CHAPTER 27

Disorders of the Peripheral Nervous System

Hereditary Motor and Sensory Neuropathies, 1435

Hereditary Motor and Sensory Neuropathies

Hereditary motor and sensory neuropathies (HMSNs) are a group of genetically acquired progressive peripheral neuropathies (Table 27–1). The most common of this group is Charcot-Marie-Tooth disease. Dyck and Lambert classified the hereditary motor and sensory neuropathies in 1968 (Table 27–2).[53–55]

CHARCOT-MARIE-TOOTH DISEASE TYPE 1

Charcot-Marie-Tooth neuropathy type 1 (CMT-1), also known as HSMN I and II, is the most common heritable chronic demyelinating neuropathy. The overall incidence of the various forms of Charcot-Marie-Tooth disease ranges from 20 per 100,000 to 1 per 2,500.[96,154] The disease is characterized by progressive weakness and atrophy of distal musculature, depressed tendon reflexes, slowed motor nerve conduction velocity, and frequently a family history of the disorder.[22] CMT-1 usually manifests in the second decade of life, but it may become evident earlier in some patients.

Genetics. Charcot-Marie-Tooth subtypes have been identified through localization of their different genetic abnormalities.[136] There are three major forms: CMT-1 (hypertrophic demyelinating form), CMT-2 (axonal form), and CMTX. CMT-1 is inherited as an autosomal dominant trait. Genetic loci for CMT-1 have been mapped to chromosome 17 (CMT-1A), chromosome 1 (CMT-1B), and a third, unknown autosome (CMT-1C).[14,33] CMT-1A is most often associated with a duplication in chromosome 17p11.2–12, an area that codes for the peripheral myelin protein 22 (PMP 22) gene, a glycoprotein expressed in the myelin sheath of Schwann cells.[155,164,172,183,230] Patients with duplications have three copies of a normal gene, a situation producing disease by what is termed a "gene dosage" effect—too much of a normal gene.[160] CMT-1B is associated with mutations in the myelin protein zero (P0 or MPZ) gene.[89] X-linked Charcot-Marie-Tooth neuropathy (CMTX) is associated with mutations in the connexin 32 gene, which codes for connexin, a gap junction protein that enhances conduction across paranodes of the peripheral nerves.[18,23,24,174] Prenatal diagnosis using molecular genetic techniques is now available.[133,162]

Clinical Presentation. Physical examination reveals atrophy of the calves, giving a "stork's leg" appearance (Fig. 27–1). Foot deformity such as pes cavus, cavovarus, or claw toes are very common. Calluses along the lateral border of the foot, particularly over the base of the fifth metatarsal, may be present. Deep tendon reflexes are diminished to absent, with the ankle reflex disappearing before the knee reflex. Distal sensation is decreased to all modalities of sensation. Motor testing varies among patients but usually reveals diminished strength in the anterior tibialis and peroneus brevis. As the patient tries to actively dorsiflex the ankle, the metatarsophalangeal (MTP) joints of the toes extend, and the great toe may dorsiflex to augment the weak anterior tibialis. Some patients have weakness throughout all of the distal calf musculature, and those with the most severe involvement have generalized muscle weakness and are unable to walk.

Observation of the gait in patients with early Charcot-Marie-Tooth disease reveals a subtle drop foot in swing phase. As the dorsiflexors become weaker, a steppage gait develops, characterized by plantar flexion of the ankle, hyperflexion of the knee, and hyperflexion of the hip in swing phase. Often the hemipelvis also elevates during the swing phase to allow clearance of the foot, and circumduction of the leg may be present.[201]

Examination of the hand reveals intrinsic atrophy. The patient may have difficulty grasping a goniometer placed between the fingers.

A careful examination of the spine should be performed. Although Charcot-Marie-Tooth disease is the most common cause of pes cavus, spinal cord pathology such as tethered cords and lipomeningocele may manifest initially with pes cavus or cavovarus. The back should be examined for evidence of underlying spinal dysraphism such as a hairy patch, dimpling, or hemangioma. Scoliosis may be seen in teenagers with Charcot-Marie-Tooth disease but is not seen in young children, so any sign of abnormal curvature in a young child should be further evaluated with magnetic resonance imaging (MRI).

Diagnostic Evaluation. Patients who are suspected of having Charcot-Marie-Tooth disease should be referred to a neurologist for further diagnostic testing. Electromyography (EMG) and measurement of nerve conduction velocities can support the diagnosis. Electrophysiologic testing reveals

TABLE 27–1 **Dyck-Lambert Features of Hereditary Motor Sensory Neuropathies**

1. The predominant involvement is of peripheral motor neurons, with lesser involvement of peripheral sensory and peripheral autonomic neurons.
2. The disorders are inherited.
3. The disorders are slowly progressive.
4. The neurologic signs are symmetric.
5. The disorders are system degenerations in that several populations of neurons of similar structure and function are affected.
6. The pathologic features are nonfocal, and the nature of the fiber degeneration is that of axonal atrophy and degeneration.

