum. Repetitive loading eventually causes the labrum to fail. Chronic impingement leads to excess bone growth at the base of the hip, motion. Forces are spread to the labrum and underlying femoral neck, compressing the labrum during physiological motion. Any deformity of the femoral head or neck, or decreased head/neck concavity (“offset”) can result in CAM impingement; these include femoral neck retroversion, Legg-Calvé-Perthes disease, and slipped capital femoral epiphysis, or malunited femoral neck fractures.

Pincer impingement happens when overcoverage of the femoral head by the acetabulum causes extra contact between the femoral head/neck and acetabulum. The extra stress on the adjacent cartilage results in excess compressive force and injury to the labrum or adjacent condral surface. CAM impingement typically presents in males, with onset of symptoms between 30 and 39 years of age. Any deformity of the femoral head or neck or decreased head/neck concavity (“offset”) can result in CAM impingement; these include femoral neck retroversion, Legg-Calvé-Perthes disease, and slipped capital femoral epiphysis, or malunited femoral neck fractures.

The pain associated with this condition is sharp or dull, and usually located in the groin. Aggravating factors include running, pivoting, walking, and flexion activities, such as climbing stairs, getting up from a seated position, and prolonged sitting. Rest and frequent position changes alleviate discomfort. The initial pain is mild, but gradually progresses to moderate or severe levels. Growing intensity limits participation in sports and other activities. Patients often note that they periodically limp during symptoms, exertion, and toward the end of more intense activity.

**Table 1**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Important Neurological Differential Diagnosis</th>
<th>Distinguishing Features</th>
<th>Helpful Imaging</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>FAI</td>
<td>Femoral Acetabular Impingement</td>
<td>Ilioinguinal neuropathy, L1-2 radiculopathy, Obturator Neuropathy</td>
<td>Age 30-45; Groin pain (no swelling); Anterior impingement on exam; typically no neurologic symptoms.</td>
<td>X-ray (AP, cross table lateral)-head/neck offset; MRI/MRA (labral, cartilage deficiencies).</td>
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<tr>
<td>SH</td>
<td>Sports Hernia</td>
<td>Ilioinguinal neuropathy, Genitofemoral Neuropathy, L1-2 radiculopathy, Obturator Neuropathy</td>
<td>Age varies; Groin pain (occ asional swelling); pain w/ resisted groin testing/stretching; typically no neurologic symptoms. Pubic tubercle tender; subtle swelling/tender inguinal ring</td>
<td>Imaging to rule out other causes, not to confirm Dx. (e.g., ultrasound hernia, or MRI osteitis pubis)</td>
</tr>
<tr>
<td>GTPS</td>
<td>Greater Trochanteric Bursitis</td>
<td>L5/S1 radiculopathy, spinal stenosis, SI Dysfunction Piriformis Syndrome, Sciatic Neuropathy</td>
<td>Age varies; pain to palpate lateral buttock; worse with standing or lying on affected side; associated w/bling in L5/S1 distribution.</td>
<td>Physical exam most useful; imaging to rule out other causes; inflammation not typically seen.</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging; MRA = magnetic resonance angiography; NSAIDs = nonsteroidal antiinflammatory drugs

insufficient anterolateral concavity. The shape of the femoral head (aspherical) promotes extra contact between the femoral head/neck and acetabulum. The extra stress on the adjacent cartilage results in excess compressive force and injury to the labrum or adjacent condral surface. CAM impingement typically presents in males, with onset of symptoms between 30 and 39 years of age. Any deformity of the femoral head or neck or decreased head/neck concavity (“offset”) can result in CAM impingement; these include femoral neck retroversion, Legg-Calvé-Perthes disease, and slipped capital femoral epiphysis, or malunited femoral neck fractures.

Pincer impingement happens when overcoverage of the femoral head by the acetabulum causes contact between the labrum and femoral neck, compressing the labrum during physiological hip motion. Forces are spread to the labrum and underlying cartilage, extending to the tip of the acetabulum. Over time, chronic impingement leads to excess bone growth at the base of the labrum. Repetitive loading eventually causes the labrum to fail and become symptomatic. Pincer impingement most often presents in females between the ages of 40 and 49, with groin pain after activity. Predisposing factors include a retroverted acetabulum, Legg-Calvé-Perthes disease, and slipped capital femoral epiphysis, or malunited femoral neck fractures.

The pain associated with this condition is sharp or dull, and usually located in the groin. Aggravating factors include running, pivoting, walking, and flexion activities, such as climbing stairs, getting up from a seated position, and prolonged sitting. Rest and frequent position changes alleviate discomfort. The initial pain is mild, but gradually progresses to moderate or severe levels. Growing intensity limits participation in sports and other activities. Patients often note that they periodically limp during symptoms, exertion, and toward the end of more intense activity.

**Diagnosis**

Physical examination shows reduced active and passive (may be pain related) hip flexion. Patients often have a slightly antalgic gait. Data suggest that the hip anterior impingement test is generally the most sensitive and specific examination technique. With the patient in a supine position, the hip is passively flexed to 90 degrees as the examiner adducts the leg and gently rotates the hip internally. Limitation of movement and pain at the end of range are important positive signs. Most patients (95%) with this condition have a positive finding. In a recent study, the involved side revealed 9° less hip flexion, 3 degrees less adduction, and 4 degrees less internal rotation.
Flexion Abduction External Rotation (FABER) testing also often reveals groin pain on the side being moved. To test for posterior impingement, the patient lies in a supine position while the examined leg is allowed into extension off the side of the table. The clinician provides external rotation of the hip as it is extending. A positive test produces pain in the groin during this motion. This test is far less sensitive than the anterior impingement test for FAI.13-17

Studies indicate that the labrum takes on some weight-bearing load at the end range of motion, with excess or repetitive force causing injury.8,11,12 Patients with FAI are often involved in athletics requiring hip flexion and/or rotation. Typical sports include hockey, tennis, martial arts, weight lifting, soccer, horse riding, and dance. All of these require frequent, and at times, forceful hip external rotation.13-17

Misdiagnoses are common; it takes an average of 2 years9,10 before FAI is identified. In one recent study, 20-25% of athletes with groin pain and 55% of patients with mechanical hip pain of unknown cause were eventually found to have a labral hip tear and a diagnosis of FAI.9,10

**Investigations**

The diagnosis is mostly made on history and physical examination. However, there are imaging findings that help support one’s conclusions.17,24,26,27 Hip X-rays are the first and most important diagnostic tool. Anterior-posterior pelvic radiographs will confirm retroversion or coxa profunda (pincer impingement).17,24,26,27 Examination of the femoral head-neck is essential. Femoral head-neck offset measures the difference between the widest diameter of the femoral head and the most prominent part of the femoral neck.13,14 Reduced offset can result in CAM impingement. Lateral and cross-table lateral views are also essential, and provide additional information regarding femoral head sphericity and head-neck relationship.13,14,24,26,27 It is important to notify the radiologist of your suspicion as findings are often subtle.

Computed tomography imaging can assess the bony architecture of the hip, and is useful for diagnosing CAM lesions, and if needed, surgical planning. It should be used with caution given its limited utility and high radiation exposure compared to magnetic resonance imaging (MRI). The latter, and especially magnetic resonance arthrography (MRA) (gadolinium), are useful in the workup of FAI and assessment of the labrum and articular cartilage.26,27 MRA distends the joint and separates the various articular structures, allowing visualization of the cartilage and labrum. MRA can localize head-neck offset, labral tears, and cartilage lesions.26,27 If the abnormality of the head-neck is not found, and only the labral/cartilage lesions are treated, the underlying cause will be missed and the problem will recur.

**Conservative Treatment**

Nonsurgical treatment should always be considered first. This includes activity modification and/or stopping the precipitating sport, at least temporarily. Often this is difficult as many patients are competitive athletes who do not want to stop. They need to be made aware of the long-term consequences of the condition if allowed to persist untreated, i.e., degenerative disease.

A course of physiotherapy to target the tight and weak muscles is typically a good initial treatment. Stretching the hip flexors and strengthening the core muscles and glutei can be helpful. A short course of nonsteroidal anti-inflammatory drugs (NSAIDs) or other pain medication can often help control pain and allow patients to take full advantage of therapy. A diagnostic and therapeutic injection (guided with ultrasound or fluoroscopy) with anesthetic/corticosteroid may help.20,21 If this reduces the pain, it provides confirmation that the hip joint is the problem. The pain control achieved with such an injection may allow increased therapy and further improvement. Alterations of lower extremity mechanics (i.e., foot/shoe orthotics) can help correct leg length discrepancies or malalignments.

**Surgical Treatment**

Open and arthroscopic treatments have been described. The open procedure involves dislocation of the hip, careful preservation of the hip’s blood supply, and treatment directed to the pathology.18,20,22 It typically involves some form of femoral osteoplasty (removal of the impinging ‘bump’) and debridement/repair of the labrum and articular cartilage. Very good short-term improvements have been noted in symptoms, function, and return to activity/sport.18,22 Long-term outcomes are still unknown.

**SPORTS HERNIA VERSUS ADDUCTOR STRAIN**

**Anatomy/Description**

SH is a nonspecific diagnosis that refers to groin pain in an athlete related to a weakness of the posterior inguinal wall.28-49 and relates to an abnormality of the internal or external abdominal oblique muscles, inguinal ligament, or conjointed tendon.28-31 It typically results in a loss of inguinal canal integrity without a clinically detectable hernia.28-30 Imbalance between the adductor and abdominal muscle strength/pull may also lead to this condition.51,36,40,46 For instance, repetitive or extreme forces applied by the adductor muscles may injure the internal oblique and/or transversalis fascia attachments to the inguinal ligament. In men, the internal oblique muscle forms the cremaster and spermatic fascia, which may be why these injuries cause scrotal and testicular pain.11,28

**Clinical Presentation**

Patients often present with insidious groin pain that gradually worsens. Increases in intra-abdominal pressure (e.g., sit-ups, cough, sneeze) or vigorous hip/leg activity (e.g., kicking a ball, pivoting) worsen the pain. In fact, reproduction of groin pain during the sporting activity is important to make this diagnosis.30,31,42-45,48,49 Symptoms typically improve with rest but recur with activity.
Diagnosis/Investigations

Four abnormalities are generally found on examination: (1) inguinal canal tenderness; (2) dilated superficial inguinal ring; (3) pubic tubercle tenderness; and (4) hip adductor origin tenderness. The most important physical examination findings are pubic tubercle tenderness and an inguinal floor tear that may be palpable, causing pain in the external inguinal ring. Unfortunately, these findings are not specific for SH.

SH is a nonspecific diagnosis made on clinical grounds. It is difficult to differentiate it from a muscle strain of the rectus abdominus and adductor group. There is no test that definitively confirms the presence of a SH. Although dynamic ultrasound has shown promise (as the patient strains, a bulge is noted at the superficial inguinal ring), the findings are subtle and extremely operator dependent. Testing is done to rule out other causes for the pain (e.g., MRI to rule out muscle tear, bone scan for osteitis pubis).

Pain on palpation in the adductor musculature and with resisted hip adduction suggests an adductor strain. Unfortunately, herniography (injecting contrast into the peritoneal cavity) has a high false positive rate and cannot be reliably trusted to diagnose a SH. Although there are numerous helpful signs/tests, none confirm this diagnosis. Often, it can only be determined at the time of surgery. In spite of all investigations to date, there is no consensus as to what constitutes a SH, and it remains a diagnosis of exclusion.

Conservative Treatment

Conservative treatment (e.g., 6 to 8 weeks of rest, activity modification, medications, physiotherapy) is often disappointing. Biomechanical abnormalities (leg length discrepancies, muscle imbalances, and leg/foot malalignments) need to be ruled out or treated. If needed, physiotherapy and the use of suitable foot/shoe orthotics can address these issues. An adequate trial of therapy should involve strengthening of the core, pelvic, and adductor muscles. The biomechanics of the sport being performed should also be assessed and errors in technique that predispose to injury should be corrected.

Therapy should focus on correcting imbalances between the hip and abdominal muscles and on endurance, coordination, and flexibility of the trunk and upper leg musculature. Transient improvement occurs when trigger activities are avoided, but pain often returns when the inciting maneuver is performed. Attempts to return to sport should be considered once the patient is pain-free. Injection treatment (corticosteroid, prolotherapy) directed to the adductor origin can temporarily relieve pain. However, literature on the results of injections for sport hernias is sparse.

Surgical Treatment

SHs, unlike most cases of groin pain, rarely improve long-term without surgical treatment. Surgery for this condition has a good success rate (60-90% symptom relief and return to sport). The most common finding is posterior inguinal wall insufficiency that creates an occult hernia, not noticeable on physical examination. Open or laparoscopic herniorrhaphy with mesh reinforcement has good success rates. The goal of surgery is generally to reinforce the abdominal muscles and/or fascia around the inguinal ligament (similar to other inguinal hernia surgeries). Additionally, a portion of the adductor muscle origin can be released to restore the balance between these muscles and the abdominal group. Postoperative care involves walking with a gradual progression to jogging by 3 to 4 weeks, as pain allows. Cutting activities should be slowly introduced at 2 to 3 months, as tolerated. Rehabilitation after laparoscopic techniques generally progresses faster than with open procedures. If patients receive appropriate postoperative treatment, a return to full activities is often possible within 3 to 4 months.

Differential Diagnosis

Adductor strain is the most common cause of groin pain in athletes. It is often seen in those involved in soccer or sports requiring pivoting (e.g., squash, hockey, tennis). The proximal musculotendinous junction of the adductor longus and/or gracilis is typically involved. An MRI can help rule out a muscle or tendon tear. If a tear is present, a period of relative rest is necessary. A thorough biomechanical evaluation is needed, similar to treatment of a SH. Acute management should attempt to reduce pain and swelling with rest, ice, and compression. This should be followed by physiotherapy to restore range of motion, reduce pain, increase strength, and eventually begin active sport-specific training and return to competition. NSAIDs and corticosteroid injections are often used, but the literature is unclear about their efficacy. Anecdotal evidence supports alternative treatments like acupuncture, mobilization, transcutaneous electrical nerve stimulation, and liniments, but additional studies on their efficacy are needed.

GREATER TROCHANTERIC PAIN SYNDROME

Anatomy/Description

Bursae, fluid-filled sacs that cushion bony regions and adjacent soft tissue structures, are abundant in the lateral hip region. The two major ones are the subgluteus maximus and subgluteus medius bursae. The former, located superficial to the gluteus medius tendon and deep to the tensor fascia latae and gluteus maximus muscles, is the biggest bursa. It contributes most to greater trochanteric pain syndrome (GTPS). The gluteus minimus bursa, located cephalad and ventral to others, is relatively minor. The varied anatomy, number, and location of these bursae create a variable clinical presentation for GTPS.

The gluteus medius and minimus muscles/tendons play an important role in GTPS. Inflammation, irritation, and/or minor tears in the musculotendinous regions present with localized pain in the lateral hip region. Secondary inflammation of the adjacent bursae
may occur, but bursitis is not typically the primary pathology. Bursitis tends to result from repetitive microtrauma between adjacent surfaces, muscle dysfunction, or tightness that causes abnormal movement mechanics or muscle overuse. In a retrospective review of MRIs in 24 patients with lateral hip pain, most had gluteus medius abnormalities (minor tears). Bursitis was uncommon.

Clinical Presentation

GTPS usually presents with insidious lateral hip and buttock pain. Exacerbating factors include lying down on the affected side, prolonged standing, and transitioning from sitting to standing. Running, walking on uneven terrain, cutting activities, and climbing stairs often provoke symptoms. Pain frequently radiates along the lateral thigh to the knee. Numbness, tingling, and frank weakness are not typically associated with GTPS. The physical examination is normal except for pain and tenderness localized to the posterolateral hip region and the origin of the gluteus medius tendon. Pain can be reproduced with resisted abduction and external rotation. In general, however, the physical exam is nonspecific and not well-correlated with imaging findings.

Diagnosis/Investigations

This diagnosis pertains to pain along the lateral buttock and hip region. It typically affects 10-25% of individuals over the age of 50, but can also afflict young athletes, especially those susceptible to buttock and leg muscle tightness (e.g., runners). Although previously known as trochanteric bursitis, the condition typically lacks frank clinical or pathological inflammation. In addition, numerous bursae in the lateral hip region are potential contributors to this condition. Numerous risk factors are associated with the development of GTPS. These include: obesity, female gender, low back pain, hip/knee/lumbar degenerative disease, age >50, and iliobibial band (ITB) tightness. It is often confused with myofascial buttock pain, spinal pathology, and degenerative joint disease.

Conservative Treatment

Most cases of GTPS resolve spontaneously with conservative treatment. NSAIDs, relative rest, ice massage, weight loss, and behavior modification (avoiding lying on the affected side, limiting climbing and other precipitating factors) may speed recovery and improve pain. Physiotherapy aimed at restoring normal biomechanics of the hip and buttock region, core muscle strengthening, and lower extremity flexibility training can also help.

If conservative care fails to resolve the pain, injections may be considered. Although no placebo-controlled trials have been completed, prospective studies suggest improvements in pain with cortisone/anesthetic up to 6 months postinjection. Repeat injections, once the initial one wears off, are also effective. Thus far, fluoroscopically guided injections have not been shown to work better than landmark guided ones. This likely relates to the numerous bursae involved and the myotendinous rather than inflammatory nature of the problem. Given the varied etiology of GTPS, peribursal injections are more likely to go into the soft tissue structures, where the problem lies.

Corticosteroid injections are a safe, simple, and effective treatment for GTPS. Injections are used to treat the condition, provide pain relief, enhance participation in therapy, and confirm the diagnosis. Ejections of blood sugar have been reported up to 21 days post-injection. Thus, care needs to be taken with diabetic patients, especially with peribursal or soft tissue injections; The most common complications postinjection involve increased pain in the injected area (2-10%), Less common complications include fat and skin atrophy (1%), infection (0.1%), and tendon rupture (especially involving the Achilles tendon and plantar fascia – 0.1%).

Little evidence supports the efficacy of one steroid preparation over another. Injectable steroids improve pain and inflammation by reducing synovial blood flow and the inflammatory response. Insoluble steroids have a longer duration of action and higher incidence of cutaneous side effects. The least soluble are triamcinolone hexacetonide, followed by triamcinolone acetonide. Methyprednisolone acetate is moderately soluble and is the most commonly used injectable steroid in North America. In a recent review from the United Kingdom, it was recommended for large joints. Betamethasone has a high solubility and shorter duration of action, and may be better for soft tissue injections, such as the trochanteric bursal region. Duration and onset of action of anesthetics vary. Bupivacaine has a 30 minute onset of action and 9 hour duration. Lidocaine has a 1-2 minute onset of action and 1 hour duration.

Surgical Treatment

Refractory GTPS can also be treated surgically. Prospective short-term studies show that bursectomy and ITB release can improve pain in such cases. Long-term studies on GTPS and surgical outcomes are needed.

SUMMARY

Hip and groin pain is a common complaint in young athletes. In this article, we discussed the clinical presentation, diagnosis, treatment, and prognosis for FAI, SH, and GTPS. As with many musculoskeletal disorders, the history and physical examination are vital to differentiate between the various causes. Investigations are used to confirm clinical findings and rule out alternate sources of symptomology.

FAI is a relatively new diagnosis that presents with groin pain in the young adult population. It is under-recognized and without a gold standard test. FAI is characterized by reduced clearance between the
femoral head/neck and the acetabulum, resulting in an “impinge-
ment syndrome.” It is diagnosed by history and physical examination,
supported with imaging findings. As our knowledge of this condition and hip anatomy/biomechanics improve, so will our
ability to recognize it and utilize additional imaging (MRA, MRI)
to diagnosis it. FAI is associated with premature hip osteoarthritis in young adults. Thus, it is important to be aware of this and to
know that early identification and treatment may delay onset and progression in this population.

SH is a nonspecific diagnosis that is not a “true hernia.” Most
conventional tests are normal; clinical features, diagnostic criteria,
and physical examination findings are nonspecific. It is mostly a
diagnosis of exclusion. Subtle findings of posterior inguinal wall
insufficiency are often found during surgery; in addition, SH often
responds favorably to surgical treatment and repair.

GTPS pertains to pain in the lateral buttock in the area of the
trochanteric bursa. Pain increases with lying on the affected side,
walking, and standing. There is no definitive diagnostic test for this
condition. One of its hallmarks is response to conservative treat-
ment, including relative rest, activity modification, corticosteroid
injections, physiotherapy, and NSAIDs. In rare instances, surgical
treatment (bursectomy, ITB release) is needed. In such cases, surgery helps, at least in the short-
term.

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INTRODUCTION

Though several discrepant definitions exist, to purists, piriformis syndrome (PS) is best defined as a neuromuscular disorder that is presumed to occur when the sciatic nerve is compressed or otherwise irritated by the piriformis muscle as it passes through the sciatic notch. Some have subdivided PS into primary and secondary forms. Primary PS comprises those cases in which sciatic nerve root entrapment occurs because of some abnormality within the muscle itself, as in anomalous anatomy or hypertrophy of the muscle and/or nerve. Secondary PS usually caused by direct, blunt trauma to the piriformis muscle. The sciatic nerve entrapment that results produces a constellation of symptoms that can include pain, tingling and numbness in the affected buttock and along the ipsilateral sensory distribution of the sciatic nerve, combined with focal tenderness directly over the muscle, deep in the sciatic notch, and worsening of symptoms with certain provocative tests. In this way, it has been likened to other nerve entrapment syndromes like carpal tunnel syndrome (CTS) and entrapment involving the ulnar, peroneal, and tibial nerve at the elbow, knee and ankle, respectively. However, unlike these other syndromes that have gained broad acceptance among clinicians and researchers alike, PS is mired in controversy. While some believe that cases of true piriformis induced entrapment are rare but do exist, others, though perhaps not questioning the patient’s symptoms, express sincere scepticism regarding the piriformis’ causative role and the use of invasive injections and surgical procedures to treat it. There is debate as to whether the syndrome is best categorized as an entrapment or a myofascial pain disorder. This manuscript claims to explore the various sources of controversy, addressing issues of PS from both perspectives as they relate to the diagnosis and management of this condition.
interventional MRI were utilized in 239 consecutive patients with sciatica who had failed to respond to traditional treatment, and the authors ultimately attributed more than two-thirds of these cases to PS (67.8%), based on diagnostic criteria which included response to local piriformis injection but not spinal injection (i.e., disc, facet and/or root). Furthermore, MR-guided injection of a local anesthetic into the piriformis muscle produced relief in almost 85% of the presumed PS patients, with 15% obtaining relief lasting more than 8 months; and piriformis surgery performed on 62 patients resulted in either a good or excellent outcome in 80%.

