Neuralgic amyotrophy (Parsonage-Turner syndrome or brachial plexus neuritis) is an uncommon syndrome whose cause is unknown. The suprascapular and axillary nerves and corresponding muscles are affected most frequently. The disorder exhibits a broad range of clinical manifestations, and patients frequently present to physicians of different subspecialties. Accurate diagnosis can be challenging and requires a thorough history and physical examination. Nerve conduction velocity and imaging studies assist in the evaluation. Treatment consists of symptomatic management. Symptoms can persist for more than a year, but most patients note resolution of symptoms over time.

Neuralgic amyotrophy (NA) was first described by Dreschfeld in 1887 and clinically defined by Parsonage and Turner in a cohort of 136 patients in 1948. It is typically characterized by attacks of neuropathic pain and subsequent patchy paresis in the upper extremity, occasionally associated with scapular winging; however, it is a syndrome with a broad range of clinical manifestations. Although this clinical condition is commonly known as Parsonage-Turner syndrome, many other eponyms exist: acute brachial neuropathy, acute brachial plexitis, Kiloh-Nevin syndrome, brachial plexus neuropathy, idiopathic brachial plexopathy, idiopathic brachial neuritis, localized neuritis of the shoulder girdle, multiple neuritis of the shoulder girdle, paralytic brachial neuritis, serum neuritis, shoulder girdle neuritis, and shoulder girdle syndrome.

The reported occurrence of NA ranges between 1.6 and 3 cases per 100,000 annually, although actual incidence is likely to be at least 20 to 30 cases per 100,000 individuals secondary to underdiagnosis and recognition. The hereditary form (HNA) is much rarer, with about 200 families known worldwide. Cases have been reported in patients as young as 3 months and as old as 81 years, but the highest incidence is between the third and seventh decades of life. Males are predominantly affected; ratios range from 1.5:1 to 11.5:1.

The cause of NA is still unknown, but autoimmune, genetic, infectious,
Table 1

Antecedent Events and Associated Illnesses Identified in Patients With Neuralgic Amyotrophy

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Virus: Epstein-Barr, varicella-zoster, Coxsackie B, parvovirus B19, cytomegalovirus, Mumps, Variola major and V minor (smallpox), human immunodeficiency virus</td>
</tr>
<tr>
<td></td>
<td>Bacteria: Leptospira, Mycobacterium tuberculosis, Yersinia, Salmonella, Borrelia burgdorferi</td>
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<tr>
<td>Immunization</td>
<td>Tetanus, hepatitis B</td>
</tr>
<tr>
<td>Stress</td>
<td>Perioperative, peripartum, exercise, burn</td>
</tr>
<tr>
<td>Drugs</td>
<td>Abacavir, streptokinase, heroin, infliximab</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Interscalene block, surgery, irradiation</td>
</tr>
<tr>
<td>Other</td>
<td>Giant cell arteritis, lymphoma, Guillain-Barré syndrome, rheumatoid arthritis, diabetes mellitus, history of allergies, polyarteritis, hepatitis</td>
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</table>

Patients typically present without constitutional symptoms but report a sudden onset of severe, unrelenting shoulder pain that radiates to the arm or neck and lasts for hours to weeks. The pain frequently can awaken patients from sleep and may be exacerbated by shoulder and elbow motion. As the pain subsides, a flaccid paralysis with muscle weakness, muscle atrophy, and sensory loss of the shoulder girdle develops. Bilateral brachial plexus involvement occurs in 10% to 30% of patients (16% simultaneously), although symptoms are usually asymmetric. Involvement of the contralateral side is often found with electromyography rather than with clinical examination. Additionally, patients can have autonomic dysfunction and (rarely) minor dysmorphic features. It is important to note that NA can differentially affect various nerves and muscles throughout the body in no consistent combination, time course, or sequence. The presentation may not coincide with a single or specific neurologic source.