From Dyck PJ: Inherited neuronal degeneration and atrophy affecting peripheral motor, sensory, and autonomic neurons. In Dyck PJ, Thomas PK, Lambert EH, et al (eds): Peripheral Neuropathy, 2nd ed, vol 2, pp 1600–1655. Philadelphia, WB Saunders Co, 1984.

slowing of motor nerve conduction velocities in the upper and lower extremities due to the loss of myelin (Fig. 27–2). Conduction is slowed uniformly from side to side and between different motor nerves.[114] EMG may show fibrillation due to denervation.

In occasional patients the diagnosis remains in question following electrical studies and genetic testing, and a nerve biopsy should be performed for definitive diagnosis. The sural nerve is chosen as the site of biopsy. A 1.5-cm-long segment of nerve is removed in the interval between the posterolateral border of the Achilles tendon and the lateral malleolus.[211] The nerve lies together with the lesser saphenous vein, and the two structures should not be confused when the surgeon is obtaining the biopsy specimen. Histopathologic study of sural nerve biopsy specimens from patients with CMT-1 show large "onion bulb" formations resulting from cycles of demyelination and remyelination. The myelin appears either folded or uncompacted on ultrastructural examination.[68] There is less demyelination and fewer onion bulbs in the X-linked form than in classic CMT-1 disease.[205] Muscle biopsy in CMT-1 shows scattered atrophic fibers and neuropathic degeneration.[59]

MRI and computed tomography (CT) of the spine show diffuse enlargement of the cauda equina, nerve roots, and ganglia.[37,159]

Orthopaedic Manifestations. The most common orthopaedic manifestation of Charcot-Marie-Tooth disease is pes cavovarus.[97,200,211] Patients often present to the orthopaedic surgeon for evaluation of pes cavovarus, and the diagnostic workup leads to the diagnosis. Atrophy and contracture of the intrinsic musculature of the foot lead to elevation of the longitudinal arch, contracture of the plantar fascia, increasing pressure on the metatarsal heads, and painful calluses along the lateral border of the foot and beneath the metatarsal heads (Fig. 27–3).[73] Varus of the hindfoot is present initially due to the plantar flexion of the first ray and forefoot equinus. Additionally, the posterior tibialis and peroneus longus remain strong relative to the weak peroneus brevis and anterior tibialis, leading to depression of the first ray and increased varus.[97,145] The Coleman block test, performed by having the patient stand on a block with the head of the first metatarsal hanging medially off the block, is useful in planning surgical correction of the foot deformity. When varus is due to plantar flexion of the first metatarsal, the heel will evert to neutral as the first metatarsal head drops off the block and is allowed to plantar flex (Fig. 27–4).[39] With time, the varus deformity becomes fixed and does not correct when the block test is performed.