Several other estimates of the percentage of patients with lower back and/or buttock pain with PS named as a cause of their symptoms have been on the order of 5 to 8%,14-20 although some have claimed a much lower percentage; in fact, suggesting that entrapment caused by the piriformis muscle is quite rare,5,7,9 and that the symptoms attributed to PS are caused by nerve impingement from some other structures, or are totally removed from any impingement at all. One survey that supports the rarity of PS is a retrospective review that examined 1293 cases of lower back pain treated at an orthopedic back pain clinic over a 12-year period, in which the incidence of PS was determined to be 0.33%.21 Clearly, differences in how PS is defined could have played a major role in these conflicting prevalence estimates. Stewart,8 for example, claims that the term is being used to denote four clinically distinct entities: (1) damage to the sciatic nerve by lesions in the vicinity of the piriformis muscle, (e.g., hematomas and aneurisms) (2) compressive damage to the proximal sciatic nerve by the piriformis muscle, usually because of some anatomic anomaly; (3) damage to the sciatic nerve by the piriformis muscle and adjacent tissue from trauma and scarring, which was termed post-traumatic PS, corresponding to the secondary PS mentioned previously; and (4) chronic buttock pain with no evidence of sciatic nerve damage. Stewart then argues that the first and fourth definitions should be excluded. Unquestionably, the number of these entities one encapsulates within the definition of PS would influence both its incidence/prevalence and the requirements for its diagnosis, both generically and in the individual patient. In terms of the latter issue, Stewart8 further recommends that patients meet five criteria prior to being assigned the second of his four piriformis definitions: symptoms and signs of sciatic nerve damage; electrophysiologic evidence of sciatic nerve damage in the absence of any abnormalities in paraspinal muscles by electromyography (EMG); imaging of the pelvis/lumbosacral spine that demonstrates no other pathology; surgical evidence consistent with piriformis-muscle induced nerve entrapment; and relief of symptoms post-surgical decompression, though he accepts the potential that chronic patients may not improve. As will become evident in further exploration, few patients meet these five criteria.

There seems to be relatively little debate at the individual level as to why many of the patients ascribed the diagnosis of PS suffer significantly, their disability largely secondary to pain that can severely restrict walking or even sitting. Additionally, many patients see several physicians and undergo years of waiting and expensive diagnostic imaging before a definitive diagnosis either is made, or they stop seeking explanations. For example, in one clinical trial of botulinum toxin (BTX) injections, the average duration of symptoms prior to inclusion in the trial was 39 months, ranging from 16 months to 7 years.22 During this time, patients may undergo lengthy trials of misdirected and fruitless therapy, injections, and even surgery. Consequently, it behaves physicians to (1) determine if, other than in very rare instances, piriformis-induced nerve entrapment truly is a cause of sciatica-like symptoms and, if so, how commonly; (2) name and/or define PS in such a way that it can be uniformly accepted, recognized and appropriately treated, as well as studied in clinical trials that generate results that are comparable between studies and can be generalized to a clearly defined population of patients; (3) identify sensitive and specific markers of disease, potentially a gold standard diagnostic test, but more likely a set of validated and universally applicable classification criteria; and (4) identify effective treatments through appropriate random, controlled and blinded clinical trials.

CONTROVERSY BEHIND PS

The controversy that surrounds PS does not just exist within the scientific community; it also affects daily clinical practice, as evidenced by widely discrepant estimates of its incidence in various settings. Further evidence of the effect of this controversy at the healthcare delivery level stems from a survey that was conducted by Silver and Leadbetter.10 Questionnaires were mailed to a random sample of 75 United States physiatrists, and of that sample, 29 responded (39%). Of these, only 72% were confident that PS was a legitimate diagnosis; moreover, reasonably similar percentages of physiatrists felt that the disorder was over diagnosed (55%) and under diagnosed (38%). On the other hand, the major controversies belying PS do not appear to be centered on whether or not these patients have true pain, but rather on what the source of that pain is and how it is best identified and treated.

Recent debate on the pros and cons of PS as a legitimate entity has included opinion papers and letters drafted by several different authors, addressing a host of different issues.4,5,7-9,23,24 Even the most adamant critics seem to accept the possibility that an occasional patient experiences piriformis induced sciatic nerve root entrapment,7,9 as in the case of a 40-year-old patient whose MRI scan demonstrated an anomalous sacral attachment of the piriformis muscle, whose piriformis was enlarged and compressing the S2 nerve root upon surgical exploration, and whose symptoms resolved immediately post operatively, leaving the patient pain free through at least 5 years of follow up.25 Similarly, Sayson and associates26 described a patient with sciatica who responded poorly to epidural steroid injection and only transiently to piriformis injection; but in whom subsequent surgical exploration of the sciatic nerve revealed a constricting band of fascia around the nerve, and the piriformis muscle lying anterior to the nerve. Arguments against the syndrome being more than just a rarity largely are defined in Table 1.
The sciatic nerve generally lies on the ventral aspect of the piriformis muscle, but considerable variation exists, with the S2 and S3 nerve roots especially documented to pass through the muscle in some asymptomatic patients,48 and in a sizeable percentage of asymptomatic live controls33 and cadavers.31-49 Due to its location within the sciatic notch and relative to the sacral nerve roots, symptoms classically include buttock pain with radiation into the ipsilateral thigh and leg.50 This pain often is exacerbated by prolonged sitting, walking, walking up inclines, and other movements.50 Symptoms other than skeletal pain include paresthesias and motor weakness, as well as dyspareunia in women, abdominal, pelvic and inguinal pain, and pain with bowel movements.2 Generally, they do not include urinary or bowel dysfunction, other than a possible increase in pain while passing stool.

On physical examination, patients are typically tender in the sciatic notch area and are focally tender on the ipsilateral side on rectal examination. In addition, a variety of provocative tests have been developed to stretch the piriformis, thereby increasing its compressive effect upon whatever nerve roots are being entrapped. The first such test to be ascribed specifically to PS is the Lasègue test, mentioned in 1947, when Robinson28 proposed a set of six criteria for what he labeled pyriformis syndrome. These criteria, which were based entirely upon his clinical experience, rather than any formal study, and are listed in Table 3.

As stated earlier, the various symptoms attributed to PS are problematic in that they all are nonspecific and are commonly reported in patients with other causes of lower back, buttock, and sciatic like pain. The same can be said of various physical findings that have been reported in these patients (Table 4). Tenderness in the buttock, even into the area of the sciatic notch, can be referred from the lumbosacral spine or sacroiliac joint, or can be the result of irritation of several different muscles within the pelvis. Rectal tenderness can be caused by something as simple and unrelated as compression of an internal hemorrhoid. Pain with external rotation of the hip is a common manifestation of early arthritis. All the various named signs (Lasègue, Freiburg, Pace, and Beatty) are nonspecific, not particularly sensitive, and are often absent in patients otherwise diagnosed with PS.8,9 Even during attempts by Fishman and associates30 to validate criteria for PS, many patients who responded to focal injections and, hence, were ultimately diagnosed with PS, exhibited only two of the three criteria used by the investigators to screen for the diagnosis. Broadhurst and as-

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**Table 1 Arguments against piriformis syndrome**

- (1) A lack of convincing evidence that the piriformis is anything more than a rare to very rare cause of sciatic nerve entrapment16;
- (2) The evidence that exists suggesting otherwise is based upon flawed studies and/or reasoning15;
- (3) Studies on cadavers as well as patients who have undergone surgery for other reasons have demonstrated that piriformis induced sciatic nerve compression is either uncommon or highly non specific1,16;
- (4) Electrophysiologic and imaging studies suggesting pathology generally are nonspecific and, consequently, potentially misleading9;
- (5) Numerous other causes of the symptoms are at least as likely5,7-9,27;
- (6) The label “piriformis syndrome” is misleading and should be changed to a more general term that does not implicate any particular anatomic structure5,7,8; and
- (7) Injections and surgical manipulations of the piriformis muscle are being performed too commonly and usually without adequate justification.

On the flip side, arguments for the syndrome being more than just a rarity largely are defined in Table 2.

**Table 2 Arguments for Piriformis Syndrome**

- (1) Piriformis syndrome is a reasonable explanation for a significant proportion of the patients with sciatic like symptoms whose pain is not explained by other, more accepted diagnoses2,23;
- (2) The anatomic location of the piriformis muscle corresponds precisely with the area of focal tenderness observed in these patients2,23,28;
- (3) The course of the muscle relative to the sacral nerve roots explains the results of a host of provocative tests that are often positive in these patients2,23,29-33;
- (4) A variety of imaging and neurodiagnostic tests now confirm the presence of piriformis pathology2,23,25,29,30,32,34-36; and
- (5) Numerous patients have responded well to either focal injections12,16-18,22,30,37-44 or surgical manipulation45,46 of the piriformis, thereby implicating it as the cause of symptoms in those cases.

Management of PS patients, including the clinical history and examination, and the use of diagnostic testing including electrophysiology, and treatment will be further discussed and these arguments and counter arguments will come into play once again.

**Clinical Findings**

Understanding the manifestations of piriformis-induced entrapment requires some familiarity with the anatomy of the muscle and surrounding structures. The piriformis muscle originates on the ventrolateral aspect of the sacrum at levels S2 through S4, and inserts into the piriform fossa of the greater trochanter.47 It is innervated by a nerve that is of S1 and S2 segmental origin. Its main functions are to externally rotate the thigh, and to abduct the thigh when the hip is flexed,2,15,47 though it also can be a weak hip flexor.
sociates\textsuperscript{51} attempted to correlate various symptoms and signs of PS with piriformis muscle morphology, as determined by ultrasound (US), and found that the odds of abnormal morphology was as high as 10.8 for the symptom of buttock pain walking up inclines, with a sensitivity of 95%; however, five of every eight patients with normal morphology also reported this symptom, for a specificity of just 38%. The odds ratios, sensitivity and specificity for pain with needling of the muscle, pain referred to the thigh, and pain with resisted abduction were 10.8, 95%, and 25%; 5.3, 80% and 57%; and 2.6, 95% and 13%, respectively.

Consequently, it appears that symptoms and physical signs alone are inadequate in establishing the diagnosis of PS as a distinct clinical entity and in establishing the diagnosis in the individual patient. Both require the addition of diagnostic testing and/or a response to disease specific treatments.

### Table 4 Signs of Piriformis Syndrome

<table>
<thead>
<tr>
<th>Sign</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Deep focal tenderness over the sciatic notch\textsuperscript{2,27,45,52}</td>
</tr>
<tr>
<td>2</td>
<td>Ipsilateral rectal tenderness (patient often exclaims that for the first time, someone has found his/her pain)\textsuperscript{53}</td>
</tr>
<tr>
<td>3</td>
<td>Palpable mass in the ipsilateral buttock\textsuperscript{2,28}</td>
</tr>
<tr>
<td>4</td>
<td>Antalgic gait\textsuperscript{2}</td>
</tr>
<tr>
<td>5</td>
<td>Traction of the affected limb reduces pain\textsuperscript{2,28}</td>
</tr>
<tr>
<td>6</td>
<td>Ipsilateral lower extremity weakness\textsuperscript{2,56}</td>
</tr>
<tr>
<td>7</td>
<td>Positive Freiberg sign (pain with passive internal rotation of the hip)\textsuperscript{2,56}</td>
</tr>
<tr>
<td>8</td>
<td>Positive Lasègue sign (localized pain over the sciatic notch, especially when the hip is flexed and knee extended)\textsuperscript{2,28}</td>
</tr>
<tr>
<td>9</td>
<td>Positive Pace sign (pain and weakness on resisted abduction external rotation of the hip)\textsuperscript{2,24,45,53}</td>
</tr>
<tr>
<td>10</td>
<td>Positive FAIR sign (pain reproduced when the hip is flexed, adducted and internally rotated)</td>
</tr>
<tr>
<td>11</td>
<td>Positive piriformis sign (patient externally rotates the affected hip when lying supine)\textsuperscript{2,52}</td>
</tr>
<tr>
<td>12</td>
<td>Positive Beatty test (abduction of affected lower extremity when lying on the contralateral side recreates sciatic symptoms)\textsuperscript{2,57}</td>
</tr>
<tr>
<td>13</td>
<td>Limited internal rotation of the affected hip\textsuperscript{2}</td>
</tr>
<tr>
<td>14</td>
<td>Gluteal atrophy in chronic cases\textsuperscript{2,28} – question disuse atrophy</td>
</tr>
<tr>
<td>15</td>
<td>Persistent sacral rotation toward the contralateral side with compensatory lumbar rotation\textsuperscript{2}</td>
</tr>
</tbody>
</table>

FAIR = hip flexed, adducted, and internally rotated

### DIAGNOSTIC IMAGING

Although there is relatively little debate as to their use in ruling out certain other causes of sciatic pain like radiculopathy, there is controversy in determining the value of using a variety of imaging modalities to document or confirm the presence of piriformis-related nerve root entrapment.

In terms of diagnostic (as opposed to therapeutic guidance) imaging, investigators have primarily reported on the use of MRI and MRN, though a single report on nuclear scintigraphy in a single patient described uptake in the distribution of the piriformis muscle on the symptomatic side after the administration of 20 mCi of Tc-99m methylene diphosphonate.\textsuperscript{58} Computed tomography (CT) scans were not found to be helpful by Benson and Schutzer in their study of post-traumatic PS,\textsuperscript{45} but both contrast CT and MRI were helpful in identifying an enlarged piriformis muscle in a 27-year-old woman with several classic symptoms and signs that included severe rectal and pelvic tenderness, as well as positive Freiberg, Pace, and Lasègue signs; injection of 10ml of 1% lidocaine and 10mg of triamcinolone acetonide produced immediate and complete relief.\textsuperscript{59}

The largest study assessing the potential utility of MRI in diagnosing PS was an imaging survey to assess piriformis muscle appearance and its relationship to sacral nerve roots in 100 patients who did not have PS.\textsuperscript{33} Because both sides were assessed, 200 piriformis muscles and sciatic nerves were viewed. Considerable variability was found in the size of the muscles and the nerve root courses. Almost one in five subjects had greater than 3mm of asymmetry in the size of their piriformis muscles, with a maximum of 8mm; and the percentage of nerve roots that traversed the muscle was < 1% for S1, but 95% and 97% for S2 and S3, respectively. The S4 root was located below the muscle in 95% of cases.

Reports supporting the diagnostic use of standard MRI in patients diagnosed with PS are limited to the single patient described above,\textsuperscript{59} who underwent CT and MRI testing, as well as three further single case reports, involving a 40-year-old man,\textsuperscript{25} and, 30-35 and 27-year-old women.\textsuperscript{59} In the first single case,\textsuperscript{58} MRI revealed an anomalous sacral attachment, with accessory muscle fibers crossing over the S2 nerve root; surgical exploration revealed S2 compression, which was surgically released via resection of approximately 1 cm of the piriformis tendon near its insertion into the piriformis fossa, resulting in total resolution of pain through 5 years of follow up. In the second case,\textsuperscript{35} MRI revealed asymmetrical enlargement of the piriformis on the symptomatic side, accompanied by anterior displacement of the sciatic nerve. Interestingly, plain radiographs revealed thoracolumbar rotoscoliosis, which was also felt to contribute to the patient’s pain and was a major focus of physiotherapy; ultimately, this woman experienced resolution of her symptoms after 3 months of conservative treatment. The final patient\textsuperscript{59} had evidence of ipsilateral piriformis muscle enlargement documented both by CT and MRI. In a fourth single case report,\textsuperscript{26} MRI was normal, even though surgical exploration of the sciatic nerve revealed a constricting band of fascia around the nerve, as well as the piriformis muscle lying anterior to the nerve. This absence of MRI findings is consistent with a lack of findings reported by Barton\textsuperscript{50} in a series of four patients, despite piriformis-related pathology identified on surgical exploration in some of them.

MRN is a relatively new technique that has been specifically developed to enhance the imaging of nerves.\textsuperscript{3,34,60} Filler and associates\textsuperscript{34} have defined it as “…tissue-selective imaging directed at identifying and evaluating characteristics of nerve morphology: internal fascicular pattern, longitudinal variations in signal intensity and calibre, and connections and relations to other nerves or plexuses.” Its ability to identify peripheral nerve pathology has been documented...
at numerous body sites, including neck, back, pelvis, and extremities. The only study on the usefulness of MRN in PS has been the Filler and associates study of 239 patients with sciatica-like pain in whom standard diagnostics and therapy failed to yield any satisfactory recovery; as stated earlier, 67% of this number were deemed to have piriformis-induced sciatic nerve root entrapment, based upon the appearance of diagnostic images, the patient's response to guided injections, or both. The authors concluded not only that MRN was a useful tool for establishing a diagnosis and aiding in the monitoring of treatment effects in PS, but that the results validate PS as a true clinical entity. Tiel disagrees with both conclusions, arguing that Filler's study was flawed on several counts, including the lack of adequate information to rule out other diagnoses, a potential for contamination from other treatments, and problems with the issues of magic angle effect and echo times. In rebuttal, Filler points out that magic angle effects only occur when echo times less than 40 ms are used, whereas MRN studies generally utilize echo times between 70 and 100 ms; and that the immediate and dramatic response to targeted injections of patients ascribed a diagnosis of piriformis in the noted study makes it extremely unlikely that other diagnoses or treatments exerted a substantial effect. Finally, in one subsequent study in which all other pathologies that might explain diagnoses or treatments exerted a substantial effect. Finally, in one subsequent study in which all other pathologies that might explain sciatic pain were ruled out prior to patient enrollment, by MRI subsequent study in which all other pathologies that might explain sciatic pain were ruled out prior to patient enrollment, by MRI.

**DIAGNOSTIC ELECTROPHYSIOLOGIC STUDIES**

As opposed to the relative dearth of evidence supporting the diagnostic use of most imaging modalities in PS, there is support for electrophysiologic testing. The main advantage of EMG testing is its ability to assist with the differential diagnosis. Perhaps the first to report using EMG to diagnose piriformis was Kipervas, in 1976. In the English language literature, Synek was the first to write about using electrophysiologic studies for this purpose, after reporting in 1987 about the detection of short-latency somatosensory evoked potentials in four patients, one of whom had PS; the other three patients had spondylarthopathic cervical radiculopathy, malalgia paraesthetica, and allodynia secondary to a femoral nerve injury. Benson and Schutzer noted abnormal EMG findings in the distribution of the inferior gluteal nerve, and the tibial and peroneal divisions of the sciatic nerve in 6 of 8 patients who later went on to have confirmatory EMG findings identified between the piriformis muscle, sciatic nerve, and the roof of the greater sciatic notch, and suggested that these findings demonstrated extrapelvic compression of the sciatic nerve. However, as Tiel and Stewart have both pointed out, there is an inherent dilemma of tautology using treatment response as the standard for diagnosis, given the absence of any way to reliably confirm the diagnosis of PS; in essence, it creates a self-fulfilling and highly convenient prophesy: patients who get better had the condition we thought they had. On the other hand, this is not so different than the situation that exists for any disorder for which there is no "gold standard" for diagnosis, like systemic lupus erythematosus (SLE), for which a set of diagnostic criteria are required. Moreover, as Filler argues, the dramatic and prolonged response seen in the majority of such patients treated by guided injection, who had failed all prior attempts at treatment, strongly implicates the piriformis as being involved in the mechanism of pain in some way.

**TREATMENT OF PS**

The absence of a widely accepted operative definition of PS, and the significant controversy over how common or rare the condition is makes it even more difficult than usual to compare different treatment modalities in its management. Traditional wisdom is that many, but certainly not all patients with PS respond to conservative management that largely consists of anti inflammatory medications, like non steroidal anti inflammatory drugs (NSAIDs), and physiotherapy. However, the percentage of patients that require more "aggressive" treatment, like injections, is difficult to ascertain, because some authors include injections under the umbrella of

conservative management while others do not. In addition, the exact nature of the physiotherapy to which patients might respond is elusive, because of the muscle’s position deep within the buttocks, where it can be neither easily palpated nor manipulated. It is beyond the scope of this paper to describe the various conservative strategies used. Sufficient it to say that stretching the piriformis muscle is a primary objective of the therapy, and only two papers describe such therapy in any detail, one written by a physiotherapist and the other by an osteopathic physician; neither author referenced any actual data to support their conclusions regarding the effectiveness of physiotherapy.

A common adjunct to NSAIDs and physiotherapy is a local injection, which can consist of a local anaesthetic alone, steroid alone, both, or more recently, BTX. In one study (30), the combination of physiotherapy and a local injection (1.5mL 2% lidocaine + 20mg triamcinolone acetonide in 0.5mL) resulted in 79% of 353 patients who had met at least two of three criteria for PS experiencing at least a 50% reduction in pain lasting over an average of 16 months follow up. Others have reported success with various injections, but the doses and methods of administration have varied. A few have attempted blind injections. Others have performed injections guided by imaging alone, using modalities like CT, MRN, US, and fluoroscopy. In the majority of studies, however, injections have been guided by EMG, nerve stimulation, or a combination of modalities, invariably incorporating imaging plus EMG, nerve stimulation, or both. Unfortunately, the only report comparing different modalities to guide injections was one designed to compare the accuracy of US versus fluoroscopic guidance to inject 20 piriformis muscles in 10 cadavers. In this study, two different-colored latex dyes were used; US was found to be superior, with subsequent dissection revealing the injected dye in 19 of 20 muscles injected via US, but only 6 of 20 muscles injected via fluoroscopy. To date, no one has compared injections guided by imaging alone, versus nerve studies alone, versus both, but such a study certainly seems warranted. Although the combination of fluoroscopy plus EMG or nerve stimulation has seemed most popular, the combination of US plus nerve stimulation may be particularly attractive for several reasons that include the ability to perform the procedure using two relatively portable and low cost devices, in the absence of any radiographic exposure. However, to date, this latter combination remains untested.

Besides the usual questions related to the efficacy and safety of treatment, questions have arisen with respect to the use of local anaesthetics and injected steroids include: Why does a local anaesthetic produce anything more than a very transient benefit? What inflammation is the steroid treating? And how can anyone be sure that it is PS that is being treated, versus nerve irritation caused by some other muscle or other structure within the sciatic notch? With respect to the latter, North and associates studied the sensitivity and specificity of several different local anaesthetic blocks in 33 patients with sciatica that had been attributed to spinal disease, and found both sensitivity and specificity to be less than 40% in almost all instances. However, their injections were not guided. Several subsequent studies specifically addressing PS management have examined the use of guided injections, and the results have been generally encouraging.

In terms of prolonged pain relief, some of the most encouraging results are from the use of BTX, usually type A. BTX-A is a 150_kD single chain polypeptide that is produced by Clostridium botulinum. Although its existence has been recognized for centuries, it has only been since the late 1970s that it has been considered for therapeutic purposes, and only since 1989 that the United States Food and Drug Administration has approved its clinical use. Its approved use was initially restricted to the treatment of strabismus, blepharo spasm, and hemifacial spasm. Over the past decade, however, its use has grown exponentially, and it is now being used for a much wider spectrum of conditions, including chronic pain disorders (i.e., cervical dystonia, myofascial pain, chronic low back pain), and focal tendopathies (i.e., tennis elbow, and PS). In chronic pain conditions, BTX presumably works by breaking the muscle spasm or subsequently the pain cycle, affording the patient a window of opportunity for traditional conservative measures to have a greater beneficial impact, but several studies suggest that a direct antinociceptive effect distinct from any reduction in muscle spasm may be at play. Again, the major benefit of BTX compared with standard therapies appears to be the prolonged duration of the response. In one study, CT-guided injections of BTX-A versus methylprednisolone were compared in 40 patients (20 per treatment arm). Both treatments resulted in a decrease in pain baseline at 30 days follow up; the beneficial effect of the steroid, but not the BTX-A, was lost by 60 days, a between-drug difference that was statistically significant. Other comparative studies of BTX versus control vehicle, using both parallel and crossover group designs, have also demonstrated a beneficial effect of both BTX-A and BTX-B. Therefore, there is some support for the use of BTX in the treatment paradigm.