Patients with HNA, in contrast to patients with INA, have higher incidences of recurrent episodes (average, 3.5 versus 1.5, respectively). These episodes may begin in childhood or adolescence (average age, 28.4 versus 41.3 years, respectively). Patients with HNA also have more frequent involvement of nerves out-
side the brachial plexus (average, 55.8% of patients versus 17.3%, respectively) and more severe maximum paresis, with a subsequently poorer functional outcome.6 Patients with HNA can also present with dysmorphic features, including hypotelorism (ie, abnormally small distance between the eyes), cleft palate, short stature, unusual skin folds, and facial asymmetry.3 This diagnosis should be considered in all younger patients regardless of family history.

The most common nerves affected in NA are the suprascapular, axillary, musculocutaneous, long thoracic, and radial. Other areas of involvement have included cervical roots, the anterior interosseous and dorsal interosseous nerves, and the lateral antebrachial cutaneous nerve.10 Affected nerves remote from the brachial plexus include the lumbosacral plexus, phrenic, recurrent laryngeal, and lower cranial (ie, VII, IX, X, XI, XII).3,5,6,31 Clinical and electrophysiologic findings have suggested the involvement of axonal lesions of the peripheral nerves, occurring singly (mononeuropathy) or in various combinations (mononeuropathy multiplex), which is reported in 75% of cases.31 Isolated involvement of a nerve branch to an individual muscle in NA is uncommon. Single phrenic nerve22,32 and anterior interosseous nerve involvement14 with focal amyotrophy have been reported. The only report of isolated involvement of a fascicle of the musculocutaneous nerve to the brachialis muscle was by Watson et al.35

Pain is the first symptom noted in 90% of cases; in approximately one in five patients, pain is episodic in nature.6 Phases of pain can exist, starting from continuous, converting to neuropathic, and subsequently becoming musculoskeletal-type pain. The pain in males, compared with that in females, initially tends to last longer (45 versus 23 days, respectively).6 Females more frequently have involvement of the middle and lower brachial plexus (23.1% versus 10.5%, respectively) and have worse functional outcomes. In general, weakness develops within 24 hours in approximately 33% of patients, within 2 weeks in 70% of patients, and within 1 month in 85% of patients.26 The most common pattern is weakness affecting the distribution of the upper part of the brachial plexus, with or without involvement of the long thoracic nerve. The muscles commonly affected include the infraspinatus, supraspinatus, serratus anterior, biceps, deltoid, and triceps.3 In 6% to 41% of patients, weakness is limited to the muscles supplied by a single nerve.20,36

Sensory changes occur in 78% of patients, with paresthesia and hypesthesia being the most common.5,6 The most common sites of sensory loss are over the deltoid, the lateral aspect of the upper arm, and the radial aspect of the forearm.29 These symptoms may go unnoticed by the patient because of the overlying pain and weakness. Although NA typically affects motor nerves, sensory dysfunction can occur, albeit rarely, in isolation.3 In pure sensory NA, the lateral antebrachial cutaneous, median, and medial antebrachial cutaneous nerves are most often affected.37,38

In approximately 15% of 246 patients with NA, signs of involvement of the peripheral autonomic nervous system, such as vegetative and trophic skin changes, edema in the involved extremity at the onset of the attack, temperature dysregulation, increased sweating, and changes in nail or hair growth, were documented.6 Sathasivam et al37 reported that one patient with HNA had a persistent Horner syndrome combined with involvement of the brachial plexus.

### Differential Diagnosis

<table>
<thead>
<tr>
<th>Differential Diagnosis for Neuralgic Amyotrophy</th>
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<tbody>
<tr>
<td><strong>Neurologic</strong></td>
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<tr>
<td><strong>Orthopaedic</strong></td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
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</tbody>
</table>

neuron diseases and peripheral nerve compression less likely,27,39 and the pattern of motor loss often suggests peripheral nerve rather than nerve root involvement.27 Similarly, in NA, sensory changes are often peripheral rather than dermatomal in distribution. In a patient with cervical radiculopathy, a meticulous neurologic examination can correlate nerve root pathology to the symptoms and signs. As the patient develops progressive weakness while pain resolves, the diagnosis of classic NA can be distinguished from a diagnosis of brachial plexus injury secondary to traumatic or iatrogenic reasons.