As a final measure, should all other treatment options fail, surgery is sometimes used in the treatment of PS patients, often sectioning the muscle to reduce or eliminate its contact with the affected sciatic nerve root(s). Debate rages as to the legitimacy and effectiveness of surgery on the piriformis muscle, spurred once again by questions as to whether or not the piriformis muscle actually is the source of symptoms. Critics cite one case of failed surgical decompression in a 44-year-old woman whose serial electrophysiological tests, plain radiographs, MRIs of the pelvis and lumbar spine, and CT myelograms all were interpreted as normal; who had failed to obtain any lasting relief from NSAIDs, physiotherapy, and multiple caudal, piriformis, sciatic, and S1 nerve root blocks; and who now was being treated chronically with sustained release morphine and paroxetine. However, straight-leg raising and diagnostic maneuvers designed to detect PS, produced buttock pain only. No mention was made of whether or not the patient had pain elsewhere, had any evidence of a chronic generalized pain condition like fibromyalgia, or any history of drug or alcohol dependency or addiction. Consequently, the value of this case as disproving PS, or of the value of surgical intervention must be considered zero.

Instead, the major concern for proponents of surgery must be the relative lack of data supporting it, limited to two small published studies. Benson and colleagues described their results of 15 opera-
tions in 14 patients (one with bilateral symptoms) with sciatica, who had failed to respond to all other measures, and whose symptoms had started following blunt trauma to their buttock. Eight of 14 patients underwent preoperative EMG, which revealed extra pelvic compression of the sciatic nerve in 6. Details of the electrophysiological assessment were superficial. At the time of surgery, all had adhesions between the piriformis muscle, sciatic nerve, and the roof of the sciatic notch, which were resected. Eleven “excellent” and 4 “good” results were attained across the 15 procedures. Meanwhile, Dezawa and associates\(^{46}\) reported their results performing arthroscopic release of the piriformis in eight limbs in six patients who met at least five of the nine criteria the authors themselves had established, and who had failed conservative treatment over 6 months. All eight procedures achieved “good results”, but further details were not provided. Otherwise, the literature contains only isolated reports of success, typically in patients who were among larger series of patients receiving injections, and who had achieved less than satisfactory long-term resolution of their pain.

CONCLUSIONS

PS faces controversy on almost all fronts. Can the piriformis muscle entrap the sciatic nerve or its individual roots? There is convincing evidence that this does occur on occasion, but how commonly this transpires remains open to debate, largely because there are no agreed upon and scientifically validated diagnostic or classification criteria. As opposed to what some critics may require, it is not necessary to have a “gold standard” for diagnosis, which is also lacking for many well-accepted clinical entities, like rheumatoid arthritis, SLE, and even CTS. A set of clinical criteria that provide reasonable assurance of accuracy is necessary, by means of achieving at least 80% sensitivity and specificity. To date, such criteria do not exist.

Controversy exists in which symptoms and signs are most characteristic, essentially because of their uniform nonspecificity; but highly sensitive and specific single symptoms or signs, again, are not necessary, so long as criteria exist that combine them and achieve adequate specificity and sensitivity. The same is true of imaging and EDX tests, though MRN has improved our ability to visualize nerves in live patients; and EDX tests that demonstrate ipsilateral slowing of nerve transmission during physical maneuvers that are presumed to increase piriformis pressure upon the nerve, like the FAIR test, certainly support the diagnosis, both generically and in the individual patient.

As for treatment, some level of controversy will always exist regarding the effectiveness of any treatment that cannot be administered in a totally double-blinded way, as with many facets of physiotherapy and various surgical procedures. However, injections can generally be blinded; and, to date, controlled. Double-blinded studies have shown that active injections are better than shams in the treatment of these patients. Guided administration of these injections has helped investigators to see what they are injecting, and these studies demonstrate superiority of active versus sham treatment. Moreover, though it remains possible that local anesthetics delivered into the sciatic notch might alter pain even if that pain originates further upstream, it is more difficult to imagine how the same could be said of a targeted and guided injection of BTX. Therefore, future investigators should use guided injections of BTX into the piriformis muscle as a “gold standard” proxy while generating and testing diagnostic criteria for this condition, so that reasonable assurances as to the diagnosis can be achieved in the individual patient prior to this expensive and somewhat invasive procedure.

Finally, from the perspective of the EDX physician, clearly there is a role for EMG, nerve conduction studies, and nerve stimulation in the diagnosis and management of this condition, though the specifics and magnitude of that role warrants further testing within the confines of formal comparative clinical trials. Presently, it appears that the most important aspect of EDX testing is in ruling out more common conditions and evaluating the differential diagnosis (e.g., peroneal entrapment at the fibular neck, an L 5 radiculopathy, or a sciatic nerve palsy).

REFERENCE


Lumbosacral Plexopathy: The Clinical and Electrodiagnostic Spectrum

Timothy J. Doherty, MD, PhD
Associate Professor and Canada Research Chair in Neuromuscular Function in Health, Aging, and Disease
Departments of Clinical Neurological Sciences and Physical Medicine & Rehabilitation
Schulich School of Medicine and Dentistry
The University of Western Ontario
London, Ontario, Canada

INTRODUCTION

The clinical and electrodiagnostic (EDX) evaluations of lumbosacral (LS) plexopathies are often complex, even for the experienced clinician. LS plexus lesions are less common than brachial plexus lesions and vary considerably in their presentations, depending on which components of the plexus are involved. The EDX assessment can be challenging because of difficulty performing motor nerve conduction studies (NCSs) for many of the proximal nerves and muscles involved (e.g., obturator to adductors), and an inability to obtain standard sensory nerve action potentials (SNAPs) for many of the sensory branches involved. Like brachial plexopathies, a LS plexus lesion should be considered when the clinical and EDX features cannot be explained by a lesion of a single nerve root (e.g., radiculopathy) or a single peripheral nerve lesion (e.g., femoral or sciatic mononeuropathy). This manuscript will review the anatomical, clinical, and EDX features of LS plexopathies.

ANATOMICAL CONSIDERATIONS

The LS plexus can be anatomically divided into the lumbar plexus and sacral plexus (Figure 1). The lumbar plexus is comprised of the anterior rami of the L1 – L4 roots and lies within the posterior portion of the psoas muscle. The anterior rami of the L2 – L4 roots divide into anterior and posterior divisions. The anterior divisions form the obturator (L2 – L4), genitofemoral (L1, L2), iliohypogastric, and ilioinguinal (L1) nerves. The posterior division forms the femoral and lateral femoral cutaneous nerves. The lumbar plexus communicates with the sacral plexus via the LS trunk (or cord).

The LS trunk is formed primarily by the L5 root, with a smaller contribution from the L4 root. The LS trunk travels a relatively long distance in close contact with the ala of the sacrum, which is in close proximity to the sacroiliac joint. The LS trunk is protected through much of its course by the psoas muscle, except at its terminal portion near the pelvic brim, where it is in close contact to bone. There it is joined by the S1 nerve root to form the sciatic nerve. The sacral plexus is formed by the anterior rami of spinal nerves L4 – S3. The anterior division forms the tibial portion of the sciatic nerve and gives rise to its peroneal component. The superior (L4 – S1) and inferior (L5 – S2) gluteal nerves arise from the posterior division of the sacral plexus. The posterior cutaneous nerve of the thigh arises from the anterior divisions of S1 – S3.

CLINICAL FEATURES OF LS PLEXOPATHY

LS plexus disorders typically present with features of motor and sensory deficits in the territories of multiple peripheral nerves or multiple nerve root territories. Pain is often a predominant feature.

Lumbar plexus disorders cause deficits in the distribution of the iliohypogastric, genitofemoral, ilioinguinal, femoral, and obturator nerves. These may result in weakness of hip flexion, knee
extension, and thigh adduction. Sensory deficits may occur over the lower abdomen, inguinal region, the medial lower leg (saphenous nerve territory), and the anterior, lateral, and medial thigh. The patellar reflex may be reduced or absent. Patients will complain of the leg giving way when standing or walking (due to knee extensor weakness), walk with knee hyperextension, and have difficulty getting in and out of bed or a car (due to hip flexor weakness).

Sacral plexus disorders produce deficits within the distribution of the gluteal, tibial, and peroneal nerves. These result in weakness of hip extension and abduction, knee flexors, ankle dorsiflexors and plantar flexors, and the extensors and flexors of the toes. Sensory deficits may occur over the posterior thigh, anterolateral and posterior lower leg, and the plantar and dorsal aspects of the foot. The ankle jerk may be reduced or absent. One important key to sacral plexus lesions is weakness in the distribution of both the gluteal and sciatic nerves. This is particularly so when both L5 and S1 innervated muscles are involved, making a single root lesion less likely.

**EDX FEATURES OF LS PLEXOPATHY**

EDX of LS plexus disorders can be challenging and perplexing for even the experienced electromyographer (Table 1). In comparison to the brachial plexus, the anatomy of the LS plexus makes it difficult to perform motor NCSs to some of the more proximal muscles. Additionally, sensory NCSs are not feasible in many cases (e.g., ilioinguinal nerve, posterior cutaneous nerve of the thigh). Nonetheless, carefully planned and executed EDX studies combined with thorough clinical assessment can usually localize the lesion.

LS plexus lesions tend to be lumped into a single entity. However, as outlined in the previous sections, it is usually more practical to approach these problems as lumbar plexus or sacral plexus lesions. Lumbar plexus problems must be distinguished from root lesions of the L1 – L4 root, or isolated lesions of the femoral or obturator nerves. Sacral plexus lesions must be distinguished from L5 or S1 root lesions, sciatic nerve injury, or mononeuropathies of the peroneal, and less commonly, tibial nerves.

Motor NCSs of the peroneal nerve to extensor digitorum brevis and the anterolateral muscles, as well as tibial motor studies to the gastrocnemius muscles and adductor hallucis are useful. These will often show amplitude reduction with involvement of the lumbar trunk and sacral plexus. Because foot drop is often a prominent clinical feature of patients with possible sacral plexus lesions, it is important to examine for the presence of conduction block across the fibular head; this indicates a peroneal mononeuropathy.

Femoral motor studies (we usually record over the vastus medialis) will reveal amplitude reduction for lumbar plexus disorders. Demonstration of conduction block is often challenging in the femoral nerve as it is difficult to perform supramaximal percutaneous stimulation proximal to the region of demyelination. Side-to-side comparisons of compound muscle action potentials are very useful for grading severity and prognosis.

Sensory NCSs for the superficial peroneal, sural, and saphenous nerves are helpful as amplitude reduction indicates a lesion at or distal to the dorsal root ganglion; these responses are usually normal in the presence of root disease. This author and colleagues routinely perform sensory studies of the lateral femoral cutaneous nerve and use near nerve recording with a monopolar electrode. These studies are most useful in diagnosing a lateral femoral nerve lesion, or so called meralgia paresthetica. Again, side-to-side comparisons are routinely made.

Carefully planned needle electromyography (EMG) is often the key to sorting out these disorders. In the case of axonal injuries, it is typically necessary to delay needle studies for 10-14 days to ensure that spontaneous activity will be present. For lumbar plexus disorders, it is necessary to study the quadriceps, adductors, and iliopsoas to rule out a femoral or obturator mononeuropathy. Examination of the upper lumbar paraspinals is also useful, as denervation indicates root disease. In sacral plexus disorders, it is important to sample muscle in the peroneal and tibial components of the sciatic nerve.
For patients presenting with foot drop, denervation in tibialis posterior or flexor digitorum, and short head of biceps femoris, indicate involvement outside the peroneal distribution. Denervation in the gluteal muscles indicates involvement outside the sciatic nerve. In some cases, it can be challenging to sort out an LS plexus lesion from an L5 root lesion; both have prominent weakness in the L5 myotome. The presence of paraspinial denervation goes against a plexus lesion, while reduction or absence of the superficial peroneal sensory response indicates a more peripheral lesion. Caveats to these guidelines apply to frequent involvement of the roots as well in diabetic LS plexopathy.

**COMPRESSIVE DISORDERS**

**Hemorrhage**

Retroperitoneal hemorrhage is a common and sometimes overlooked cause of LS plexopathy. Large hematomas within the psoas muscle lead to diffuse compression of the lumbar plexus with involvement of both the femoral and obturator nerves. More commonly, the intrapelvic component of the femoral nerve is compressed by smaller haematomas within the indistensible fascia of the iliaca muscle. This leads to an isolated femoral lesion. These usually occur in the setting of therapeutic anticoagulation, but can also be seen with clotting disorders, leaking aneurysms, or trauma.

Patients typically present with acute onset of lower abdominal and groin pain with referral into the thigh. Weaknesses of hip flexion and knee extension as well as sensory deficits occur shortly thereafter. Patients may adopt a posture of hip flexion and external rotation to reduce the severe pain. There is usually an associated drop in the hematocrit, and computed tomography (CT) of the abdomen and pelvis will reveal the hematoma. Treatment is normally conservative, with management of pain, reversal of anticoagulation, and transfusion. Outcomes are variable, with most patients experiencing partial recovery; the extent depends on the degree of axonal injury.

**Neoplastic LS Plexopathy**

Neoplastic LS plexopathies are relatively uncommon. They occur as a result of direct invasion or external compression of the plexus by a tumor. Pain, in association with weakness and sensory loss, is the most typical presenting feature. The most common tumors associated with LS plexopathy include: colorectal, lymphoma, genitourinary, breast and lung carcinoma, as well as a range of sarcomas. Both CT and magnetic resonance imaging (MRI) are useful in the evaluation of suspected cases. Treatment is specific to the underlying malignancy. It often involves chemo- and radiation therapy, with surgery in some cases. Pain control usually requires narcotics. The addition of gabapentin, pregabalin, or tricyclics is often helpful.

**Pregnancy and Post-partum**

Compressive LS plexopathy can develop during late gestation, but symptoms usually manifest during labor, with pain in the sciatic distribution and the development of foot drop a few hours post-partum. Young, primagravidae women of short stature are most susceptible. The usual mechanism of LS plexopathy is direct pressure of the fetal head against the plexus as it descends into the pelvis during the second stage of labor. The peroneal component of the sciatic nerve is most commonly affected, with weakness of ankle dorsiflexion and eversion as well as sensory loss over the dorsum of the foot. Peroneal motor studies reveal decreased amplitudes with no block across the fibular head. The peroneal SNAP is absent or decreased. Needle studies performed 10 to 14 days post-partum will reveal denervation in peroneal innervated muscles as well as

<table>
<thead>
<tr>
<th>Spinal Root</th>
<th>Muscle</th>
<th>Motor Nerve</th>
<th>Sensory Nerve</th>
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</thead>
<tbody>
<tr>
<td>Lumbar plexus</td>
<td>L3/L4</td>
<td>Adductor longus</td>
<td>Obturator</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Femoral</td>
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<td></td>
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<td>Saphenous</td>
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<tr>
<td>Iliopsoas</td>
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<tr>
<td>Vastus</td>
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<tr>
<td>Tensor Fascia</td>
<td>L5</td>
<td>Gluteus Medius</td>
<td>Superior Gluteal</td>
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<tr>
<td>Tibialis Anterior</td>
<td>S1</td>
<td>Peroneal</td>
<td>Superior Peroneal</td>
</tr>
<tr>
<td>Peroneus Longus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibialis Posterior</td>
<td></td>
<td>Tibial</td>
<td></td>
</tr>
<tr>
<td>Gluteus Maximus</td>
<td></td>
<td>Inferior Gluteal</td>
<td></td>
</tr>
<tr>
<td>Biceps Femoris (long)</td>
<td></td>
<td>Sciatric (tibial)</td>
<td>Sural</td>
</tr>
<tr>
<td>Biceps Femoris (short)</td>
<td></td>
<td>Sciatric (peroneal)</td>
<td>Sural</td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td></td>
<td>Tibial</td>
<td></td>
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</tbody>
</table>

Table 1: Muscles and sensory nerves to consider for electrodiagnostic evaluation of lumbosacral plexopathy
short head of biceps femoris, with sparing of gluteal muscles and paraspinals.7 Prognosis is usually good, with most patients gradually recovering over the course of 3 to 4 months.

Trauma

Traumatic lesions of the LS plexus are far less common than traumatic brachial plexopathy. The most typical causes are motor vehicle accidents and severe falls that result in fractures of the pelvic ring or sacrum.12 The entire LS plexus may be involved, but the sacral plexus is more commonly affected with predominant involvement of the gluteal nerves and peroneal component of the sciatic nerve. This relates to the proximity of these fibers to the sacrum and sacroiliac joint.12 Clinical examination is often difficult in these patients due to pain and orthopaedic injury. This makes EDX assessment essential to characterize the extent of neurological involvement and provide prognosis. Treatment is usually conservative unless there is the possibility of removing a compressive mass.

Vascular Disease

Compression of the LS plexus can occur as a result of expansion of iliac or hypogastric artery aneurysms. A slowly leaking abdominal aortic aneurysm may lead to accumulation of a large retroperitoneal hematoma that results in LS plexopathy.8 Back and leg pain with the presence of a pulsatile mass in the abdomen are features of this syndrome. CT scan of the abdomen and pelvis will confirm the presence of the hematoma and aneurysm and allow for urgent surgical assessment and treatment.

NONCOMPRESSIVE DISORDERS

Diabetic LS Radiculoplexopathy

Diabetic LS radiculoplexopathy (DLRP), often referred to as diabetic amyotrophy or proximal diabetic neuropathy, is a relatively common disorder usually seen in older men and women. It often results in severe impairment and disability that affects 1-2% of diabetics (typically, Type II).5 Nondiabetic LRP is a more recently recognized condition,3 with clinical features and etiology that appear very similar to DLRP.5 Both DLRP and LRP typically present with severe, acute onset of lower-limb pain and weakness. Frequently, these occur in concert with a large concomitant weight loss. In many cases, affected patients have not been diabetic for a long period of time.

Symptoms are usually unilateral and involve proximal lower limb segments, such as the hip flexors and knee extensors. They may spread more distally, and to the contralateral side over a few days. While pain, often requiring narcotic analgesia, is the most severe initial manifestation, weakness typically develops in the first few days as well. Often, it has severe effects not only on the hip flexors and knee extensors, but also the more distal muscles, including the ankle plantar and dorsiflexors. Gait aids or wheelchairs are often required for mobility.

In both DLRP and LRP, the cerebrospinal fluid will reveal elevated protein. This provides evidence that the disease process is proximal at the level of the spinal roots. Some patients will have elevated erythrocyte sedimentation rate, positive rheumatoid factor, positive antinuclear antibody test, or other indicators of immune mediated disorders.5

Some authors have proposed two subtypes of patients with DLRP—those with EDX evidence of a more generalized diabetic peripheral neuropathy, and those without it.13 However, a large community-based cohort study of diabetics did not support this hypothesis. Most patients who developed DLRP had not been diabetic long enough to develop a distal symmetric diabetic polyneuropathy.5 In addition, the occurrence of diabetic polyneuropathy is highly associated with diabetic retinopathy and nephropathy, and the majority of patients who developed DLRP had neither of those. Thus, it is likely that those with DLRP and a polyneuropathy simply reflect the end of the spectrum with more severe underlying disease rather than a specific subgroup.5

The EDX features of DLRP and LRP are very similar. Needle EMG reveals axonal injury or denervation in affected muscles in multiple nerve territories, often with severe loss of recruitment implying substantive loss of axons. Motor and sensory action potential amplitudes are often reduced, with only mild slowing of nerve conduction velocities. Paraspinal denervation is typically present in both DLRP and LRP (29 of 30 patients in one series).3

Earlier studies suggested that the pathophysiology of DLRP was diabetes-induced vasculopathy. More recent investigation, however, provides strong evidence that DLRP, and similarly, LRP, are caused by an immune-mediated attack and microvasculitis of nerve.3,5 Given that both of these disorders are potentially immune mediated, early initiation of immunotherapy may limit the extent of disease.

Some evidence from small open cohort studies suggests that immunotherapy (intravenous immunoglobulin, prednisone) may be of benefit.11 One open-label trial of weekly intravenous infusions of methylprednisolone for 11 patients with LRP reported marked improvement in pain and weakness.4 However, there was no control group, and LRP tends to improve in most untreated patients. Without evidence from controlled trials, most clinicians reserve immunotherapy for those most severely affected.

Given that axonal loss is the mechanism, the time course of recovery is typically many months.5 In the author's experience, most of these patients do well if provided with supportive treatment, followed by appropriate physical therapy in the form of resistance exercise and gait retraining.

REFERENCES


Neuromuscular Disease and the Hip: An Orthopedic Perspective

Timothy P. Carey, MD, FRC(C)

Associate Professor
Department of Orthopedic Surgery
University of Western Ontario
London, Ontario, Canada

INTRODUCTION

By definition, neuromuscular disease involves an alteration in the normal function of musculotendinous units, and can lead to secondary effects on the skeletal system. The hip is commonly affected. Muscle imbalance due to disease can alter forces across the joint, eventually leading to subluxation or dislocation, with subsequent development of painful degenerative arthritis. Management of the hip in patients with neuromuscular disease involves awareness of potential pathology, preventative measures, appropriate surveillance, and an array of reconstructive techniques to address the varied and often challenging situations encountered.

This manuscript brings an orthopedic perspective to neuromuscular diseases of the hip. It covers clinical considerations, identifies conditions associated with increased and decreased muscle tone; and reviews the assessment, treatment, and management of hip pathologies.

OVERVIEW

Knowing age of onset can help physicians anticipate clinical issues they may encounter in patients with hip disorders. Neuromuscular disease leading to muscle imbalance around a child’s developing hip will alter normal forces transmitted to the changing skeleton, and affect growth and development. Frequently, the result is progressive dysplasia and subluxation of the hip joint, culminating in accelerated degenerative changes in the femoral head and distortion of the acetabular anatomy. Adult onset conditions do not lead to dysplastic changes, but can result in contractures and functional issues secondary to muscle imbalance around the hip. Degenerative changes from aging are not directly related to neuromuscular condition, but their management can be complicated or compromised by muscle imbalance.

The multiple neuromuscular conditions that can affect the hip can be classified into two broad categories: those involving spasticity, and those with a flaccid-type paralysis. In children, examples of the former include cerebral palsy (CP) and brain and spinal cord injury; in adults, they include cerebrovascular accidents, Parkinson’s disease, and acquired brain and spinal cord injury. Conditions with decreased muscle tone or flaccidity include myelomeningocele, polyneuropathies, and myopathies. Poliomyelitis, although rare, is a classic example.

Patients with a neuromuscular hip disease may need treatment for two general reasons: the disease process (e.g., CP or myelomeningocele) has led to dysplasia of the hip, which in turn, has evolved into degenerative arthritis; or the degenerative joint disease has developed independently of the neurologic disease (e.g., Parkinson’s disease).

In the child with hip dysplasia, efforts are typically directed at restoring normal anatomy and normalizing soft tissue balance and muscle forces early, before irreversible degenerative changes to the articular cartilage develop. Treatment ranges from bracing and tone reduction to soft tissue releases and femoral and pelvic osteotomies. In the adult with degenerative changes, reconstructive options include total joint arthroplasty in addition to osteotomies. Salvage procedures can include joint excision, soft tissue releases, and arthrodesis, but all are associated with functional compromise.
EVALUATION

Assessment of hip pathology begins with a focused history and physical examination. Ambulatory patients require a visual gait analysis, measurement of joint range of motion (ROM), contractures, and evaluation of muscle strength and tone. Tools, such as the modified Ashworth or Tardieu scores, are often used to quantify the degree of spasticity. Imaging of the hip with plain anterior-posterior (AP) and lateral radiographs is routine. AP pelvic views allow comparison with the contra-lateral hip. Indications for additional imaging depend on the clinical scenario. Additional information on bony dysplasia can be obtained with special views, such as the false profile view of the acetabulum. Cross-sectional imaging with computed tomography scans can help delineate more complex changes in the bony anatomy.

3-D computed gait analysis has evolved significantly since its introduction as a research tool, and is now routinely performed at most centers that deal with children who have CP. Advantages include a multimodal approach with video recording, kinematic and kinetic data, electromyography (EMG), and energy consumption measurements. Costs of the computer hardware and software have decreased significantly, but a useful gait laboratory requires sufficient investment in physical resources and, most importantly, trained staff.

CONDITIONS ASSOCIATED WITH INCREASED MUSCLE TONE

CP

The incidence of hip subluxation/dislocation in children with CP ranges from 2-75%. Hip dislocation/subluxation with severe or total body involvement is more common. Recent literature shows a direct correlation between the incidence of hip displacement (subluxation to dislocation) and functional level measured by the Gross Motor Function Classification System. Recommended hip surveillance schedules for children with CP are shown in Table 1.

Table 1: Recommended hip surveillance schedules for children with cerebral palsy

<table>
<thead>
<tr>
<th>Gross Motor Function Classification System</th>
<th>Functional Description</th>
<th>Recommended Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Walks without limitations</td>
<td>Clinical and x-ray 12-24 months; clinical at 3, 6 years</td>
</tr>
<tr>
<td>Level II</td>
<td>Walks with Limitations</td>
<td>Clinical and x-ray 12-24 months; repeat q12 months until MP stable; ages 5, 10 years</td>
</tr>
<tr>
<td>Level III</td>
<td>Walks using a Hand-Held Mobility Device</td>
<td>Clinical and x-ray 12-24 months; repeat q 6 months until MP stable; repeat q 12 months until age 7; if MP stable, review prepuberty, follow until skeletal maturity</td>
</tr>
<tr>
<td>Level IV</td>
<td>Self-Mobility with Limitations; May use Powered Mobility</td>
<td>Clinical and x-ray 12-24 months; repeat q 6 months until MP stable; repeat q 12 months until age 7; if stable, review prepuberty, follow until skeletal maturity – if scoliosis or pelvic obliquity present, follow q 6 months until skeletal maturity</td>
</tr>
<tr>
<td>Level V</td>
<td>Transported in a Manual Wheelchair</td>
<td>Clinical and x-ray 12-24 months; repeat q 6 months until age 7; if stable, review q 12 months until skeletal maturity – if scoliosis or pelvic obliquity present, follow q 6 months until skeletal maturity</td>
</tr>
</tbody>
</table>

MP = migration percentage


Deformities of the hip joint in patients with CP produce pain and prevent ambulation. In the most profoundly affected, they can also interfere with sitting ability and hygiene. The most common pattern of muscle imbalance results in the hip adductors and flexors overpowering the hip abductors and extensors, leading to progressive “uncovering” of the hip as measured by Reimer’s migration index (Figure 1).

This can eventually progress to frank dislocation of the hip joint. Frequently, patterns of asymmetric tone lead to “windswept” posturing of the lower limbs, with severe adduction of one hip with abduction of the contralateral side. This is often associated with pelvic obliquity and scoliosis. Early surgical treatment during childhood consists of muscle releases to obtain balance and early femoral varus rotation or acetabular osteotomies for containment of the femoral head. Without early surgical intervention, the uncovered femoral capital epiphysis becomes deformed from the tremendous pressures generated by the overlying capsule and spastic abductor muscles, leading to painful arthritic changes in adolescents and adults (Figures 2A and 2B).

In adults, the aim of treatment is to prevent contractures that lead to hip subluxation or dislocation. With end-stage arthritis, treatment goals are to eradicate pain in the affected arthritic joint and preserve motion, if possible. Surgical options include resection/interposition arthroplasty, arthrodesis, and total hip replacement arthroplasty.

TREATMENTS

Proximal Femoral Resection Interposition Arthroplasty

Resection of the femoral head and neck is used to treat end-stage arthritis in the dislocated hip. Interposition of local soft tissue between the acetabulum and the remaining femur prevents impingement and subsequent pain. The procedure is reserved for patients who are unable to walk and whose functional needs might...
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include improved hygiene and ease of positioning. Although good results have been reported in terms of pain relief, significant complications are not uncommon. Heterotopic bone formation at the surgical site is the most problematic effect.

In our series, only half of parents and caretakers would recommend the procedure to others. Most centers have moved away from it. Subtrochanteric valgus osteotomy (+/- femoral head resection) is more commonly performed to relieve pain while maintaining some stability of the leg. This limits shortening and decreases the incidence of proximal migration and heterotopic bone formation (Figure 3).4,42

Hip Arthrodesis

A subluxed hip makes arthrodesis a poor choice for most patients with severe painful arthritis. The majority are nonambulatory and have significant musculoskeletal involvement. They often have scoliosis and contralateral hip pathology. These conditions preclude any compensatory movements to accommodate the arthrodesed hip, as occurs in otherwise healthy patients with unilateral hip disease. For these and other reasons, the procedure is rarely performed in CP patients.12,30

Total Hip Arthroplasty

The clinical success of total hip arthroplasty for painful degenerative arthritis is well-documented in the literature. Many large series include a small number of patients with neuromuscular issues, and in general, good results can be expected even in this patient population. However, those with CP present many significant challenges that need to be addressed.

Careful selection of appropriate candidates is of paramount importance. The concerns with total hip arthroplasty (THA) include the patient’s age (patients are usually young), the abnormal muscle strength, the spasticity and contractures that are often present, and poor compliance with postoperative regimens. Indications for performing a total hip replacement in the spastic patient usually include the following:

- Hip pain refractory to medication;
- Decreased function in standing, limited sitting, and difficulty with perineal hygiene; and
- The potential for standing or walking, transfer ability, or upright sitting in a wheelchair.
Figure 3 Severe degenerative changes secondary to paralytic hip dislocation treated with femoral head and neck resection and subtrochanteric osteotomy

Contraindications include active or previous hip joint infection, poor general medical condition, insufficient bone stock, and limited functional goals. The literature is relatively sparse, but case series demonstrate acceptable results. Complications, such as increased incidence of heterotopic ossification, dislocation, and loosening are more frequent in patients with CP compared to those without it.

Patients with CP require extensive preoperative planning. The surgery is technically challenging, and modular or custom components are often required. Nonetheless, THA is a valuable option. Incapacitating pain can be relieved and function improved in the majority of patients. Longevity of the implant can also be expected (>95% at 10 years).

Surgeons should pay attention to adductor spasticity that might need an adductor tenotomy at the time of surgery. Modification of surgical technique to favor stability over ROM, and the use of constrained components may afford protection from instability. If instability is a concern intraoperatively, postoperative support with a hip abduction orthosis or even a hip spica cast may be needed. If death is a concern intraoperatively, postoperative support with a hip abduction orthosis or even a hip spica cast may be needed. If death is a concern intraoperatively, postoperative support with a hip abduction orthosis or even a hip spica cast may be needed.

Parkinson’s Disease

The prevalence of Parkinson’s disease in the general population older than 60 years of age is 1%. The incidence rate is 20.5 persons per 100,000, with concomitant dementia 3 times more frequent than in a control group. Current medical management effectively controls tremors, rigidity, and akinesia. Degenerative arthritis of hips may occur through natural processes or after hip fractures.

The literature on the treatment of hip fractures in patients with Parkinson’s disease is extensive. Regardless of fracture type, morbidity and mortality are high, with pneumonia the most frequent complication. Patients treated with surgery have better functional results and improved quality of life. However, standard internal fixation techniques have a high failure rate. Due to the often compromised medical status of this patient population, many authors recommend hemiarthroplasty or THA for treatment of hip fractures.

In 1988, Staeheli and colleagues investigated treatment of femoral neck fractures (Garden III and IV) in patients with Parkinson’s Disease. They reported high rates of complications at 6 months (mostly urinary tract infections and pneumonias) and a high mortality rate (20%) after 50 hemiarthroplasties in 49 patients. Despite these outcomes, functional results were good: 80% of the survivors could walk. The authors attributed the positive result to rapid postoperative mobilization of patients and the release of contracted adductor muscles at the time of surgery.

THA performed for fracture or degenerative arthritis has similar results. Restoration of motion and pain relief is good, but the complication rate is high compared to primary THA in an age-matched non-Parkinson’s population. Significant increase in function and decrease in pain is seen at 1 year postoperatively, but function continues to deteriorate with time. This is evidenced by an increased use of gait aids and a decrease in walking distance. The decline is mostly due to progression of the underlying Parkinson’s disease, as neurological deterioration appears to parallel decreasing functional scores.

Although THA in Parkinson’s patients can be quite successful, careful preoperative assessment is necessary to optimize surgical results. In particular, screening for low-grade or asymptomatic infections is necessary to decrease the rate of this common complication. As with the CP patient, operative techniques often need to be modified to deal with preexisting soft tissue contractures and bone quality issues. Ultimately function is determined by progression of the neurological disease.

Spasticity Due to Brain/Spinal Cord Injury

Hip joint contractures are a frequent complication in adult onset spasticity caused by brain or upper spinal cord injury. Additionally, heterotopic ossification around the hip can decrease ROM significantly in patients with brain injury. Prevention of fixed contrac-
tures is of paramount importance, and early management with an aggressive physical therapy program of ROM exercises. Additional modalities include tone reduction measures, such as botulinum toxin or phenol injections.

Surgery plays a small role in these situations, but it offers another option if limb position doesn’t improve over time, and contractures interfere with sitting, hygiene, or achieving full rehabilitation potential. Generally, adduction and flexion contractures are the most significant problems, and soft tissue releases can help to restore ROM. Again, physical therapy is an integral part of the treatment to maintain gains achieved with surgery. In select cases, postoperative bracing may be used.

In head injuries, significant heterotopic ossification will occasionally cause loss of joint ROM. This condition often responds well to surgical excision and therapy, but careful timing is required, and
operations are not usually performed until there is evidence of a maturing of the heterotopic bone.

THA is occasionally indicated in elderly patients with spasticity, usually secondary to stroke. As in the other cases, acceptable results with respect to pain relief and mobility can be achieved. Contractures can be dealt with at the time of surgery, and care must be taken to ensure stability of the prosthesis. A higher incidence of heterotopic ossification postoperatively has been reported in this patient population; prophylactic treatment with low-dose radiation is often recommended.18,15,39

CONDITIONS ASSOCIATED WITH DECREASED MUSCLE TONE

Poliomyelitis

Poliomyelitis, although rarely seen in the modern era due to vaccination programs, is a classic example of pure flaccid paralysis. The result of a viral infection targeting the anterior horn cells, permanent muscle paralysis occurs in varying anatomical distributions. After the acute phase of the illness, treatment is aimed at addressing the effects of the paralysis on the locomotor system.

Although the disease is static, there can be deterioration in aging polio victims, a condition known as post-polio syndrome (PPS). Primary criteria necessary for the diagnosis of PPS are a history of paralytic poliomyelitis, partial or complete recovery of neurological function followed by a period of stability (usually several decades), persistent new muscle weakness or abnormal muscle fatigability, and the exclusion of other causes of new symptoms.38

Orthopedic treatment of the manifestations of poliomyelitis is rarely indicated. Physiotherapy and orthotic management are the mainstays of treatment. However, patients with significant complications may require surgical intervention. Those who did not have adequate medical attention during childhood can have residual deformities. These will occasionally require tendon transfers and bony reconstructive work. Surgery to address limb length discrepancies and joint arthrodeses for severely unstable joints are other common procedures.

Specific deformities involving the hip occur when the flexors and adductors overpower the weaker abductors and extensors, causing hip subluxation, and occasionally, dislocation. In the young child, coxa valga and excessive femoral anteversion contribute to the development of the hip instability. Significant hip abduction contracture can also uncover the hip on the “high” side. In this situation, release of the adductors, as recommended by Eberle, may result in reduction just by leveling the pelvis.14 When surgical treatment is indicated for a subluxed hip, muscle transfers must be considered to address the muscle imbalance at the root of the hip problem. Boney reconstruction that doesn’t address the contractures and imbalance is less likely to be successful.24,33

Myelomeningocele

The management of children with myelomeningocele has evolved over the years. Early closure of the spinal defect, aggressive shunting of hydrocephalus, and improved management of renal disease have increased lifespan and quality of life.

Involvement of the lower extremities is classified on the basis of the lowest functioning intact nerve root, or neurosegmental level. These generally determine not only the patient’s ability to walk, but also the risk of developing hip instability. High-level involvement, such as thoracic or high lumbar levels, rarely results in hip instability; these patients are wheelchair ambulators. Those with an L2 level only walk with braces and crutches, and generally become wheelchair-bound by their adolescent years.

L3 and L4 level children have good quadriceps and the potential to be community ambulators, although they may require orthotics. Their prognosis improves if hamstring activity is also present. The incidence of hip subluxation is greatest in patients with lesions at these levels because hip flexors and adductors remain intact and hip extensors and abductors are absent or weak. Patients at an L5 or sacral level rarely develop significant hip pathology.11,3

Surgical reduction of dislocated hips in myelomeningocele is unnecessary for patients with neurosegmental levels of L2 and higher. Successful maintenance of the reduction is difficult, and the presence of a dislocation does not affect ambulation, pain, or quality of life. Indications for surgery in the mid lumbar level child are still controversial. The surgical reconstruction can be challenging; soft tissue contractures and bony deformities need to be corrected; and muscle transfers to address the absent abductor function are typically recommended.37

Still, recurrence of dislocation is not uncommon, and stiffness, wound breakdown, and fractures have all been reported. Except for a small improvement in energy expenditure in gait, studies in operative and nonoperative cohorts fail to show a significant benefit in quality of life.25,36

Hereditary Motor Sensory Neuropathies

Charcot-Marie-Tooth (CMT) disease is the most common form of heritable peripheral neuropathy, with a prevalence estimated at 1 in 2500. Two types are recognized. Type 1 (demyelinating), the more common form, affects 60-80% of the CMT population; Type 2 (axonal) affects 20-40% of patients. Clinically, the disease is characterized by distal limb weakness that affects both extrinsic and intrinsic musculature in the lower limbs. Sensory deficits and areflexia are also seen.

The muscle weakness can gradually produce secondary deformities in the musculoskeletal system. The most common are cavovarus foot deformities. Often progressive, these are aggravated by the weakness of ankle dorsiflexion due to extrinsic involvement. Management includes use of foot orthotics and ankle foot orthoses (AFOs). Surgical intervention is aimed at correcting deformities and muscle imbalance by tendon transfers.19,20
Hip dysplasia is a problem that occurs more frequently than previously thought. Kumar and colleagues first reported the association between CMT and hip dysplasia in 1985. Since then, numerous studies have addressed this issue. One series found a prevalence rate of 8.1%, with radiographic abnormalities in a higher proportion of patients. Hips in children with CMT are normal at birth, but progressive weakness from the neuropathy affects the hip extensors and abductors, leading to a more shallow acetabulum and a valgus, antverted femoral neck. Hip subluxation is subsequent to these changes (Figure 4).

**Figure 4** Hips in children with CMT are normal at birth, but progressive weakness from the neuropathy affects the hip extensors and abductors, leading to a more shallow acetabulum and a valgus, antverted femoral neck. Hip subluxation is subsequent to these changes. CMT= Charcot Marie Tooth disease

Hip dysplasia can be asymptomatic. As with CP patients, regular surveillance should be instituted. The natural history of hip disease in CMT is not yet defined, but a baseline AP pelvis film is suggested when the diagnosis is made, with follow-up films every other year during skeletal immaturity. If dysplasia exists, as defined by established radiographic criteria, there are no effective nonsurgical options.

Surgical intervention requires correction of both the acetabular deficiencies and restoration of more normal proximal femoral anatomy. Patients with CMT may be more sensitive to pressure or stretch of peripheral nerves, and this should be taken into account when planning surgical treatment. Early mobilization to prevent aggravation of weakness is also important in postoperative rehabilitation.

**SUMMARY**

Numerous neuromuscular conditions can affect the normal development and function of the hip joint. A useful approach to hip pathology categorizes the underlying neurological disease into spastic or flaccid paralysis, and pediatric or adult onset. Within this framework, specific approaches to hip pathology can be developed and incorporated into the overall management of patients.

**REFERENCES**


INTRODUCTION

The hip joint is surrounded by multiple neural and vascular structures that are susceptible to both traumatic and iatrogenic injuries. These may cause extremely disabling motor or sensory dysfunction. Appropriate management includes imaging and electrodiagnostic (EDX) studies to determine which injuries will spontaneously recover, and which may benefit from intervention.

This manuscript describes the anatomy of the hip joint, the causes of specific nerve injuries, how they present, and effective evaluation and diagnostic techniques. It also covers recommendations for intervention, treatment options, and prognoses for the various types of injuries.

ANATOMY

The hip joint is surrounded by multiple major motor nerves (sciatic, superior gluteal, inferior gluteal, femoral, and obturator) and multiple sensory nerves (lateral femoral cutaneous, ilioinguinal, iliohypogastric, and genitofemoral). Each of these are at risk from either trauma or various medical interventions. Knowledge of the relevant anatomy assists in appropriate diagnosis and treatment.

The sciatic nerve arises from the L4 to S3 nerve roots and exits the pelvis through the greater sciatic foramen. It passes under the piriformis muscle and over the other external rotators of the hip to the gluteus maximus muscle. Computed tomographic (CT) studies demonstrate that the sciatic nerve lies less than a centimeter from the posterior column of the pelvis adjacent to the acetabulum (Figure 1). The intraneural anatomy of the sciatic nerve contains distinct peroneal and tibial divisions, with the former more susceptible to injury.

The superior gluteal nerve arises separately from the L4 to S1 nerve roots and exits the pelvis through the greater sciatic foramen before supplying gluteus medius, gluteus minimus, and tensor fascia lata. Surprisingly high rates of superior gluteal nerve palsy have been reported with lateral approaches to the hip, but modifying the surgical approach protects the nerve.

The femoral nerve arises from the L3 to L4 nerve roots and travels on the ventral surface of the iliopsoas muscle. It enters the femoral triangle as it passes beneath the inguinal ligament. At this point, the nerve is almost directly anterior to the hip joint, and at risk during anterior or anterolateral approaches to the hip, particularly from retractor placement.

The obturator nerve arises from the L2 to L4 nerve roots and leaves the pelvis through the obturator foramen. It then innervates the adductors of the medial thigh. Of the major motor nerves around the hip, it is the one that receives the fewest injuries.
SPECIFIC NERVE INJURIES

Superficial sensory nerves

The sensory nerves that arise from the T12 to L2 roots provide sensation to the inguinal region and the ventral surface of the thigh (Figure 2). All are at risk from various surgical interventions. The ilioinguinal, iliohypogastric, and genitofemoral nerves are at particular risk during inguinal hernia repairs, particularly when prosthetic mesh is used.2 Other causes include blunt and postappendectomy trauma.23

Patients present with symptoms consistent with a Type II complex regional pain syndrome. Burning neuropathic pain is common and is frequently positional. Some patients experience worse pain with hip extension; others when they sit. Sexual dysfunction secondary to cutaneous hypersensitivity is common. Physical examination reveals hypersensitivity and allodynia in the distribution of one or more of the three nerves. A positive Tinel sign may be elicited at the particular site of injury, but significant overlap of the sensory territory of these nerves makes it difficult to be certain which of the nerves is causing the symptoms (Figure 3).

In general, imaging studies do not help assess the causes of pain. Diagnostic nerve blocks with electromyography (EMG) guidance help localize the cause of pain, and for some patients, may alleviate it.33 Other nonoperative therapies, such as gabapentin or pregabalin, may also help.

Operative treatment mirrors that of painful neuromas in other anatomic locations. Proximal neurectomy alone risks regrowth of regenerating axons into adjacent cutaneous areas. Burying the resected nerve
end into muscle “satisfies” the regenerating nerves, and is preferred. Surgical options include a so-called “triple neurectomy” through an anterior or retroperitoneal approach via a flank incision.

Amid reported that out of 100 patients, 80% experienced complete pain relief from an anterior approach triple neurectomy, but follow-up was short. This outcome still mirrors our own experience. In summary, patients who continue to experience significant and disabling pain despite a reasonable trial of nonoperative therapy, should be considered for surgical treatment.

Sciatic Nerve Injuries

The sciatic nerve is the one most often injured. The relative tethering of the peroneal nerve at the fibular neck renders the peroneal division more susceptible to traction injury. Axonotmetic injuries of the sciatic nerve have a poor prognosis due to the significant distance from injury site to motor end-plates and sensory receptors. Common mechanisms include gluteal injection, hip dislocation, as well as iatrogenic damage after surgery for acetabular fractures or total hip arthroplasty. Cross-sectional imaging and EDX testing to evaluate sciatic nerve injury are advocated. They’re also complementary.

Yuen and colleagues reviewed the EDX features of 100 sciatic nerve injuries and found a surprisingly high frequency of normal sural and peroneal sensory nerve action potentials (SNAPs) despite the presence of postganglionic sciatic nerve injury. Thus, normal SNAPs “do not necessarily exclude sciatic neuropathy.” One important take home point in this retrospective analysis deals with the importance of contralateral limb studies.

Only 18 of the 27 normal sural reports had comparisons with the contralateral sural SNAP (65 abnormal of 92 studies). This further emphasizes the importance of bilateral sensory studies to look for sensory axonal involvement in nerve injury. In addition, this study found that the compound motor action potential of the extensor digitorum brevis was the best predictor for prognosis.

The peripheral nerve surgeon seeks the following information from the EDX physician: (1) nature of the lesion (neuropraxic versus axonotmetic); (2) localization of the lesion; (3) associated nerve injuries; and (4) evidence of recovery. (Table 1)

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<th>Table 1</th>
<th>Key information peripheral nerve surgeon requires from electromyographer.</th>
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<td>1.</td>
<td>Is the injury neuropraxic or axonotmetic?</td>
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<td>2.</td>
<td>Where is the injury anatomically (localization)?</td>
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<td>3.</td>
<td>Are there other associated nerve injuries (are possible nerve transfer options injured)?</td>
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<td>4.</td>
<td>Is there evidence of recovery?</td>
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Distinguishing neuropraxic from axonotmetic lesions allows the surgeon to inform the patient about prognosis as well as the potential need (in the case of axonal injuries) for surgery. It is also useful in planning follow-up since axonal injuries not only require closer scrutiny, but also decisions on intervention by 4 to 6 months postinjury. Sciatic nerve injuries frequently present as peroneal nerve deficits, making localization of the lesion crucial. In a systematic review, Marciniak and colleagues concluded that motor nerve conduction studies (NCs)—particularly across the fibular neck—were useful to assess and localize peroneal nerve palsies.