**Diagnosis**

Understanding the chronology of NA is critical because the diagnosis is clinical, supported by imaging and findings on electromyography (EMG). A thorough history can identify previous infections, surgeries, injuries, and medical conditions that may be suggestive for conditions other than NA. Patients should be questioned regarding the onset of symptoms, the severity and location of the pain, and alleviating factors. The distribution of pain in the extremity (or elsewhere) should be ascertained; the radiation of the pain, if present, may indicate the underlying nerve root or peripheral nerve involvement. In addition, a complete physical examination can help exclude other orthopaedic diagnoses as well as medical conditions such as pulmonary embolism and diaphragmatic paralysis. In some instances, a Valsalva maneuver results in less aggravation of pain in patients with NA than it does in patients with cervical radiculopathy. Dermatomal sensory assessment and (in our experience) two-point discrimination can help to differentiate NA from other neurologic conditions and from a possible cervical disk herniation. The skin and extremities should be evaluated for trophic skin changes or other abnormal findings that could indicate underlying neurologic involvement.

Shoulder radiographs should be obtained and evaluated for calcific tendinitis, another diagnosis that can present with severe, incapacitating pain. Chest radiographs may reveal a diaphragmatic palsy or Pancoast tumor (especially with Horner syndrome), if present.7 MRI has been shown to be sensitive for detecting signal abnormalities in the muscles of the shoulder girdle of patients with NA.40 T2-weighted images demonstrate early changes resulting from edema and show diffuse high-signal intensity involving one or more muscles innervated by the brachial plexus (Figure 1). As NA progresses, an increased intramuscular T1-weighted signal suggests atrophy with fatty infiltration and can involve one or more muscle groups of the shoulder girdle.10 The supraspinatus, infraspinatus, deltoid, and teres minor muscles most commonly exhibit MRI changes, and the nerves supplying these muscles often display abnormalities on EMG.40 Other causes of high T2 signal intensity must be considered, including trauma, inflammatory disorders, rhabdomyolysis, exercise, and tumors (especially in the superior sulcus region). The distribution and clinical history, however, allow for differentiation between these entities.10

Although NA is primarily a clinical diagnosis, an EMG examination is abnormal and compatible with NA
in 96.3% of patients and thus may help confirm the diagnosis. EMG and nerve conduction testing on patients with cervical disk disease often show abnormalities in specific affected nerve roots. By contrast, EMG testing in NA reveals acute denervation, with positive sharp waves and fibrillation potentials 3 to 4 weeks after the onset of symptoms in both a peripheral nerve and nerve root distribution. Also, an EMG performed 3 to 4 months after the onset of initial symptoms may show chronic denervation and early reinnervation with polyphasic motor unit potentials. In the only study investigating pure sensory NA, Seror reported that electrodiagnostic studies demonstrated sensory nerve action potential amplitude reduction (without velocity impairment) that conformed in distribution to the impaired clinical area in all eight patients. These studies support the diagnosis of NA and/or serve to exclude a radicular problem, hereditary neuropathy with liability to pressure palsies, and multifocal motor neuropathy in painless cases. In general, the difficulties with electrophysiologic examinations include knowing which affected muscles to study and when to study them. Furthermore, motor nerve conduction studies may not be particularly informative unless the paresis is severe.

Laboratory studies can help exclude other causes of shoulder pain, but they remain largely inconclusive for the diagnosis of NA. Blood tests may reveal elevated levels of liver enzymes, positive measures of antian- glioside antibodies, or a positive antinuclear antibody test result. Examination of the cerebrospinal fluid is usually normal, although mildly elevated protein levels, slight pleocytosis, and oligoclonal bands have been reported. Blood counts and erythrocyte sedimentation rates remain normal.

**Management**

The natural history of NA is one of resolution over time, with abatement of neuropathic pain followed by gradual return of muscle strength and function. No specific treatment protocol currently exists. Anecdotal evidence and a single, uncontrolled retrospective case series show some evidence to suggest that early corticosteroid therapy may have a positive influence on pain in some patients and possibly hasten recovery in a few. The primary role of physical therapy in the early phase of the syndrome is to provide the patient with strategies to help alleviate the traction on the involved nerves, which may have an increased mechanical sensitivity because of inflammation. Patients should use the affected limb as fully as possible, avoid strength training, and adhere to physiotherapy so that biomechanical stability can be maximized. Shoulder stabilization with nonsurgical and/or surgical management has been shown to be effective in patients with instability; however, shoulder stabilization is not as well studied in the context of NA. A substantial proportion of patients experience chronic strain, pain, and fatigue as they balance between residual impairments and activities of daily living. This scenario is typical of neuromuscular disorders and consequently brings increased importance to the recognition and accurate diagnosis of concomitant shoulder pathology. In patients with known multidirectional instability based on clinical examination criteria, the clinical picture can be challenging because some component of brachial plexus irritation may be present from primary shoulder pathology. Stabilization of the shoulder in these select cases may improve the clinical scenario; however, in true cases of concomitant NA, there is likely to be residual neurologic impairment.