Looking for associated neuromuscular deficits can help localize sciatic nerve injury and plan reconstructive surgery; for instance, transfer of the tibialis posterior tendon for persistent peroneal nerve palsies requires assurance that the tibialis posterior as well as other plantar flexors are functioning normally. In addition, the technique of nerve transfers, which has “exploded” in upper extremity nerve reconstruction, is likely to become more popular in lower extremity nerve reconstruction.

For example, branches to the lateral head of the gastrocnemius may be transferred to injured branches of the peroneal nerve (Ross, unpublished data, 2009). Therefore, the surgeon requires assurance that potential donor nerve branches of the tibial nerve are functioning normally. Finally, recovery on EMG testing predates that from
the clinical examination by several months. This is also very useful when considering surgery.

Injection Injuries

Injection injuries are common, particularly in children. Severity is highly dependent on the injected agent. Cephalosporins produce relatively mild injury while some steroid agents, such as hydrocortisone, produce severe damage. Children who are born prematurely or have medical conditions requiring intensive care are at higher risk. The typical presentation is that of a foot drop with or without an accompanying pain syndrome. In the perinatal period, this may be misdiagnosed as either congenital club foot or spinal cord dysfunction.

A paucity of literature documents the natural history of these injuries, making definitive recommendations about observation versus intervention difficult. Several authors have advocated surgical intervention if spontaneous recovery does not occur. Senes and colleagues found that EDX testing helped identify less clinically obvious tibial nerve involvement, thereby confirming the level of involvement at the sciatic nerve rather than more distally at the common peroneal nerve.

Of 17 children with sciatic nerve palsies secondary to injection injuries, 3 recovered spontaneously within a few months. Of the remaining 14, 5 were referred more than 2 years after injury and underwent reconstructive procedures, such as tendon transfers, but no nerve surgery. Thus, 9 children underwent nerve surgery, most commonly neurolysis.

The most important predictor of outcome was time from injury to intervention. Of the children treated after 6 months postinjury, 4 achieved Medical Research Council (MRC) grade 4 or higher, whereas only 1 of the 4 children treated after 6 months did so. The other 3 achieved MRC grades of 1 or 0. The authors, and most peripheral nerve surgeons, advocate exploration if there is no significant clinical or electrophysiologic evidence of recovery by 4 months postinjury.

Injuries Associated With Hip Trauma

The sciatic nerve may be injured from trauma or iatrogenically during treatment of hip trauma. The frequency of sciatic nerve injury from hip dislocations varies among series, but is approximately 10% in adults and 5% in children. It is thought that the incidence is lower in children because dislocation is often associated with low-energy trauma whereas adult’s injuries are typically high-energy (i.e., motor vehicle accidents). As is typical in many sciatic nerve injuries, the peroneal division is more commonly injured. Unlike the tibial division, the tethering of the peroneal nerve at the fibular neck may render it less able to dissipate the stretch forces incurred at the moment of injury.

The frequency of primary sciatic nerve injury is also related to the pattern of hip injury, with the highest incidence in dislocations associated with fractures of the posterior wall and/or column of the acetabulum. In addition, the length of time that the hip remains dislocated may affect outcomes. Hillyard and Fox reviewed 106 patients with hip dislocations and sciatic nerve dysfunction and found that increasing periods of dislocation correlated with both a higher incidence and greater severity of sciatic nerve injury.

Sciatic nerve injury may also occur during operative treatment of hip injuries. Reasons include retractor or hardware placement, and prolonged hip flexion and/or knee extension (placing greater tension on the nerve). Some authors advocate intraoperative somatosensory evoked potential monitoring to lessen the incidence of nerve injuries. Others, however, suggest that such monitoring is ineffective.

Finally, sciatic nerve dysfunction may occur sometime after injury and operative treatment secondary to heterotopic ossification (HO). Incidence increases with associated closed head injuries, complex fracture patterns, and postoperative hematoma formation. Both indomethacin and low-dose radiation have been used for prophylaxis against HO.

Assessment of these injuries includes clinical examination, imaging, and EDX testing. Symptoms may mimic a radicular pattern with buttock pain, sensory disturbances in the sciatic nerve distribution, and motor deficits with a predominance in the peroneal division. Imaging may include plain films, CT, and magnetic resonance imaging (MRI). Plain films may be helpful in identifying HO, errant hardware, and fracture fragments that can potentially impinge on the nerve.

CT scanning more precisely identifies HO location, more fully defines the posterior acetabular wall and columns, and assesses for possible confounding spinal pathology. MRI may be compromised by metal artifacts, but helps assess spinal pathology, in particular. EDX testing may be extremely helpful as stated previously.

Findings from the literature that describe the natural history of these lesions are mixed. Epstein found that 60% of sciatic nerve injuries associated with posterior fracture-dislocations “fully recovered.” In a more detailed study, Fassler and colleagues reported on 14 post-trauma patients with sciatic nerve injuries, with particular attention to the severity of initial injury and prognosis. Those who presented with a “mild” peroneal palsy had a good prognosis, typically with mild permanent sensory deficits and no motor deficits. Of 10 patients with initially severe peroneal deficits alone or in combination with tibial deficits, only one recovered with a MRC grade > 3.

A relative paucity of literature exists on outcomes of surgical interventions after hip trauma. Isaak and colleagues reported on 10 patients with sciatic nerve palsies after acetabular trauma. All sciatic nerves were released; none were grafted. Every patient reported improvement in sensory symptoms, including pain, but only 4 of 7 with motor deficits improved.

Benson and Schutzer found good results after piriformis release and sciatic neurolysis (n=14), although all patients were injured by low energy, blunt trauma. Precise indications for surgical inter-
vention are not available due to small patient numbers. However, a reasonable guideline for those with significant neuropathic pain, paraesthesia, and/or motor deficits is a lack of progressive recovery at 6 months postinjury.

Injuries Associated With Total Hip Arthroplasty

Nerve injuries occur in 1-2% of total hip arthroplasty (THA) procedures; more than 90% of these involve the sciatic nerve.12 Factors that increase the risk of sciatic nerve injury include revision arthroplasty (rate 3-8%) and procedures for congenital hip dysplasia (rate 5.8%).32 Mechanisms of injury include direct mechanical trauma from retractors, cautery, and reamers; also mechanisms specific to THA, such as cement extrusion and/or heating. Excessive limb lengthening can also cause injury. In addition, sciatic nerve dysfunction may occur years after THA secondary to inflammation caused by wear debris from the prosthesis.11

The recurring pattern of a predominance of injury to the peroneal division of the nerve is seen once again (>90% of all injuries32). Although the diagnosis is typically made on clinical grounds, this may underestimate the frequency of injury. Weale and colleagues36 prospectively studied 42 patients undergoing primary THA. Although all were asymptomatic postoperatively,4 had denervation potentials on EMG testing. Foot drop as well as neuropathic pain were common symptoms. Precise cause of injury is often unclear, but if clinical examination and/or imaging suggest reversible causes, such as hematoma or cement extrusion, early exploration is warranted, and the prognosis is good.15

Factors that predict a poor prognosis include severe neuropathic pain or complete lesions involving both the tibial and peroneal divisions. Schmalzreid and colleagues32 examined patients at a minimum of two years postinjury; 19% were normal, 64% had a mild persistent deficit, and 17% had a major persistent deficit. Farrell and colleagues15 cautioned that, “The majority of nerve injuries, whether complete or incomplete, never fully resolved.”

Few papers have examined the role of nerve exploration/reconstruction in the context of THA. In a large, heterogeneous group of patients with sciatic nerve injuries from various causes, Kline and colleagues24 reported on 13 patients with sciatic nerve dysfunction after THA. Nine underwent exploration and were treated with either neurolysis (4 of 9) or grafting. Recovery was good for the tibial division in both groups (MRC grade >3 in 3 of 4 with neurolysis, and 3 of 5 with grafting), but the prognosis was poor for the peroneal division, with only 1 of 9 recovering useful function. If there is no evidence of recovery at 4 to 6 months postinjury, most peripheral nerve surgeons support exploration of sciatic nerve injuries associated with hip trauma.

Nerve Injuries Associated With Hip Arthroscopy

Hip arthroscopy is a new and increasingly popular treatment for hip pathology, such as femoroacetabular impingement.7 Complications are uncommon. In a review by Ilizaliturri,19 nerve injuries occurred in 0.9-2% of cases. Injury is typically due to traction on the joint (required for arthroscopic access) and surrounding structures, and the perineal post used for countertraction. The most commonly injured nerves are the perineal and pudendal, followed by the sciatic and femoral. Fortunately, virtually all injuries are neuropathic, and therefore, resolve spontaneously. Indications for nerve exploration are similar to those outlined above for other kinds of injuries.

OTHER MOTOR NEUROPATHIES

Although much less common than sciatic nerve injuries, both the femoral and obturator nerves may be injured after trauma or surgery. Farrell and colleagues15 noted that only 3 of 47 injuries post THA involved the femoral nerve; none involved the obturator. The superior gluteal nerve may also be injured in isolation after antegrade femoral nailing for fractures as well as after THA.13 The small numbers in these studies make it difficult to extrapolate findings for these less common neuropathies. Recommendations for exploration mirror those for THA and hip trauma.

SUMMARY

Nerve injuries around the hip are relatively uncommon, but disabling when they occur. Appropriate evaluation requires clinical examination, imaging, and electrodiagnostic testing. Surgical assessment and intervention should be considered for nerve deficits that persist longer than 4 to 6 months postinjury.

REFERENCES

Critical Care

Charles F. Bolton, MD, FRCP(C)
Simon Podnar, MD, DSc
Andrea J. Boon, MD
Ted M. Burns, MD
Shawn J. Bird, MD

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2621 Superior Drive NW
Rochester, MN  55901
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Critical Care

Faculty

Shawn J. Bird, MD
Associate Professor
Director, Electromyography Laboratory
Department of Neurology
University of Pennsylvania
Philadelphia, Pennsylvania

Dr. Bird is director of the EMG laboratory and clinical neurophysiology fellowship program, as well as the Muscular Dystrophy Association and myasthenia gravis clinics at the University of Pennsylvania. He is an associate professor of neurology at the University of Pennsylvania. He received his undergraduate degrees in electrical engineering and biology from Cornell University. He attended medical school at the Johns Hopkins University School of Medicine. He completed his neurology residency and fellowship training in neuromuscular disease and electrodiagnostic medicine at the University of Pennsylvania. He is an active member of the AANEM, is currently on the AANEM’s Course Committee, and has served on the Journal, Special Interest, and Historical Committees. He is a member of the American Academy of Neurology and the American Neurological Association. His main research interests include neuromuscular disorders associated with critical illness, immune-mediated neuropa-thies and myasthenia gravis.

Andrea J. Boon, MD
Department of Physical Medicine and Rehabilitation
Mayo Clinic College of Medicine
Rochester, Minnesota

Dr. Boon graduated from medical school in New Zealand before completing her residency in physical medicine and rehabilitation (PMR), followed by a fellowship in clinical neurophysiology at the Mayo Clinic, Rochester, MN. She has been on staff at Mayo since 2000, with a joint appointment as assistant professor in the Departments of PMR and Neurology, Mayo Clinic College of Medicine. Dr. Boon has introduced diagnostic ultrasound into the clinical and academic practice of the Mayo EMG lab, where over 12,000 patients undergo testing annually. Her current research focus is in this area, in addition to her musculoskeletal practice where she has been investigating the role of botulinum toxin in painful musculoskeletal disorders. Dr. Boon is a member of the Continuing Medical Education committee of the AAPMR and the Professional Practice committee of the AANEM, as well as serving as the AANEM CPT advisor and the AANEM alternate RUC advisor to the AMA.

Charles F. Bolton, MD, FRCP(C)
Faculty
Department of Medicine Division of Neurology
Queen’s University
Kingston, Ontario, Canada

Dr. Bolton was born in Outlook, Saskatchewan, Canada. He received his medical degree from Queen’s University and trained in neurology at the University Hospital, Saskatoon, Saskatchewan, Canada, and at the Mayo Clinic. While at the Mayo Clinic, he studied neuromuscular disease under Dr. Peter Dyck, and electromyography under Dr. Edward Lambert. Dr. Bolton has had academic appointments at the Universities of Saskatchewan and Western Ontario, at the Mayo Clinic, and currently at Queen’s University. He also recently received the AANEM Distinguished Physician Award. His special interests are investigations of neuromuscular problems in the intensive care unit, and of neuromuscular respiratory insufficiency.

Course Chair: Shawn J. Bird, MD

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Ted M. Burns, MD

Associate Professor
Department of Neurology
University of Virginia
Charlottesville, Virginia

Dr. Burns is an associate professor of neurology at the University of Virginia in Charlottesville. He graduated from Kansas University Medical School and completed his neurology residency at the University of Virginia (UVA). He later completed 1-year fellowships in electromyography/neuromuscular diseases at UVA, and peripheral nerve diseases at the Mayo Clinic in Rochester, Minnesota. He is board certified in neurology, clinical neurophysiology, and electrophysiology. Dr. Burns is the director of the EMG laboratory at UVA, director of the UVA neurology residency program, and director of the UVA clinical neurophysiology fellowship program. He is the editor of the weekly podcast for *Neurology*. He is also the editor of the AANEM’s *Nerve and Muscle Junction* podcasts. He is a member of the AANEM’s Continuing Medical Education committee and also a member of the American Board of Psychiatry and Neurology’s (ABPN) Neurology Clinical Neurophysiology committee, and the ABPN Neurology Recertification and Maintenance of Certification committee.

Simon Podnar, MD, DSc

Division of Neurology
Institute of Clinical Neurophysiology
University Medical Center
Ljubljana, Slovenia

Dr. Podnar graduated in 1992 from the University of Ljubljana Medical School, in Ljubljana, Slovenia. In 1996 and 2002 he received his masters, and the doctorate degrees. Since April 2001 he has worked as a neurologist and clinical neurophysiologist at The Institute of Clinical Neurophysiology in Ljubljana, Slovenia. His main interests are uroneurology, quantitative EMG and respiratory neurophysiology. He is co-author of 10 chapters, and is the first author on over 50 papers in peer reviewed, Science Citation Index cited journals. He is on the editorial board of *Muscle & Nerve*, and regularly reviews papers for several other journals, including *Clinical Neurophysiology, European Journal of Neurology, Journal of Neurology, and Neurosurgery & Psychiatry*. He has been an invited speaker at neurologic, clinical neurophysiologic, and urologic meetings in Europe and North America. Since 2004 he has been president of the section for clinical neurophysiology of the Slovenian medical society.
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Critical Care

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OBJECTIVES

Neuromuscular disorders are a common cause of prolonged weakness and failure to wean from mechanical ventilation. Participants will learn (1) up-to-date information on various electrophysiologic techniques used to assess patients with neuromuscular respiratory failure, (2) current approaches to the management of myasthenic crisis, and (3) the recognition of critical illness polyneuropathy and critical illness myopathy.

PREREQUISITE

This course is designed as an educational opportunity for physicians.

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Michael T. Andary, MD, MS
East Lansing, Michigan
Electrophysiologic Approach to Neuromuscular Weakness in the Intensive Care Unit

Charles F. Bolton, MD, FRCP(C)
Division of Neurology
Queen's University
Kingston, Ontario, Canada

INTRODUCTION

An electrophysiological approach to neuromuscular (NM) weakness in the intensive care unit (ICU) may be time consuming. It involves comprehensive clinical and electrophysiological assessment, as well as other studies when indicated.1,2 There are two main reasons for NM consultations in the ICU. One reason is the unexplained difficulty in weaning patients from the ventilator after cardiac and pulmonary causes have been excluded. The second reason involves observed limb weakness and reduced deep tendon reflexes.

Appropriate arrangements should be made in advance with the ICU staff. Information on the patient's history and physical examination, possible diagnoses, main treatments including use of NM blocking agents and steroids, and ventilator settings should be obtained. The best time for the bedside clinical and electrophysiological assessment should be indicated. Additionally, the patient should be on the least amount of sedation. Knowledgeable members of the ICU staff including a nurse, resident, and a respiratory technologist should be available.

There are two main categories to be considered in the differential diagnosis which will be discussed.

CONDITIONS DEVELOPING ACUTELY BEFORE ADMISSION TO THE ICU

In this scenario, the respiratory muscles are predominantly involved and an NM condition has not been previously considered. The patient presents to the emergency room in acute respiratory failure. An endotrachial tube is inserted, the patient is placed on a ventilator, and continues to be managed thereafter in the ICU. After acute cardiac and pulmonary conditions have been addressed, a consultation from an electrodiagnostic (EDX) physician is requested because an NM problem is suspected.

In this acutely developing situation, clinical signs may be confusing. The differential diagnosis should be approached systematically, and the relevant conditions should be eliminated.

Brain

Somatosensory evoked potentials (SEPs) are valuable in determining the severity of encephalopathy, particularly anoxic ischemic encephalopathy. Severe trauma or metabolic toxic illnesses affecting the brain may interfere with respiration though a lack of central drive to the extent that endotracheal intubation and mechanical ventilation are required. The results of limb conduction studies and phrenic nerve conduction studies (NCSs) are normal. A needle electromyography (EMG) of limb muscles shows an absence of or a decrease in the number of motor unit action potentials (MUAPs). The pattern of firing of MUAPs in the diaphragm is abnormal. For example, Cheyne-Stokes respiration indicates diffuse disturbance of the central hemispheres.

Spinal Cord

In acute disorders of the high cervical spinal cord, the traditional signs of localized spinal cord disease such as compression resulting from neoplasm, infection, or acute transverse myelitis may be
absent. Hyperreflexia is usually abolished by spinal shock, with the sensory level difficult to determine, particularly in high cervical lesions. Thus, magnetic resonance imaging (MRI) of the spinal cord on an emergency basis is often necessary.

In motor NCSs, the amplitude of compound muscle action potentials (CMAPs) is decreased due to anterior horn cell disease when the injury occurred at least 5 days earlier. When sensory conduction is normal and clinical sensory loss is present, the lesion is proximal to the dorsal root ganglion, usually indicating myelopathy. Needle EMG abnormalities appear after a 10 to 20 day interval, depending on the distance between the muscle and the site of injury along the nerve. The pattern of needle EMG signs of denervation should assist in localizing the segmental level, in determining whether it is unilateral or bilateral, and in providing a rough estimation of the number of segments involved, although the results may not be precise due to the considerable overlap of innervation, particularly of the paraspinal muscles.

If the high cervical spinal cord is damaged, the results of motor and sensory NCSs of limb nerves are normal. Because the phrenic nerves arise from spinal segments C3 - C5, the amplitude of CMAPs from the diaphragm may be considerably reduced or absent, although latency is relatively preserved. Needle EMG shows an absence of or a decreased number of MUAPS. Muscles innervated by the involved high cervical segments demonstrate fibrillation potentials and positive sharp waves 2 weeks after the lesion occurs. To confirm the localization further, needle EMG of the cervical paraspinal and the shoulder muscles supplied predominantly by C4 should also show evidence of denervation.

In lesions of the lower cervical spinal cord, respiratory difficulty is the result of upper motor neuron (MN) weakness of chest wall muscles. Thus, the findings of phrenic NCSs and needle EMG of the diaphragm are normal. However, there is a relative lack of firing of MUAPS from chest wall muscles, and fibrillation potentials and positive sharp waves are not present.

Motor Neuron Disease

Amyotrophic lateral sclerosis may be initially misdiagnosed as severe respiratory insufficiency. The typical combined upper and lower MN signs of hyporeflexia or hyperreflexia, muscle wasting and fasciculations, atrophy, and fasciculations of the tongue may not be obvious. Electrophysiological studies, including phrenic NCSs and needle EMG of the chest wall, diaphragm, and the limb muscles, often suggest the diagnosis. However, it still may be necessary to proceed with MRI studies. Atypical MN disease, such as motor neuropathy with multifocal conduction block, should be excluded.

Acute Polyneuropathy

Acute polyneuropathy is suspected in the presence of muscle weakness, hyporeflexia, distal sensory loss, and the absence of upper MN signs or bladder dysfunction, but these signs may not always be obvious. Bladder dysfunction and extensor plantar responses are seen occasionally in Guillain-Barré syndrome (GBS).

In an acute inflammatory demyelinating polyneuropathy such as GBS, the electrophysiological features are those indicating demyelination of peripheral nerve. In the initial stages, conduction velocities may be decreased only mildly, but the diagnosis is suggested by the prolongation or absence of F waves, evidence of conduction block, and an absence of abnormal spontaneous activity in muscle, with the remaining MUAPS firing rapidly. Thus, even within hours after onset, the findings often strongly suggest GBS. Phrenic NCSs and needle EMG of the diaphragm are particularly valuable in establishing the type and severity of the involvement of the phrenic nerve and diaphragm. Serial electrophysiological studies that follow the course of treatment, such as plasmapheresis and hyperimmune globulin are valuable. In the author’s experience, symptomatic improvement may precede electrophysiological improvement.

Variants of GBS are primarily axonal, rather than demyelinating. Most, but not all of them are likely to have Campylobacter jejuni as the factor precipitating the immune mediated polyneuropathy. Positive results on serological testing or stool culture for C. jejuni may be the earliest evidence of these axonal variants.

The acute axonal form of GBS (acute motor and sensory axonal neuropathy) presents with a rapidly developing paralysis that reaches completion within hours and requires early admission to the ICU and full ventilatory assistance. Although the severity of the condition varies, all muscles of the body, including cranial, eye, and papillary muscles, may be completely paralyzed. Therefore, it clinically simulates the syndrome of brain death, but the electroencephalogram (EEG) is relatively normal. All peripheral nerves may be unresponsive to electrical stimulation.

In acute paralytic syndromes of children and young adults with acute motor axonal neuropathy, symmetrical ascending weakness develops over days, sensation is normal, deep tendon reflexes are often preserved, and the concentration of protein in the cerebrospinal fluid is increased. The amplitude of CMAPs is reduced, but the latency is normal. Sensory conduction is normal. Respiratory paralysis may be significant. Good recovery eventually occurs.

Other polyneuropathies such as acute porphyria, Lyme disease, or human immunodeficiency virus infection should be considered.

Chronic Polyneuropathies

Chronic polyneuropathies may evolve as rapidly developing respiratory insufficiency. Although rare, this situation may occur in chronic inflammatory demyelinating polyneuropathy and diabetic polyneuropathy. The typical clinical and electrophysiological signs should be noted, and phrenic NCSs and needle EMG of the diaphragm should be performed.
Neuromuscular Transmission Defects

Initially, both myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) may present with respiratory insufficiency. In MG, this appears to be a syndrome. Levels of acetylcholine antibodies are normal, but muscle-specific tyrosine kinase-seropositive antibodies may be abnormal. LEMS, hyocalcemia, hypermagnesemia, and wound botulism may also be identified electrophysiologically. In organophosphate poisoning, a repetitive discharge appearing after a single electrical shock to a peripheral nerve is diagnostic.