The acute pain of NA responds best to a combination of a long-acting nonsteroidal anti-inflammatory drug with a slow-release opiate; the increased mechanical sensitivity sometimes needs treatment with coanalgesics. The use of tricyclics and antiepileptics is not advocated because of the latency period associated with the use of these medications before the onset of benefit. Patients with positive serologic tests or a history of an infection can be treated with appropriate medications. Weakness, atrophy, and decreased range of motion can be addressed with physical therapy and rehabilitation. In one study, wasting managed nonsurgically with rehabilitation showed no difference in brachialis muscle size between both upper extremities at 14 months.

Patients should be followed at monthly intervals to assess progression in reinnervation. This can be done with electrodiagnostic studies and physical examination. A persistent Tinel sign at sites of entrapment along the course of a regenerating nerve represents halted axonal extension. It is essential to realize that denervation that persists for >1 year is unlikely to recover well; any intervention to restore function should ideally be undertaken well before this time. In general, if by 6 to 9 months there is no clear evidence of regeneration or early recovery within a nerve distribution, then nerve transfer procedures or nerve decompressions, such as ulnar nerve transposition, radial tunnel release, carpal tunnel release, and Guyon canal release, may be considered, as indicated. Furthermore, microneurolysis and decompression of the long thoracic nerve are effective in reversing scapular winging. Most recently, Pan et al surgically explored five
cases of brachial neuritis with hourglass-like constrictions in the absence of external compression of individual peripheral nerves; these authors found neurolysis to be superior to neurorrhaphy and nerve grafting. Other procedures include pectoralis major transfer for serratus anterior paralysis,\textsuperscript{41} scapular stabilization, and tendon transfers.\textsuperscript{34}

### Prognosis

The course of NA has been shown to be quite variable, with some patients showing resistance to therapy\textsuperscript{46} and others demonstrating complete recovery within a month after nonsurgical management.\textsuperscript{6} Tsairis et al\textsuperscript{29} noted excellent recovery in 36% of patients within 1 year, 75% of patients by 2 years, and 89% of patients by 3 years. A more recent study found chronic pain and persistent functional deficits in almost one third of affected patients after an average follow-up of >6 years.\textsuperscript{6}

Two thirds of patients show beginning recovery of motor function within 1 month of the onset of weakness.\textsuperscript{26} Patients with predominantly upper trunk involvement tend to have a better prognosis than do those with lower trunk involvement. In addition, in general, the duration of pain is correlated to the duration of muscle weakness. Prolonged recurrent pain with no sign of motor recovery after 3 months is associated with a poor prognosis. One study suggests that it may take as long as 8 years for patients to regain full strength.\textsuperscript{27} Seror\textsuperscript{37} showed all patients with pure sensory NA to have spontaneous improvement without serious physical disability. No relationship was found between recovery and age.\textsuperscript{6}

With regard to recurrence, at 6-year follow-up, HNA was found to have a higher rate than INA (74.1% versus 26.1%, respectively), and 12% of patients have a recurrent attack within the first year.\textsuperscript{6} These events may be less severe than the initial episode.\textsuperscript{27,29}

### References

**Evidence-based Medicine:** Levels of evidence are described in the table of contents. References 19, 25, and 31 are level III studies. The remaining references are level IV studies.

References printed in **bold type** are those published in the past 5 years.


Authors found neurolysis to be superior to neurorrhaphy and nerve grafting. Other procedures include pectoralis major transfer for serratus anterior paralysis,\textsuperscript{45} scapular stabilization, and tendon transfers.\textsuperscript{34}