Myopathies

Myopathies do not usually pose a difficult diagnostic problem because the diagnosis is usually evident, having been established previously in chronic cases such as muscular dystrophy. However, respiratory muscles are occasionally involved, and these patients may require intubation and admission to the ICU. In acute myopathies, such as necrotizing myopathy with myoglobinuria, the diagnosis is evident due to the high levels of creatine phosphokinase (CPK) and, at times, myoglobinuria.

CONDITIONS DEVELOPING AFTER ADMISSION TO THE ICU

1. Critical illness polyneuropathy (CIP) occurs commonly and manifests as flaccid limbs and respiratory weakness. Electrophysiologically, the findings are consistent with an axonal motor and sensory polyneuropathy. The duration of the CMAP is normal, and there is a response on direct muscle stimulation. The CPK is near normal. Muscle biopsy reveals atrophy of both type I and type II fibers. The prognosis is variable.

2. NM transmission defects commonly occur following the use of NM blocking agents. There are flaccid limbs and respiratory weakness. Repetitive nerve stimulation shows the typical post synaptic defect. Creatine kinase (CK) is normal, as is the muscle biopsy. Prognosis is good.

3. Critical illness myopathy (CIM) can be subdivided into several different types.

Thick filament myosin loss has the distinctive feature of a deficiency of thick filament myosin on muscle biopsy. This occurs commonly in patients who have been treated with NM blocking agents and steroids, but are often septic as well. The limbs are flaccid and there is a respiratory weakness. EMG may show a myopathic pattern. There is mild elevation in the CK. The duration of the CMAP is increased, and there is an equally reduced response in amplitude on both stimulation of nerve and direct stimulation of muscle. Prognosis is good.

Diffuse (cahectic) myopathy occurs commonly in patients who have been recumbent for long periods in the ICU. Weakness and wasting of muscle may be considerable. However, electrophysiological studies are normal, as is serum CK. Muscle biopsy is normal or reveals type II fiber atrophy. The prognosis is good.

Combined polyneuropathy and myopathy is likely a common occurrence with the proportion of each depending on a variety of factors. The limbs are flaccid and there is respiratory weakness. Electrophysiological studies indicate a combined polyneuropathy and myopathy. The CK is variably elevated. Muscle biopsy often shows a mixture of denervation, necrosis, and atrophy of either type I or type II fibers, or both. The prognosis is variable.

Mononeuropathies

A variety of mononeuropathies and plexopathies may occur in isolation or coexist with CIP and CIM. These may occur as a result of nerve compression from prolonged recumbency, direct trauma, ischemia, or hemorrhagic compression, complicating anticoagulant therapy. One or both phrenic nerves may be damaged by mechanical trauma in major accidents, following surgery, or trauma of a thermal nature, as in the application of ice during cardiac surgery, or induction of heat in the procedure of radio frequency ablation for auricular fibrillation.

Clinical Assessment

A reasonably comprehensive neurological assessment can be performed, especially if the patient is under minimal sedation and there is little evidence of septic encephalopathy. With the patient receiving only a pressure support of 9 cm H2O, the strength and pattern of respiratory muscles from central drive can then be accurately observed, including paradoxical respiration from severe paralysis of both diaphragms. The accuracy of sensory testing will depend on the degree of patient alertness and level of cooperation.

Protocol for Electrophysiological Studies

1. Record skin temperatures.

2. Perform needle EMG of chest wall muscles and diaphragm. This can be performed under the condition of least sedation and on a pressure support of only 9 cm H2O so there is maximum possible central drive. In conditions of difficult
access to the diaphragm (e.g., edema or obesity), an ultrasound-guided technique may be helpful. Needle EMG of limb muscles should also be performed at this time.

3. Administer an intravenous narcotic for the remainder of the studies, as the tests can be quite uncomfortable, especially in patients who have GBS.

4. Perform phrenic nerve, motor, and sensory conduction tests of limb nerves. In addition to observing any reductions in the CMAP, a possible increase in duration is an important sign of CIM.

5. Perform repetitive nerve stimulation to investigate for defects in NM transmission. While the patient is under narcotic sedation, these tests can be performed at slow and rapid rates of stimulation with reasonable comfort and can be used to investigate for pre synaptic and post synaptic defects in NM transmission.4

Other Tests of Neuromuscular Investigation in the ICU

If there is any possibility that acute respiratory insufficiency is based on cervical myelopathy, MRI scans of the cervical area should be performed before electrophysiological studies. Computed tomography, head scans, EEG, and SEPs may be necessary. If after all the above investigations have been explored there is still uncertainty, muscle biopsy is often quite helpful in a prognosis. For example, in acute rhabdomyolysis, despite severe muscle weakness and very high levels of CK, if the muscle biopsy is relatively normal, it harbors a good prognosis. On the other hand, massive necrosis of muscle may indicate a poor prognosis. Since open biopsy of muscle may be difficult to arrange in ICU patients, needle biopsy may be worthwhile.5

References

Phrenic Nerve Conduction Studies

Simon Podnar MD, DSc
Division of Neurology
Institute of Clinical Neurophysiology
University Medical Center Ljubljana
Ljubljana, Slovenia

TECHNIQUE

Phrenic nerve conduction studies (NCSs) have been used for a number of years in the evaluation of patients with respiratory failure due to suspected neuromuscular (NM) disorders. The first phrenic NCSs were performed by Heinbecker and associates in 1936 using specimens obtained from operations or harvested from cadavers. Later, “in vivo” studies were also performed, using invasive recording electrodes (either esophageal or needle electrodes inserted through the chest). However, the modern era of phrenic NCSs began in 1967 with the publication of Newsom Davis’ work. Davis demonstrated the clinical feasibility and utility of surface electrodes for recording the diaphragm compound muscle action potential (CMAP) on phrenic nerve stimulation. A pair of surface electrodes that were separated for 5 cm and positioned at the antero-lateral chest in the eighth or ninth intercostal space were used. In these early studies, the phrenic nerve was stimulated at the upper margin of the thyroid cartilage behind the posterior border of the sternocleidomastoid (SCM) muscle.

Seventeen years later, another important contribution to phrenic nerve conduction techniques was provided by Markand and colleagues. A similar stimulation technique was used, but it involved exploring recording montage in detail. Using a remote reference (knee), it was discovered that a surface electrode placed at the ipsilateral seventh intercostal space produced a higher amplitude electropositive response, and that a surface electrode placed at the xiphoid process generated a minimal amplitude electronegative response. Simultaneous recordings from the xiphoid process (G1), and the ipsilateral seventh intercostal space (G2) resulted in summation of opposite polarity activity, and in a higher amplitude electronegative response similar to typical CMAP, as recorded from distal limb muscles.

In a 1992 study, Swenson and Rubenstein further refined the position of recording electrodes. Using electrode arrays, they found the maximal phrenic nerve CMAP amplitude at the intersection of the anterior axillary line and the transverse plain through the xiphoid. The researchers also mapped out the “motor point” area of the diaphragm for the phrenic NCS.

The technique that is most widely used today in phrenic nerve studies was established in 1995 by Chen and associates. They discovered that phrenic nerve stimulation in the supraclavicular fossa just above the clavicle is easier than stimulation at the level of the upper margin of the thyroid cartilage, which had been used before. Furthermore, use of a recording montage similar to that used by Markand and colleagues was suggested, but instead of counting intercostals spaces, the G1 electrode was placed 5 cm above the tip of the xiphoid process, and the G2 electrode was placed 16 cm from G1 on the rib cage margin, ipsilateral to the phrenic nerve stimulation. In using this approach, the G2 in most subjects was at the level of the seventh intercostal space, which made G2 electrode positioning much easier, particularly in obese subjects.

Since the publication of that article in 1995, only small changes in technique were suggested in 2008 by Resman-Gašperšič and Podnar. Instead of phrenic nerve stimulation at the posterior border of the SCM muscle, these authors proposed stimulation between both heads of the SCM muscle. It had been their experience that stimulation at the posterior border of the SCM muscle often resulted in difficulties obtaining a well formed and
reproducible supramaximal diaphragm CMAP. When using stimulation at the posterior border of the SCM muscle, concomitant brachial plexus stimulation had proven to be a problem reported by others as well.1-4,6

The authors’ current approach is very similar to that described by Bolton. It includes phrenic nerve stimulation in the supraclavicular fossa just above the clavicle with the anode above the cathode. First, stimulation between both heads of the SCM muscle (Figure 1) is attempted. Both heads of the SCM muscle become more prominent when the subject flexes the neck for a moment during stimulation electrode positioning. During stimulation, firm pressure of a bipolar stimulating electrode is applied using lateral inclination pointing beneath the SCM muscle.5 Stimulation strength is continually increased, and no attention is given to breathing. When amplitude stops increasing, in spite of an increase in stimulation strength, voltage is increased another 20% to ensure a supramaximal stimulation strength. This usually occurs at 70 to 90 mA with 0.1 ms pulse duration.5 Again, five responses are recorded at the supramaximal stimulation strength, and the breathing cycle is disregarded. The highest amplitude and artifact-free CMAP is used as the result.7 If supramaximal stimulation response is not obtained at 100 mA, other stimulation electrode positions are used. These include the posterior border of the SCM muscle with anterior inclination of the bipolar stimulating electrode and stimulation at higher levels in the neck, instead of in the supraclavicular fossa. These differences in optimal position of stimulation electrodes are likely due to anatomical variability in phrenic nerve course.

Two disposable, self-adhesive disc electrodes are used for recording; the G1 electrode is fixed on the sternum 5 cm above the xiphoid process tip, and the G2 electrode is placed ipsilaterally to the stimulation electrode 16 cm from G1 along the rib cage border (Figure 1).4 The distance between both electrodes is fixed and should only be proportionally reduced in small children to the approximate location of the anterior axillary line. The ground electrode is usually fixed to the middle of the sternum.

The setting of the electromyography (EMG) machine is the same as for other NCSs (filters 2 Hz to 10 kHz). However, the amplitude is usually set at 200 µV, and latency is set to 3 ms per division.

Bilateral studies are performed in all subjects. At supramaximal stimulation strength, phrenic nerve CMAP onset latency (ms), peak latency (ms), amplitude (mV), duration (ms), and area of the negative phase (mVms) are measured.5

PHRENIC NERVE CMAP PARAMETERS: UTILITY AND CONFIDENCE INTERVALS

The most regularly used CMAP parameters are onset latency and amplitude. Exact confidence intervals for these two parameters vary somewhat between different studies (Table 1).

CMAP onset latency has a well-established role in phrenic nerve demyelination.1,2,6 It was found to correlate with the subjects’ age4,8 and height.5 However, as seen in patients with hereditary demyelinating polynuropathies (e.g., Charcot-Marie-Tooth 1A, Figure 2), latency poorly correlates with respiratory function. Therefore, it can be regarded as a surrogate marker of neuropathy. In general, longer latencies were reported in studies that used phrenic nerve stimulation at the upper level of thyroid cartilage1,2,6 than in studies that used stimulation in the supraclavicular fossa (in Table 1 non-standard and standard, respectively).4,5,8,9 Using the latter stimulation site, latencies > 8.0 ms can be regarded as prolonged.5

In contrast, amplitude is very useful in assessing phrenic nerve function (Figure 3), and is usually regarded as the main CMAP parameter in phrenic NCSs. It is particularly helpful in the detection of neuronal or axonal lesions.2 However, the variability among the results of previous studies is even larger (Table 1). This may be primarily due to technical reasons (i.e., differences in stimulation efficiency and in recording montage). Stimulation at the posterior border of the SCM muscle is not likely always supramaximal, due to concomitant brachial plexus stimulation. With a slightly more medial position in the supraclavicular fossa the anode is above the cathode (Figure 1). The ground electrode is usually fixed to the middle of the sternum.

Figure 1 Position of stimulation and recording electrodes for phrenic nerve conduction studies. Stimulation electrodes (shown on subject’s right) are positioned between the sternal and clavicular heads of the sternocleidomastoid muscle (shown schematically on subjects’ left), cathode being distal to anode. The position of the recording electrodes is as described by Chen and colleagues (G1 5 cm above xiphoid process, and G2 ipsilateral to stimulation 16 cm infero-laterally from G1 over the chest margin).4 In addition, positions for electromyographic (EMG) needle electrode insertions into the diaphragm are also shown on the subject’s left side.5
Amplitude becomes larger during inspiration, which can be recognized as more peaked traces. Several explanations for this observation have been discussed. The flattening of the diaphragm during inspiration increases the angle that the moving dipole subtends at the recording electrode, which, according to the theory of volume conduction, would result in increased CMAP amplitude. Shortening (shorter path) and thickening (faster conduction) of muscle fibers during contraction (inspiration), both of which shorten the conduction time along the diaphragm muscle fibers, could also contribute to this variance. Similarly, the lower right phrenic nerve CMAP amplitude during inspiration might be explained by the higher position of the diaphragm dome (smaller angle, longer and thinner muscle fibers) on that side due to the subjacent liver. No such difference was observed during expiration. The explanation is further complicated by the fact that both recording electrodes (G1 and G2) used in phrenic nerve CMAPs are active.

Due to lower sensitivity to the respiratory cycle, and no differences between the left and right sides, the CMAP area was proposed to be used instead of amplitude. However, the clinical utility of phrenic nerve CMAP area is not yet well established.

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Technique</th>
<th>Latency (mean ± SD; upper limit)</th>
<th>Amplitude (mean ± SD; lower limit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>Non-standard</td>
<td>7.7±0.80; 9.3</td>
<td>0.16 - 0.50;</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>Non-standard</td>
<td>L: 7.74±0.76; 9.26</td>
<td>L: 0.77±0.22; 0.33</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>Non-standard</td>
<td>R: 7.77±0.77; 9.31</td>
<td>R: 0.79±0.19; 0.41</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>Standard</td>
<td>6.54±0.77; 8.08</td>
<td>0.66±0.10; 0.26</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>Standard</td>
<td>6.1±0.7; 7.5</td>
<td>0.67±0.16; 0.35</td>
</tr>
<tr>
<td>6</td>
<td>32</td>
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<td>7.4±0.9; 9.2</td>
<td>0.51±0.12; 0.26</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>Non-standard</td>
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<td>R: 0.50±0.19; 0.12</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>Non-standard</td>
<td>L: 6.81±0.75; 8.31</td>
<td>L: 0.40±0.18; 0.02</td>
</tr>
<tr>
<td>9</td>
<td>29</td>
<td>Standard</td>
<td>6.55±0.69; 7.93</td>
<td>1.00±0.27; 0.46</td>
</tr>
</tbody>
</table>

The lower and upper normative (cut-off) limits were calculated as mean ± 2 SD - for amplitude lower limit, because study data do not enable us to calculate this value. Non-standard and standard techniques are as described in the “Technique” portion of this text; SD = standard deviation.
Using a rectangular pulse of 0.1 ms duration, CMAPs usually appear at a stimulation strength of less than 50 mA in most control subjects. None of them require stimulation with more than 85 mA to record the maximal amplitude CMAP. However, in extremely obese patients (body mass index > 40 kg/m²) with short, thick necks, stronger stimulation strengths (longer pulse durations) are often needed to record supramaximal amplitude CMAPs. Higher response thresholds are usually observed in men.

In addition to normative data for absolute values, normative data for interside differences are also available. Although the value is currently unclear, they are expected to be particularly useful in patients with asymmetric or unilateral phrenic nerve involvement.

**INDICATIONS**

Phrenic NCSs have several indications. When used with needle EMG of the diaphragm, these studies are useful in evaluating patients with respiratory failure due to suspected NM disorders. However, in contrast to needle EMG of the diaphragm, phrenic NCSs are noninvasive. They can also be safely performed in intensive care unit (ICU) patients with catheters in the supra and infra clavicular fossae, as well as in those with implanted cardiac devices.

Nevertheless, in most of these patients, phrenic NCSs are probably even more useful than needle EMG of the diaphragm. Normal amplitude phrenic nerve CMAP virtually excludes the important lesion of the phrenic nerve or diaphragm. Needle EMG of the diaphragm is useful only in patients with nonrecordable or very low amplitude phrenic nerve CMAPs. In this situation, it may not only confirm the phrenic NCS findings, but also provide data in regards to severity, mechanism, time course, and collateral reinnervation. Therefore, phrenic NCSs can and should be performed even by electrodiagnostic (EDX) physicians who are not accustomed to performing needle EMG of the diaphragm.

In general, referrals to respiratory EDX studies can be divided into several groups. The first group includes patients with known NM conditions where respiratory failure is either expected (e.g., amyotrophic lateral sclerosis [ALS]) or possible (e.g., different myopathies, Guillain-Barré syndrome [GBS], chronic inflammatory neuropathy) along the disease course. It is often useful to follow these patients using regular respiratory EDX studies along with pulmonary function tests in order to be prepared for the occurrence of respiratory failure, and treat it in a timely manner. Although needle EMG of the diaphragm will provide more detailed information, phrenic NCSs alone will usually demonstrate the severity of NM involvement of the peripheral respiratory system. CMAP amplitude is particularly useful in this respect, and is expected to fall steadily in progressive diseases (e.g., ALS) along with failing respiratory function.

The second group consists of patients with minor respiratory symptoms and signs of partial restrictive respiratory failure. Such patients will most often note reduced exercise tolerance and report difficulties in the ability to lay flat. These complaints often lead to a referral to a pulmonologist and a chest x-ray will be ordered, which may demonstrate the elevation of either a single diaphragm leaf or both leaves. This is confirmed by poor movement of the diaphragm on chest fluoroscopy or ultrasound study. The most common localization of the lesion in this group is the phrenic nerve itself. These disorders may be confined to the phrenic nerve unilaterally (Figure 4), or bilaterally. However, they may also be evident in other parts of the peripheral nervous system. In some of these patients, systemic lupus erythematosus (SLE), Lyme disease, and Herpes zoster (Martić V., personal communication) can be diagnosed. In those with severe neck and shoulder pain following infection, surgery, or vaccination, a diagnosis of neuralgic amyotrophy is usually made (Figure 4). Phrenic nerves were affected in 7 of 99 consecutive patients with neuralgic amyotrophy, but isolated phrenic nerve involvement was reported only a few times in this condition. However, painless (bilateral) isolated phrenic neuropathy has been proposed as a distinctive entity, a shared opinion among others as well. In some of these patients, other concomitant autoimmune disorders such as myasthenia gravis and SLE suggest an immunological...
The last group is comprised of ICU patients. Some will be admitted to the ICU due to restrictive respiratory failure of unknown cause. Many of these patients have ALS, which occasionally presents with respiratory failure (Figure 3). Other patients from this group may have severe neuropathies (e.g., GBS, porphyria), myelopathies, or encephalopathies. Phrenic NCSs will be very useful in these patients to differentiate between lower and upper motor neuron lesions. Additional EDX studies performed in other regions will be helpful in revealing the extent and mechanism of disease process. Severe respiratory failure that requires admittance to the ICU may also be observed in patients with isolated, usually bilateral, phrenic nerve lesions due to the mentioned etiologies, particularly if their respiratory function is compromised for other reasons. The other important group includes patients that need phrenic NCS at some point and are admitted to the ICU due to severe medical or surgical conditions, of which respiratory failure is not the leading component. Respiratory failure will often become obvious at the moment an attending physician would expect them to be weaned from the mechanical ventilator. This typically occurs when such patients become alert and responsive.

Table 2. Reference intervals for phrenic nerve conduction studies obtained in 29 normal volunteers.5

| Parameter               | Mean±SD | L/U limits    | 5th/95th
|------------------------|---------|---------------|-----------
| Response threshold (mA)| 32.41±12.02 | 8.38/56.45     | 15/48     |
| Maximal response (mA)  | 55.86±13.76 | 28.34/83.39    | 37/83     |
| Onset latency (ms)     | 6.55±0.69 | 5.18/7.92      | 5.53/7.72 |
| Peak latency (ms)      | 12.89±1.25 | 10.39/15.39    | 11.08/14.94 |
| Amplitude (mV)         | 1.00±0.27 | 0.46/1.54      | 0.66/1.46 |
| Duration (ms)          | 14.99±3.14 | 8.70/21.28     | 11.18/20.25 |
| Area (mVms)            | 8.23±1.91 | 4.40/12.05     | 5.58/11.31 |

L/U – lower/upper limits obtained after mathematical transformations; 5th/95th – 5th/95th percentile limits. Clinically more relevant limits are underlined.

basis for this disorder. A patient was seen by this author with severe idiopathic thrombocytopenic purpura and bilateral phrenic nerve lesion presenting soon after laparoscopic splenectomy (Podnar, unpublished personal data). In some patients, other diagnoses could have been made if the presentation occurred earlier in the disease course. Presentations may also occur soon after surgery, a trigger cause of phrenic nerve lesions (e.g., cardiac or thoracic surgery). Phrenic nerve lesions in these patients may be unilateral or even bilateral, and their prognosis depends on the exact mechanism of the nerve lesion (i.e., traction or compression versus section). Similarly, in nonsurgical patients, some phrenic nerves will recover, while others will not. In general, the prognosis is slower and worse than in typical neuralgic amyotrophy.11 Phrenic nerve CMAP amplitude will often be very useful in these patients to confirm presence and the extent of the phrenic nerve injury. Interestingly, in some patients, bilateral phrenic nerve lesions will be demonstrated in imaging studies even when only a unilateral lesion was suspected.15

Characteristically, these patients have a tendency to move their limbs poorly, a result of diseased muscle or nerve. These conditions are referred to as critical illness myopathy or neuropathy, respectively. They are supposedly caused by systemic inflammatory response that accompanies severe illness (e.g., sepsis, multiorgan failure, etc). Although a diagnosis can often be made by limb NCSs and limb muscle needle EMG, due to the importance of respiratory function in this clinical situation, phrenic NCSs should also be considered.

Furthermore, phrenic NCSs may be also used in patients with high cervical spinal cord lesions to identify candidates for phrenic nerve or diaphragmatic pacing. For these patients, mechanical ventilation via a tracheostomy is a standard therapy. Potential problems associated with the use of mechanical ventilation include high cost, risk of infection, tracheal injury, and equipment malfunction. Pneumonia remains the most common cause of death after spinal cord injury. A demonstration of normal or near normal amplitude phrenic nerve CMAPs can serve as a useful indicator of viable phrenic motor neurons that are needed for this type of treatment.18

CONCLUSION

Phrenic NCS is an established technique that is not only fast and easy to perform, but can provide important information in patients with suspected NM causes of restrictive respiratory failure. Additionally, it can usually be effectively applied in ICU patients.

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Needle Electromyography of the Diaphragm

Andrea J. Boon, MD
Assistant Professor of Physical Medicine and Rehabilitation
Assistant Professor of Neurology
Mayo Clinic College of Medicine
Rochester, Minnesota

C. Michel Harper, MD
Professor of Neurology
Mayo Clinic College of Medicine
Rochester, Minnesota

NEEDLE ELECTROMYOGRAPHY OF THE DIAPHRAGM

Indications

Needle electromyography (EMG) of the diaphragm is a useful electrophysiologic technique in patients presenting with unexplained dyspnea or failure to wean from the ventilator. Underlying etiologies include lack of central drive (such as in high spinal cord injury or encephalopathy), anterior horn cell or nerve root disease (at C3 - C5 levels), polynuropathy (including critical illness polyneuropathy and Guillain-Barré syndrome), myasthenia gravis or other disorders of neuromuscular transmission, myopathy (including critical illness myopathy), and phrenic neuropathy (which may be traumatic, compressive, or inflammatory such as in Parsonage Turner syndrome).

Needle EMG can provide important information regarding the underlying pathophysiology. It can assist in differentiating between neuropathic, myopathic, and central disorders, as well as prognostic information regarding potential for meaningful recovery, that may not be elicited on clinical grounds alone. Although the diaphragm is an inherently high-risk muscle to examine due to nearby vital structures (liver, spleen, colon and lung), when performed with appropriate technique, the actual risk appears to be quite low.

Anatomy

It is important to understand the anatomy and normal function of the diaphragm prior to attempting needle EMG. The diaphragm is a musculotendinous structure that receives its motor innervation from the phrenic nerves (C3 - C5) and its sensory supply from the phrenic, intercostal (T5 - T11), and subcostal (T12) nerves. The muscular part of the diaphragm lies peripherally, with fibers converging radially onto a central tendon. It is fixed to the thoracic cage and superior lumbar vertebrae, allowing only the central portion to move. The costal part of the diaphragm consists of wide muscular slips attaching to the costal cartilages and ribs (forming a dome on either side). The muscle contracts (the domes flatten) during inspiration, then relaxes during expiration. Based on anatomical studies, there is at least 1.5 cm between the pleural reflection and the lower costal cartilage upon which the diaphragm inserts, and with quiet inspiration, the lung does not descend to enter the pleural space.

Technique

Several techniques for needle EMG of the diaphragm have been described, including two which approach the muscle from the abdominal wall, advancing the needle rostrally beneath the costal margin, towards the diaphragm. However, both can be technically difficult, particularly in more obese patients, and may require a long needle to reach the diaphragm. More recently, Bolton and colleagues have described a technique initially reported by Koepke which is technically very feasible and has been demonstrated in a cadaveric study to be safer than the abdominal approach.

This technique involves insertion of the EMG needle just above the costal margin at any interspace between the medial clavicular line.
and the anterior axillary line (Figure 1). The interspace chosen is based on palpation and examiner preference, as in some cases cartilage may bridge the interspace, making needle insertion difficult, and another interspace must be chosen. The needle is inserted as far medially and caudally within the chosen interspace as possible. The angle of entry is perpendicular to the chest wall, with the needle passing first through skin and subcutaneous tissue before encountering the external oblique or rectus abdominus muscle, followed by external and internal intercostal muscles, and finally passing into the diaphragm (Figure 2).

At rest, the intercostal muscles should be fairly quiet; however, they can be easily activated with vigorous inspiration, forced expiration such as coughing, or slight twisting of the chest wall. Entry into the diaphragm is signaled by bursts of motor unit action potentials (MUAPs) firing with each inspiration. This can be accentuated by asking the patient to sniff quickly in through the nose. Small redirections of the needle may be required to achieve complete entry of the needle into the diaphragm; however, if motor units are initially heard to fire with inspiration, but are no longer audible with further advancement of the needle, this suggests the diaphragm has been completely traversed and the needle should be withdrawn and redirected. MUAPs in the diaphragm are typically shorter in duration, have lower amplitude, and are more numerous than MUAPs in the intercostal or limb muscles.

**Risks**

Prior to attempting needle EMG of the diaphragm, it is prudent to discuss the potential risks with the patient, to obtain informed consent (either written informed consent or verbal consent documented in the EMG report), and to instruct the patient to notify the electrodiagnostic (EDX) medicine physician if they feel a deep aching or very sharp pain any time after the intercostal muscles have been entered, as this may represent penetration of the pleura or peritoneum. Chiodo and associates performed a cadaveric study evaluating three different techniques of needle insertion, just lateral to the xiphoid process, beneath the costal margin at the anterior axillary line, and through the sixth, seventh, and eighth intercostal spaces at the anterior axillary line. This was a small study with only 10 needle insertions per technique and was performed in cadavers (in which the diaphragm is elevated, similar to a paralyzed diaphragm). The authors reported a 100% success rate with insertions above and below the seventh rib (Bolton’s technique), and only 50% accuracy with the other approaches.

Bolton reported a series of 49 cases with no pneumothorax, and based on a telephone survey, two cases of pneumothorax in over 1000 needle examinations of the diaphragm, both in patients with severe chronic obstructive pulmonary disease (COPD). Anecdotally, this is a low-risk procedure, and pneumothorax is more commonly seen after examination of chest wall muscles (such as serratus anterior, rhomboid) than after examination of the diaphragm. However, this may in part reflect the greater number of chest wall muscles that are examined in a particular laboratory in addition to the relative experience of the EDX medicine physician.

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**Figure 1** Insertion points for diaphragmatic needle electromyography examination are marked by an X. The needle is inserted just above the costal margin between the medial clavicular line and the anterior axillary line. The needle is inserted as far medially and caudally within the chosen interspace as possible and the lowest interspace that can be entered is targeted.

**Figure 2** Anatomy of needle electromyography (EMG) of the diaphragm. The angle of needle entry is perpendicular to the chest wall, with the needle passing first through skin and subcutaneous tissue before encountering the external oblique or rectus abdominus muscle, followed by the intercostal muscles, and finally passing into the diaphragm. The pleural reflection is usually at least 1.5 cm rostral to the lower costal margin.
ULTRASOUND-GUIDED NEEDLE EMG OF THE DIAPHRAGM

Rationale

Ultrasound (US) imaging provides excellent direct and real time visualization of soft tissues. It provides details about anatomical landmarks, fascial planes, and neurovascular structures adjacent to the intended target. With recent advances in technology, high-quality US machines are affordable and portable, and have subsequently become more widely available for a variety of clinical applications. For the past several years, the use of US imaging has been integrated into a number of aspects of daily clinical and academic practice in a large, tertiary referral EMG laboratory.

Although Bolton's described technique is relatively safe and technically feasible, in certain cases, such localization is not always possible or may be inaccurate based on anatomical landmarks (i.e., when the diaphragm is completely paralyzed or very atrophic, in obese patients, in patients with altered anatomy, or in patients with severe obstructive pulmonary disease with hyperinflated lungs). For this reason, the use of diagnostic US has been introduced to help localize the diaphragm. By providing direct visualization during needle placement, this enhances the safety and accuracy of the examination and may also provide additional information regarding diaphragmatic function which cannot be elicited on the basis of needle EMG alone. Many of the benefits of complementary US in the assessment of respiratory failure were highlighted in a recent case report in which US enabled physicians to evaluate whether the diaphragm was actually contracting during phrenic nerve conduction studies and whether there was any volitional activation of the diaphragm with the ventilator turned off. In addition, it provided real time visualization of needle placement into the diaphragm and allowed for detection of any associated bleeding in a patient on warfarin with an international normalized ratio of 4.1.3

Technique

US examination of the diaphragm can be easily performed at the bedside using a portable machine. Depending on the US system utilized, depths of up to 10 cm can be visualized using a linear probe at frequencies of 8 to 12 Hz. (In larger adults, a curvilinear transducer may be necessary to adequately image the diaphragm). The seventh, eighth, and ninth ribs in the region of the anterior axillary line are identified, and the probe is initially placed perpendicular to the ribs, centered over the eighth intercostal space. Each rib is easily identified by the bright signal generated at the bony cortex, and the acoustic shadowing deep to it. Subcutaneous tissue lies superficial to the ribs, and two layers of intercostal muscle bridge the space between any two adjacent ribs. Deep to the ribs, the diaphragm can be visualized (Figure 3a).

The muscle layers are easily recognized by their location and appearance. Longitudinally, muscles have a mixed echogenic appearance, consisting of hypoechoic (dark) muscle fibers separated by hyperechoic (bright) fibroadipose septae (perimysium). Transversely, the mixed echogenicity pattern of muscle produces a “starry night” appearance. The diaphragm is typically identified by its deep location, curved geometry, and muscular echotexture. In addition, the diaphragm will thicken during inspiration as a result of muscular contraction unless severely atrophic, in which case it will appear as a very thin strip beneath the intercostal muscles and may not move with inspiration.

In the region of the lower intercostal spaces, the liver on the right and the spleen on the left can be visualized deep to the diaphragm and appear as homogeneous, low-intensity structures punctuated by occasional blood vessels (Figure 3). However, when the patient inhales deeply, the pleura and lung will enter into the field of view; the lung will appear as a bright high-intensity shadow coming in from above and displacing the diaphragm and underlying liver or spleen (Figure 3b).

After initial identification of the anatomy perpendicular to the long axis of the ribs, the transducer is then turned parallel to the ribs overlying the intercostal space. Typically, the seventh intercostal space is initially evaluated, but other spaces are subsequently evaluated as necessary to identify the space that will provide the best visualization of the diaphragm, where the muscle is thickest, with minimal encroachment of the pleural space and or lung. Under real-time US guidance, the needle can be inserted either parallel or perpendicular to the long axis of the transducer. A personal preference is to insert the needle parallel to the transducer (long axis approach), providing direct visualization of the needle throughout the examination (Figure 3b) while simultaneously monitoring the pleural space descending in to the field of view as the patient takes in a deep inspiration. The scanning depth and transducer frequency should be adjusted to allow the highest frequency to be used that will allow visualization at a sufficient depth to see the pleura. If a short axis approach is used, caution must be exercised to stop advancing the needle as soon as the bright tip of the needle is identified on US, as the appearances of the needle tip and the shaft (i.e., the tip has moved beyond the plane of the US beam) are nearly indistinguishable.

Applications

US is utilized on a regular basis when examining the diaphragm. Even in relatively uncomplicated cases, US can easily identify the rib space that provides the best view of the diaphragm, without pleural or lung encroachment. In addition, the depth of needle penetration necessary to reach the diaphragm can be quickly gauged. This is also helpful when attempting a nonguided approach.

It is particularly helpful in more challenging cases, such as larger patients where ribs may be more difficult to palpate, patients with altered anatomy where landmarks cannot be relied upon for accurate guidance, patients with COPD and associated hyperinflation of the lungs, patients on anticoagulation or with coagulopathy who would otherwise not be candidates for needle EMG, and patients with severe atrophy or denervation of the diaphragm where the normal sound of MUAP firing cannot be relied upon to guide...
AANEM Course

Needle Electromyography of the Diaphragm

US imaging not only provides information on the proximity of nearby vital structures, but also allows the EDX physician to assess the quality and degree of motion of the diaphragm, both with respiration and in response to phrenic nerve stimulation.

REFERENCES


Figure 3 Ultrasound guided needle electromyography of the diaphragm.
3(A): The transducer is initially placed perpendicular to the ribs, and the different layers of tissue are identified: subcutaneous tissue (SC), two layers of intercostal muscles (IC) spanning the ribs, diaphragm (D), and pleura (P) which is just coming in to the field of view with inspiration. 3(B): The transducer is then aligned parallel to the ribs, overlying the intercostal space. As the patient takes a deep inspiration, the bright shadow of the lung is seen coming into the field of view from the superolateral direction, displacing the diaphragm and underlying liver. 3(C): The needle is inserted parallel to the long axis of the transducer under real time ultrasound guidance until the needle tip (arrow) enters the diaphragm. The left side of the image is cephalad.
INTRODUCTION

Myasthenic crisis is defined as myasthenic weakness leading to respiratory failure requiring intubation and mechanical ventilation or delayed postoperative extubation for more than 24 hours due to myasthenic weakness.\(^6\)\(^,\)\(^23\) Approximately 15-20% of myasthenia gravis (MG) patients experience crisis at some time during the course of their disease. Respiratory failure caused by myasthenic weakness has historically represented the “gravis” of MG, with 60-80% mortality reported in the first half of the 20th century.\(^4\)\(^,\)\(^47\) With advances in critical care and treatment, myasthenic crisis mortality rates have dropped to < 5%.\(^2\)\(^,\)\(^48\)

Although the diagnosis of MG is often known at the time of myasthenic crisis, some undiagnosed patients may develop crisis in the setting of medical illnesses or surgical procedures. When such undiagnosed patients present with respiratory failure associated with extraocular and bulbar weakness, the differential diagnosis might include Guillain-Barré syndrome, tick paralysis, botulism, Lambert-Eaton myasthenic syndrome, organophosphate intoxication, and brainstem ischemia. A clinical diagnosis of MG may be supported by edrophonium testing; by electrophysiological studies, including repetitive nerve stimulation studies and single-fiber electromyography; and by acetylcholine receptor and muscle-specific receptor tyrosine kinase (MuSK) antibody testing.\(^23\)

This manuscript explores the critical muscles, clinical manifestations, and management of patients with myasthenic respiratory failure. It also focuses on risk factors, complications, weaning criteria, and perioperative care.

CRITICAL MUSCLES INVOLVED IN MYASTHENIC VENTILATORY FAILURE

Respiratory failure in myasthenic crisis develops from critical weakness involving respiratory muscles, upper airway muscles, or both muscle groups. Respiratory muscles of inspiration include the diaphragm and external intercostals, with the scalene and sternocleidomastoid muscles acting as accessory inspiratory muscles. Exhalation in quiet breathing occurs with passive recoil of the lungs, and may be augmented by contractions of the abdominal muscles and the internal intercostals. Vital capacity and negative inspiratory force are ventilatory indices that reflect the strength of inspiratory muscles. Positive expiratory force measurements reflect the strength of expiratory muscles. Compared with vital capacity, maximal inspiratory and expiratory force measurements may be more sensitive indices of respiratory muscle function in patients with MG.\(^2\)\(^5\)\(^,\)\(^33\)

CLINICAL MANIFESTATIONS OF EVOLVING MYASTHENIC CRISIS

Patients experiencing an MG exacerbation leading to crisis can deteriorate quickly, and thus, warrant close observation. For example, 68% of patients in one series (44 patients with 63 crises) needed mechanical ventilation within 1 to 3 days of the start of deterioration. This illustrates the importance of closely monitoring patients at risk.\(^7\)
A focused history and examination that assess ventilatory status and the muscles of the head and neck region are essential. Features of impending myasthenic crisis include severe bulbar weakness, increased respiratory rate due to decreased tidal volumes, marginal vital capacity (i.e., less than 20 mL/kg), weak cough with difficulty clearing secretions, and paradoxical breathing while supine. Serial vital capacity measurements and peak inspiratory and expiratory pressures are customarily used to monitor ventilatory capacity in impending crisis.

To establish the timing of intubation, the “40/30/20” guide (vital capacity < 20mL/kg; peak inspiratory pressure < -30 cm H2O; peak expiratory pressure < 40 cm H2O) may be helpful. Results must be compared to prior readings to identify trends, and they must also be placed in the proper clinical context. These indices have notable limitations; for example, when there is significant bulbar weakness, measurements may be limited by difficulty sealing the lips around the spirometer mouthpiece or by an inability to seal the nasopharynx. Furthermore, vital capacity measurements may not reliably predict respiratory failure in MG.

Other indicators that suggest the need for intubation include evidence of fatigue with increasing tachypnea and declining tidal volumes, hypoxemia despite supplemental oxygen administration, hypercapnea, and difficulty with secretions. Many patients initially maintain partial pressure of carbon dioxide in the blood (PaCO2) in the range of 35 mm Hg because of a subjective sense of dyspnea with low tidal volume, or because of hypoxia from atelectasis and increasing dead space. When the PaCO2 begins to rise in this setting, respiratory failure may be imminent.

Patients with features of impending crisis should be admitted to an intensive care unit and monitored closely. Patients should receive nothing by mouth to prevent aspiration. In acute respiratory failure due to myasthenic crisis, noninvasive mechanical ventilation with bi-level positive pressure ventilation (BiPAP) may circumvent the need for intubation in myasthenic patients who have not developed overt hypercapnea (PaCO2 > 50 mm Hg).

Bulbar manifestations usually accompany respiratory weakness due to MG, and patients will often have flaccid dysarthria, dysphagia, and chewing fatigue. They may exhibit facial weakness with difficulty holding air within the cheeks. Jaw closure is sometimes weak. Tongue weakness may be assessed with protrusion of the tongue into each cheek. Neck muscle weakness is a very common accompaniment of crisis. For example, of the 73 episodes of myasthenic crisis at Columbia Presbyterian Medical Center from 1983 to 1994, 92% of patients had neck weakness at the time of intubation.

Very rarely, vocal cord abductor paralysis may cause laryngeal obstruction with associated stridor. When upper airway dysfunction due to oropharyngeal and laryngeal muscle weakness compromises respiration, tidal volume and vital capacity may be deceptively normal. Direct laryngoscopy may be useful to demonstrate vocal cord paralysis when bulbar myasthenic findings are not otherwise overt.

**RESPIRATORY MANAGEMENT OF THE PATIENT IN MYASTHENIC CRISIS**

Nasotracheal tubes are more comfortable than orotracheal tubes, therefore nasotracheal intubation is preferred. Mechanical ventilation is started using intermittent mandatory ventilation (IMV) or a synchronized IMV mode with additional positive end-expiratory pressure or pressure support to reduce alveolar collapse and atelectasis. The duration of ventilator requirement is often relatively prolonged in myasthenic crisis, with most patients requiring mechanical ventilation for nearly 2 weeks.

Predictors of prolonged intubation (> 2 weeks) include preintubation serum bicarbonate ≥ 30 mg/dL, vital capacity < 25 mL/kg within 6 days of initial intubation, and age over 50 years. For patients requiring more than 2 weeks of mechanical ventilation, a tracheostomy should be considered; the procedure decreases the risk of tracheolaryngeal injury related to prolonged intubation, facilitates suctioning of oropharyngeal secretions, reduces dead space, and is often more comfortable for chronically ventilated patients.

Aggressive respiratory treatment—including suctioning, intermittent positive-pressure breathing, bronchodilator treatments, sighs, and chest physiotherapy—may reduce prolonged respiratory complications of atelectasis and pneumonia, and shorten periods of mechanical ventilation and intensive care.

**RISK FACTORS AND PRECIPITATING FACTORS OF MYASTHENIC CRISIS**

Approximately 15-20% of MG patients experience a crisis; of these, an estimated 33% will have a second episode. Risk factors are shorter duration of disease, history of previous crisis, thymoma, and anti-MuSK antibodies. Crisis usually occurs early in the disease course. For example, a recent case series from Columbia Presbyterian Medical Center reported a mean interval between symptom onset and myasthenic crisis of 8 months (range 0 to 22 years); 53% of patients experienced the first crisis within 1 year of symptom onset, and 21% during the second year. Other series show longer intervals. A series in Leipzig, Germany, found a mean interval of 37 months (range 0 to 18 years).

The prevalence of thymoma is greater in MG patients who experience crisis than in those who do not. For example, approximately one-third of patients in the Columbia Presbyterian cohort had thymoma—a figure higher than the overall prevalence of 10-15% in MG. Patients with anti-MuSK antibodies may also have a higher risk of crisis. Bacterial pneumonia,
for example, was a precipitant in 16% of cases in the Columbia Presbyterian cohort; viral and bacterial upper respiratory infections were identified in another 14%.48 Other noteworthy precipitating factors include sepsis and pregnancy.

Corticosteroid-related exacerbations of MG may follow initial treatment with steroids and result in transiently increased myasthenic weakness. Increased weakness usually begins within 1 to 2 weeks after beginning drug therapy and lasts up to 1 week before strength improves. Patients at highest risk are those with more severe bulbar and generalized MG. Those with marginal respiratory or bulbar muscle function may lapse into crisis after starting steroids and should be observed carefully for the first 2 weeks.

Excessive dosing of cholinesterase inhibitors, such as pyridostigmine, can potentially increase weakness due to depolarization blockade at functionally compromised neuromuscular junctions in MG. The muscarinic effects of cholinesterase inhibitors may also increase oropharyngeal and bronchopulmonary secretions that can obstruct the airway and be aspirated.23 With limited therapeutic options before the widespread use of immunotherapy, some patients in myasthenic crisis experienced a “cholinergic crisis” due to excessive dosing of cholinesterase inhibitors.

In addition to weakness indistinguishable from the underlying myasthenic crisis, signs of cholinergic crisis include muscle fasciculations, miosis, excessive lacrimation, salivation, bronchial secretions, abdominal cramping, diarrhea, diaphoresis, and bradycardia.

Cholinergic crisis is now rare.48 It is common practice to avoid repeated dose escalations of cholinesterase inhibitors in impending myasthenic crisis and to discontinue the use of cholinesterase inhibitors following intubation. These approaches reduce muscarinic complications and facilitate an uncontaminated observation of the response to immune modulation with plasma exchange (PEX) or intravenous immunoglobulin (IVIg). Table 1 lists some commonly prescribed drugs that can exacerbate MG.

### TREATING MYASTHEIC WEAKNESS, INCLUDING MYASTHEIC CRISIS

PEX is an effective short-term treatment for myasthenic crisis, and is used to prepare symptomatic MG patients for surgery.3,7,11,16,27,36,37,48 For patients in crisis, many centers perform a series of 5 to 6 exchanges of 2-3 L every other day. Fewer exchanges (e.g., 3) are typically prescribed for surgery preparation. Onset of improvement varies, but generally begins within 2 to 3 days. Improvement in strength following PEX is only temporary and lasts several weeks at best unless an immune suppressant agent is used. Many of the complications of PEX (e.g., venous thrombosis, infection, and pneumothorax) are associated with large-bore central venous catheters or with the large volume shifts that occur during procedures (e.g., hypotension, bradycardia, and congestive heart failure).

IVIg is an alternative short-term immunomodulating treatment for myasthenic exacerbations or crises. It is also used for surgical preparation in patients who are poor candidates for PEX due to vascular access problems or septicemia.14,20 A randomized, controlled trial of IVIg at 1.2 or 2.0 gm/kg over 2 to 5 days in myasthenic exacerbations and crises demonstrated comparable efficacy, but the sample size was relatively small.14 In a retrospective multicenter study of myasthenic crisis, PEX facilitated extubation at 2 weeks and improved 1-month functional outcome more than IVIg.37 In both studies however, patients treated with PEX experienced a higher rate of cardiovascular and infectious complications. Treatment failures with IVIg that subsequently responded to PEX have been reported.46

Chronic, oral immunosuppressant medications (e.g., azathioprine) do not produce improved strength for weeks to months after a therapeutic dosage is reached; they are therefore ineffective for the acute treatment of myasthenic crisis or exacerbation. Chronic immunosuppression, on the other hand, will decrease the likelihood of recurrence of crisis.24,42 A center in Hungary, for instance, treated myasthenic crisis patients with corticosteroids only during their intensive care unit stay. After 1997, however, patients were started on azathioprine and prednisolone at the time of their crisis. Both oral medications were continued after hospitalization until pharmacological remission. Prednisolone was then gradually tapered. This practice of daily oral immunosuppression during and following myasthenic crisis dramatically reduced the rate of recurrent crisis from 74% to 19%.42

Cholinesterase inhibitors treat symptoms of MG but do not alter the autoimmune attack of the postsynaptic acetylcholine receptor complex. For this reason, and because of their potential for increased weakness due to depolarization blockade and more secretions, they are generally discontinued upon intubation.8,23 After several days, when patients exhibit a definite response to immune modulation (PEX or IVIg), enteral pyridostigmine may be restarted at a low

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<th>Table 1</th>
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<td>Antibiotics</td>
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<td>Aminoglycosides, particularly gentamycin</td>
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<td>Macrolides, particularly erythromycin and azithromycin</td>
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<td>Cardiovascular agents</td>
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<td>Corticosteroids</td>
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<td>Antacids, laxatives, intravenous tocolytics</td>
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<td>D-Penicillamine</td>
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Complications of Myasthenic Crisis

The main causes of mortality in myasthenic crisis are medical complications associated with the crisis itself and its treatment. 

Fever, pneumonia, atelectasis, diarrhea, bronchitis, depression, and anemia requiring transfusion are relatively common complications. 

Sepsis and cardiac arrhythmias or failure are particularly serious complications during crisis. 

Hospital mortality rates in MG crisis are approximately 5%.

Patients with crisis and fever should be evaluated with appropriate chest imaging and cultures for infections, particularly bronchopulmonary. Aggressive respiratory treatment may reduce prolonged complications of atelectasis and pneumonia, and shorten periods of mechanical ventilation and intensive care.

Because Clostridium difficile enterocolitis is a complication of broad-spectrum antibiotic therapy, caution regarding antibiotic treatment should be exercised in the absence of documented infection. Medications that may increase myasthenic weakness (Table 1) should be discontinued and avoided.

Weaning Criteria

After patients exhibit a clear trend of improved respiratory muscle strength (i.e., negative inspiratory force greater than 20 cm H2O, positive expiratory force greater than 40 cm H2O, vital capacity greater than 10 mL/kg), weaning trials should begin. The initial goal should be to eliminate mandatory ventilations, then to reduce the amount of pressure support by about 2 cm H2O every 3 hours, as tolerated.

The weaning trial should end if patients develop signs of respiratory fatigue, including shallow, rapid respirations, diaphoresis, tachycardia, or agitation. Intubated myasthenic patients with significant residual bulbar weakness may exhibit favorable respiratory parameters (vital capacity, negative inspiratory force, positive expiratory force) but retain the potential for significant upper airway dysfunction when the stenting effect of the nasotracheal or orotracheal tube ends upon extubation. 

For this reason, clinical assessment of surrogate bulbar muscles is as important as respiratory parameters. It has been proposed that extubation can be attempted when patients are breathing comfortably, do not become fatigued, have a force vital capacity ≥ 15 mL/kg, and have a negative inspiratory force of ≥ -20 cm H2O.

A recent study from the Mayo Clinic found that male gender, previous crisis, atelectasis, and intubation for more than 10 days were all associated with failure to extubate. Reintubation after extubation is relatively common following crisis. In the Mayo Clinic study, 26% of extubated MG patients required reintubation. In these patients, the need for reintubation could be predicted based on lower pH and vital capacities at the time of extubation, BiPAP use after extubation, and atelectasis. In another series, extubation failure occurred 27% of the time. Median time to reintubation was 36 hours. Older age, atelectasis, and pneumonia were associated with extubation failure.

Perioperative Care

Myasthenic crises may occur in the context of surgical procedures and manifest as prolonged postoperative intubation. Prior to the common use of preoperative PEX, for example, nearly one-third of myasthenic patients undergoing transsternal thymectomy required supported ventilation for 3 days or more postoperatively. 

Risk factors for postsurgical (especially post-thymectomy) extended ventilation vary among case series. This is due, in part, to different pre- and perioperative management, surgical techniques, and MG disease severities. Taken together, however, studies indicate that poor preoperative respiratory condition (e.g., pulmonary function test performance) and disease (e.g., bulbar) status signify increased risk for extended ventilation.

Preoperative PEX in patients with bulbar and generalized myasthenia has reduced postoperative time on mechanical ventilation and in the intensive care unit. 

In a study of thymectomy patients with an undetectable level of myasthenic weakness, PEX treatment prior to surgery eliminated the need for postoperative ventilation or reintubation and reduced the mean length of hospital stay to 5 days.

IVIg has also been used to prepare patients for thymectomy, although the time to maximal response varies (range 3 to 19 days). 

To prevent delayed postoperative extubation or reintubation, PEX (or IVIg) should be performed in patients with respiratory, bulbar, or generalized weakness prior to surgery. For patients who are poor PEX candidates due to difficult vascular access, IVIg may achieve a similar improvement in strength. When in doubt, preoperative pulmonary function testing may help document the function of respiratory and upper airway muscles. This author typically performs 3 to 5 preoperative PEX treatments in patients with bulbar or generalized weakness, or with abnormal pulmonary function studies relating to MG.

The last PEX should ideally be performed 24 to 48 hours prior to surgery to allow for repletion of coagulation factors and more time for the treatment effects of PEX to take hold. Cholinesterase inhibitors should be tapered concurrently so that true myasthenic weakness is not masked and the risk for cardiac arrhythmias relat-
ing to vagal effects is minimized.\textsuperscript{21} With adequate preoperative PEX preparation, use of cholinesterase inhibitors and associated cholinergic risks may be eliminated. Post-thymectomy pain control and ventilatory function may be improved by administration of epidural morphine.\textsuperscript{26}

A number of anesthetics-related considerations are specific to MG. In brief, MG patients generally demonstrate relative resistance to depolarizing neuromuscular blockers (e.g., succinylcholine) and sensitivity to nondepolarizing neuromuscular blockers (e.g., vecuronium, atracurium).\textsuperscript{5,13,25} Long-acting nondepolarizing muscle relaxants, such as pancuronium should be avoided.\textsuperscript{1,13} Many inhaled anesthetic agents, such as isoflurane and sevoflurane, cause neuromuscular junction depression that can magnify weakness in patients with MG.\textsuperscript{1,30} Asymptomatic MG patients (e.g., in remission) can also demonstrate sensitivity to nondepolarizing agents and volatile anesthetics.\textsuperscript{13,30}

**SUMMARY**

The outlook for myasthenic patients experiencing crisis has improved markedly over the past half century. With timely recognition, respiratory support, and appropriate immunotherapy, those experiencing crisis or undergoing surgical procedures should incur minimal morbidity and mortality.\textsuperscript{23}

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Critical Illness Polyneuropathy and Critical Illness Myopathy

Shawn J. Bird, MD
Department of Neurology
Director, Electromyography and Neurodiagnostic Labs
University of Pennsylvania
Philadelphia, Pennsylvania

INTRODUCTION

The development of severe, acquired neuromuscular (NM) weakness is common in the intensive care unit (ICU). The two syndromes that account for the vast majority of cases of acquired weakness in the ICU are critical illness polyneuropathy (CIP) and an acute myopathy, critical illness myopathy (CIM). These disorders contribute significantly to prolonged ventilator dependence, as well increased morbidity, costs, and persistent neurologic deficits. The mean increase in ventilator days is 11.6 days in a patient with one of these disorders as compared to those without CIP or CIM.13

There are numerous potential causes of NM weakness in the ICU. They are generally separated into disorders that produce weakness severe enough to result in ICU care, such as myasthenia gravis or the Guillain-Barré syndrome. These disorders should be differentiated from disorders that develop as a consequence of critical illness, CIP, and CIM. In the ICU setting, considerations of acquired weakness should also include severe hypokalemia, hypermagnesemia, or prolonged NM blockade. The latter should be considered in those who have received nondepolarizing NM blocking agents, particularly if there is renal or hepatic disease where the active metabolites may persist.4

INCIDENCE AND RISK FACTORS

In general, the incidence of CIP and/or CIM appears to be about 50% in patients who are critically ill in the ICU for more than a week.14,15,19,23,27,31 This has been demonstrated in small, single-site prospective studies, as well as larger multicenter studies. Khan and colleagues recently conducted a prospective cohort study of patients with severe sepsis in the ICU.18 Twenty patients survived the analysis period and half (50%) of those developed CIP, CIM, or features of both, most by day 14 of illness. Of those affected, 10% were found to have CIP, 10% had CIM, and 80% had both.

Stevens and colleagues performed a systematic review of 24 studies (19 prospective) of critically ill patients who developed CIP and/or CIM.27 Most of these studies avoided the problem of distinguishing between the two disorders (see below) by combining them as an endpoint. Of the total 1421 patients included in the studies, 655 (46%) developed CIP, CIM, or both.

Three large prospective studies (61 to 95 patients each) have examined risk factors in critically ill patients for the development of NM weakness.2,14,15 The studies concur that measures of illness severity (Acute Physiology and Chronic Health Evaluation (APACHE) III score, presence of systemic inflammatory response syndrome [SIRS], or organ failure assessment scores) correlate with the development of CIP/CIM. The likelihood of developing CIP and/or CIM is strongly influenced by the severity of illness. For those with a high APACHE III score (>85) and those with the presence of sepsis at the time of study entry (day four of mechanical ventilation), the probability of developing CIP/CIM by 30 days was 72%. This compares to only 8% in patients with low APACHE III scores (<70) and no sepsis.15 This is almost a 10-fold higher risk in severely ill patients.

The causative association between high-dose corticosteroids, nondepolarizing NM blocking agents (NMBAs), and sedative drugs like propofol with acquired ICU weakness, particularly for CIM, is likely but not established. The first reports of CIM were in patients with status asthmaticus treated with high dose corticosteroids and NMBAs. Many of the early reports of critically ill patients with
severe CIM emphasized the prodromal use of corticosteroids and NMBAs. However, the results from prospective trials have been inconsistent. Of the reports that detailed this information, there was no significant univariate association with corticosteroids, NMBAs, midazolam, or aminoglycosides. Multivariable analysis identified a relationship between corticosteroids and CIP/CIM in one of the two studies that addressed this. In this study, the use of corticosteroids was a significant risk factor (Operations CIM in one of the two studies that addressed this. The studies that did not show an association were limited, due to the relatively small number of patients included that had received substantial doses of corticosteroids and/or NMBAs.

DIFFERENTIATING CIP AND CIM

There is a large cohort of patients in the ICU who have clinical and electrodiagnostic (EDX) features common to both disorders. These patients are not as easily classified as purely CIP or CIM. The clinical presentation of both disorders is dominated by limb weakness that develops in the ICU, usually accompanied by a delay in weaning the patient from mechanical ventilation.

On electrophysiologic examination, one typically finds features common to both disorders. This includes reduced compound muscle action potential (CMAP) amplitudes on nerve conduction studies (NCSs) and the presence of fibrillation potentials on needle electromyography (EMG) examination. Sensory NCSs are often hampered by technical factors (limb edema and electrical noise from the ICU equipment), or the sensory responses may be low amplitude due to preexisting neuropathies. Furthermore, the assessment of motor unit action potential (MUAP) morphology and recruitment is often limited by the patient's encephalopathy or sedation. Direct muscle stimulation and measures of the CMAP duration may be helpful in identifying CIM, but specific diagnostic criteria for these techniques have not been formally established. Of course, establishing the presence of CIM by direct muscle stimulation or prolonged CMAP amplitudes does not address the presence or absence of CIP. Despite the limitations in differentiating CIM from CIP, suggested criteria have been proposed (Tables 1 and 2).

In addition to the technical considerations that may limit these studies, the risk factors for the two disorders overlap and many patients have a variable combination of both disorders. Nonetheless, the recognition that the cause of acquired limb weakness and failure to wean in the ICU is due to CIP, CIM, or a combination of both, is helpful to the ICU staff.

CIP

A sensory motor axonal neuropathy commonly develops in the ICU. This was first described by Bolton and colleagues who gave it the name critical illness polyneuropathy, or CIP. They described a cohort of patients who, during a period of critical illness with sepsis and multiorgan failure, developed a severe sensory motor neuropathy. CIP was convincingly shown to be a distal sensory and motor axonal neuropathy that could be differentiated from the Guillain-Barré syndrome on electrophysiologic and morphologic studies. The clinical, electrophysiologic, and pathologic features have been detailed by Bolton and colleagues. In the setting of critical illness, these characteristics define a distinctive form of acute polyneuropathy.

Clinical features

The clinical features of CIP are similar to other length dependent neuropathies with distally predominant limb weakness and reduced reflexes. Difficulty weaning the patient from mechanical ventilation due to phrenic nerve involvement is common, and is often the first recognized manifestation of CIP. Muscle atrophy isn’t usually present until the second or third month of illness, and it parallels the degree of axonal loss. Sensory loss is usually present distally, but is difficult to demonstrate. These patients often have coexistent septic encephalopathy or are sedated in the ICU, limiting the sensory examination that is dependent upon patient responses. Cranial nerve involvement in CIP is rare and should suggest the presence of another NM disorder.

An early, illustrative prospective study detailed 43 ICU patients who had sepsis and multiple organ failure. The patients were in the ICU for a mean of 28 days when evaluated and diagnosed with septic encephalopathy. Thirty-five percent had clinical findings consistent with neuropathy, defined as distal weakness and hyporeflexia, or as an inability to wean from the respirator. More than half (70%) had electrophysiologic evidence of an axonal neuropathy. Only half of those patients survived the ICU stay. Of

<table>
<thead>
<tr>
<th>Table 1 Suggested diagnostic criteria for critical illness polyneuropathy</th>
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<td>1. The patient is critically ill (sepsis and multi organ failure, SIRS)</td>
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<tr>
<td>2. Difficulty weaning the patient from mechanical ventilator support after non neuromuscular causes, such as cardiac and pulmonary disease, have been excluded</td>
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<td>3. Possible limb weakness</td>
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<tr>
<td>4. Electrophysiologic evidence of an axonal sensory and motor neuropathy</td>
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<tr>
<td>5. Under the appropriate clinical circumstances, other causes of acute neuropathy should be excluded (i.e., porphyria, acute massive intoxications from arsenic or thallium, fulminant vasculitis, etc.)</td>
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SIRS = systemic inflammatory response syndrome
the survivors, the course of recovery followed that expected of an acute axonal neuropathy.

The prognosis for recovery from CIP is variable, although it is good for most patients. As with other acute nerve injuries, recovery depends on the severity of axonal loss and the distance over which nerve regeneration must occur. Patients who have had only mild to moderate axonal loss recovered fully over months as a result of collateral sprouting from remaining motor neurons. Those with severe axonal loss due to CIP may take longer to recover. In these patients, permanent distal sensory and motor deficits may occur, although deficits severe enough to preclude ambulation are uncommon.31,32

Electrophysiologic Features

Electrophysiologic studies of CIP are those of an axonal neuropathy.7,9,10,32,33 NCSs are characterized by reduced sensory and motor response amplitudes. There are no features that suggest demyelination. In general, conduction velocities and distal motor latencies are not significantly affected. Repetitive nerve stimulation studies of NM transmission are normal, unless there is persistent pharmacologic NM blockade. Needle EMG examination of limb muscle is often notable for abnormal spontaneous activity (fibrillation potentials and positive sharp waves) with the muscle at rest. The degree of abnormal spontaneous activity varies from nothing detectable to profuse. With voluntary muscle activation of significantly weak muscles, MUAPs are recruited with an increased recruitment ratio. These needle EMG findings are consistent with acute denervation.

In those with severe CIP, phrenic NCSs are often absent and needle EMG examination of the diaphragm can demonstrate denervation.32

Pathologic Features and Pathophysiology

Sural nerve biopsy and postmortem autopsy studies in patients with CIP show features of an acute axonal neuropathy. The pathology is consistent with axonal degeneration of both sensory and motor nerve fibers, with no evidence of significant inflammation or of primary demyelination.7,8,33

The pathogenesis of CIP is uncertain. Prospective studies have not supported a causative role of pharmacologic agents.27 No specific toxin, infectious agents, or nutritional deficiencies have been identified in CIP. Cytokines and free radicals associated with SIRS may adversely affect the nerve microcirculation, producing endoneurial hypoxia and distal axonal degeneration.7 This view is supported by the finding that critically ill patients with high APACHE III scores and SIRS are most prone to the development of CIP.

Sepsis activates humoral responses locally in tissues as antigen presenting cells that produce pro-inflammatory cytokines such as tumor necrosis factor, interleukin1, and free radicals. These interact with adhesion molecules on platelets and endothelial cells producing platelet fibrin aggregates that reduce capillary flow. Cytokines released in sepsis have histamine like effects that increase microvascular permeability and produce endoneurial edema. This may result in endoneurial hypoxia. In addition, an increase in local tissue nitric oxide may cause arteriolar dilatation, further reducing capillary flow. The microvascular structures of nerve lack auto regulation, which may make it particularly vulnerable to deleterious effects.7

CIM

Clinical Features

As with CIP, the clinical presentation of CIM is that of limb and respiratory muscle weakness that develops acutely, but is often difficult to recognize early in the course of disease due to coexistent encephalopathy, sedation, or both. The weakness varies from mild to complete quadriplegia. The weakness is not in a strictly length related pattern where distal muscles are weakest, a pattern typical of CIP and most neuropathies. In patients with CIM, there is usually as much proximal limb weakness as there is distal.
Respiratory muscles are frequently involved, delaying weaning from mechanical ventilation. Failure to wean from mechanical ventilation may be the first recognized manifestation. Neck flexor or facial muscle weakness may be present, but the presence of ophthalmoparesis should suggest the existence of another disorder. Sensation is spared, but often cannot be clinically evaluated in an encephalopathic, sedated, and intubated patient. As with other myopathies, reflexes are decreased in parallel with the decrease in strength.

### Laboratory and Pathologic Features

The serum creatine kinase (CK) is elevated in less than half of the reported patients, and is usually only mild. One prospective study in patients with severe sepsis found the mean CK at day 7 was 365 (range 128 to 1397; normal < 250).

A spectrum of pathological findings, mostly such nonspecific abnormalities such as myofiber size variability or atrophy (especially of type 2 fibers), are found in CIM. Lymphocytic inflammation and significant muscle fiber necrosis is not seen. Muscle biopsy may show a characteristic patchy loss of myosin thick filaments. This is the hallmark pathologic finding of CIM and has led some to call this disorder "thick filament myopathy." This characteristic pathologic finding of myosin loss can be seen in up to 50% of those with CIM. Even though the diagnosis of CIM may be strongly supported by such pathological findings, muscle biopsy is invasive and is not routinely performed for diagnostic confirmation.

### Electrophysiology

Motor NCSs in patients with CIM differ from those found in most myopathies. The motor response CMAP amplitudes are reduced, or even absent, when recording from distal limb muscles. The motor response amplitudes generally increase during clinical recovery of strength. In many patients, the CMAP durations are abnormally prolonged (see below). There is preservation of sensory nerve action potential amplitudes, unless there is coexistent CIP or preexistent neuropathy. Sensory and motor response conduction velocities, as well as distal motor and F-wave latencies, are normal. Repetitive nerve stimulation studies do not show an abnormality of NM transmission.

On EMG examination, abnormal spontaneous activity in the form of fibrillation potentials and positive sharp waves, is variably present. It is not infrequently seen, but is generally sparse. Reduced insertional activity may be seen in patients with severe weakness and markedly reduced CMAP amplitudes, another feature of reduced muscle membrane inexcitability. With voluntary muscle activation of significantly weak muscles, one generally sees small amplitude, short duration MUAPs with an early recruitment pattern.

### Muscle Membrane Electrical Inexcitability - Direct Muscle Stimulation

There are several features that are unique to this CIM. The myopathy develops in the setting of critical illness and there are features that are unlike most other myopathies. The presence of severe weakness (often quadriplegia) are absent or markedly reduced. CMAP amplitudes are difficult to reconcile with normal CK values and minimally abnormal muscle pathology. An acquired disorder of muscle membrane inexcitability would fit these observations.

There are several lines of evidence indicating that muscle membrane inexcitability plays a role in CIM. These include:

1. Absent or reduced responses with direct electrical stimulation of muscle.
2. Increased CMAP durations.
3. Muscle fiber conduction velocity is slowed.
4. All features improve with clinical recovery.
5. Animal models of these disorders.

Muscle membrane inexcitability can be demonstrated by direct stimulation of muscle in patients with severe CIM. In contrast, muscle is easily excitable by this technique in patients with CIP and other acute and chronic neuropathies. The muscles most commonly studied are the tibialis anterior (TA) and the biceps. In this technique, the peroneal nerve is stimulated at the fibular head and the CMAP is recorded from the TA muscle. The stimulating and recording locations for the nerve evoked CMAP are the same as those used with routine NCS techniques. However, the active recording electrodes are either a 12 mm subcutaneous stainless steel electrode, or a concentric needle EMG electrode inserted near the end-plate. Most favor the latter electrode. The direct muscle stimulation CMAP is performed with the same recording locations and electrodes. The muscle is directly stimulated with a monopolar EMG electrode 2 to 5 cm distal to the active recording electrode away from the endplate region.

This is a semi-quantitative technique without well established normative values. Using this technique, an absent direct muscle stimulation CMAP is strongly supportive of CIM. When a direct muscle stimulation CMAP can be obtained, an amplitude from the tibialis anterior of less than 2 mV with subcutaneous recording electrodes, or 3 mV with a concentric needle recording electrode is also consistent with CIM (Bird, personal communication, 2009). This technique is not helpful in differentiating mild or moderate myopathy from normal, where there is a relatively preserved direct muscle stimulation CMAP amplitude. Serial studies using this technique in patients with CIM have shown recovery of muscle membrane excitability as strength improves and an increase in CMAP rise.

### Prolonged CMAP duration

An interesting observation in many patients with CIM is that the CMAP duration is significantly increased, concomitant with a drop in amplitude. During recovery of strength, the CMAP amplitude...
increases and the CMAP duration shortens, with no change in the distal motor latency.\(^6\)

Park and colleagues\(^26\) reported the first series detailing prolonged CMAP durations in clinically defined CIM. This retrospective review of nine patients reported a prolonged distal CMAP duration in all of the motor nerves studied. For example, the median nerve distal CMAP durations ranged from 9.2 to 21.4 ms (normal < 7.2 ms). A larger study of 32 patients with CIM also noted prolonged CMAP durations.\(^1\) They found a mean median nerve CMAP duration of 9.0 ms. This was abnormal (normal > 6.8 ms) in 72% of nerves. Similarly, the mean tibial CMAP duration was 9.4 ms. This was abnormal (normal > 6.2 ms) in 63% of the nerves studied. However, in this study, only the medial and tibial motor nerves were studied.

Increased CMAP durations are frequently seen in demyelinating neuropathies as well.\(^29\) However, both groups\(^1,26\) have indicated that there are important differences in the prolonged CMAP durations seen in CIM and demyelinating neuropathies, such as CIDP. In CIM, the durations of the distal and proximal CMAP are the same. In many patients with demyelinating neuropathy, the CMAP with proximal stimulation is considerably longer than the distal CMAP, reflecting abnormal proximal to distal temporal dispersion. In CIM, other features of demyelination are also absent. The distal motor latencies are normal and the conduction velocities are normal or minimally reduced (not less than 80% lower limit of normal).

**Pathophysiology**

The mechanism involved in the development of CIM is likely multifactorial.\(^4,5\) The use of nondepolarizing NM blocking agents and corticosteroids may result in myosin loss and changes in other structural proteins. Inactivity and sepsis can increase the ubiquitin proteasomal mediated proteolysis induced by corticosteroids. The up regulation of corticotosteroïd receptors due to immobilization, sedation, or NMBAs may increase muscle fiber susceptibility to the myotoxic effects of steroids. Sepsis may alter the muscle bioenergetic machinery with unknown deleterious effects. Impaired muscle membrane excitability probably plays a more significant role in producing weakness in the acute stage. Muscle membrane inexcitability is likely due to abnormal sodium channel inactivation.\(^28\)

**REFERENCES**