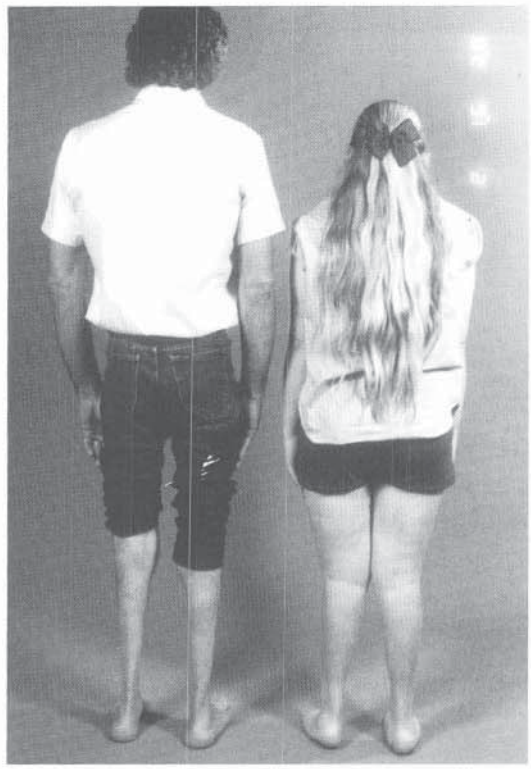
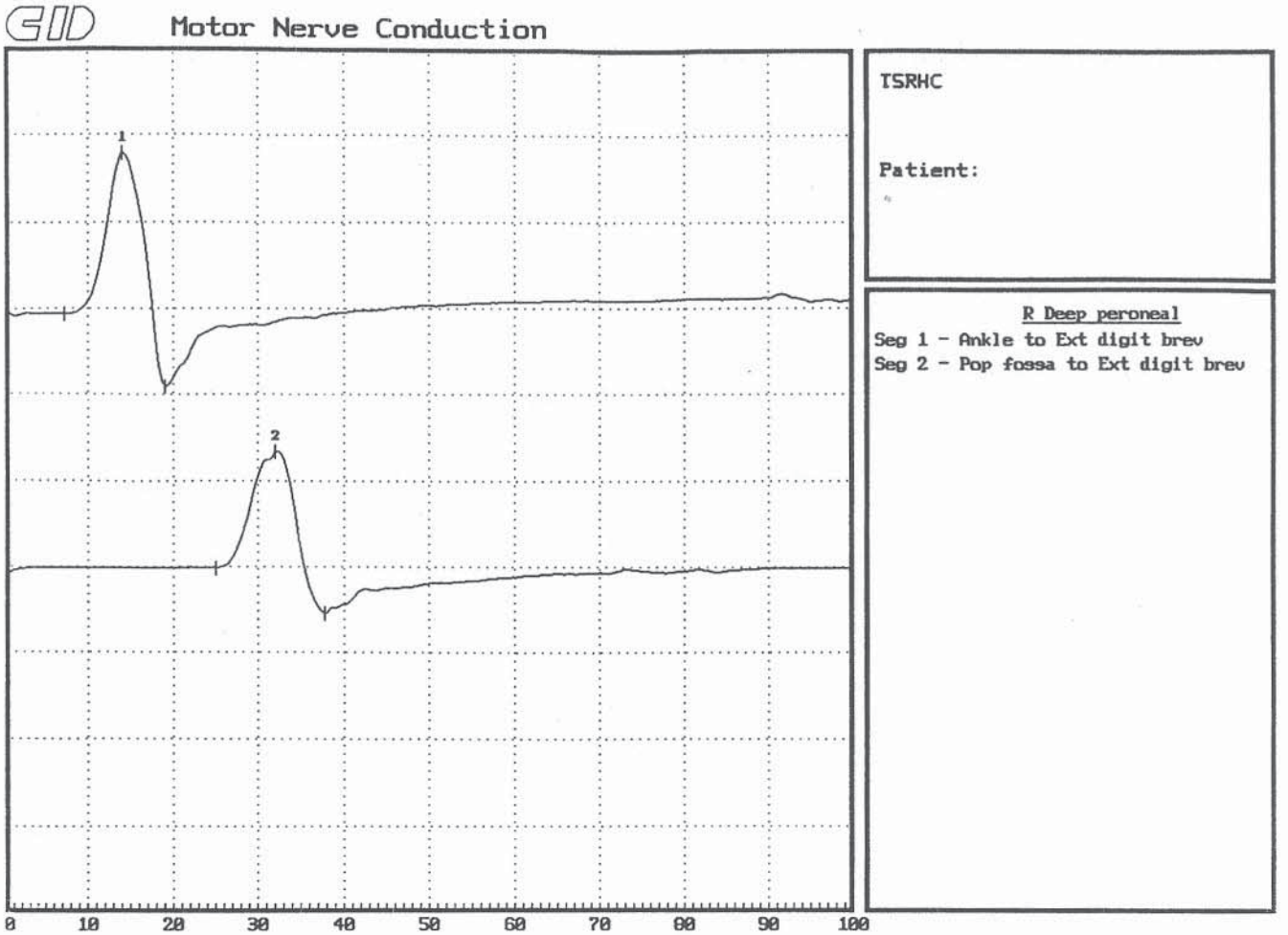


FIGURE 27–1 Father and daughter with Charcot-Marie-Tooth disease type 1. Atrophy of the calves is striking, particularly in the father.

The treatment of cavovarus foot is described in greater detail in Chapter 22, Disorders of the Foot. When addressed early in the disease in young patients, soft tissue surgery with tendon transfer may be sufficient to postpone or avoid triple arthrodesis.[152,173,198,204,213,219] Tendon transfers used in Charcot-Marie-Tooth disease include transfer of the posterior tibialis tendon to the dorsum of the foot and transfer of the peroneus longus to the peroneus brevis. The anterior tibialis tendon is not transferred, as it is usually weak in this disease. Proximal metatarsal osteotomies of either the first metatarsal alone or of multiple metatarsals corrects plantar flexion of the forefoot in patients who have flexible varus hindfeet (Fig. 27–5).[73,152,173,204,246] Care must be taken when performing a proximal first metatarsal osteotomy in a young

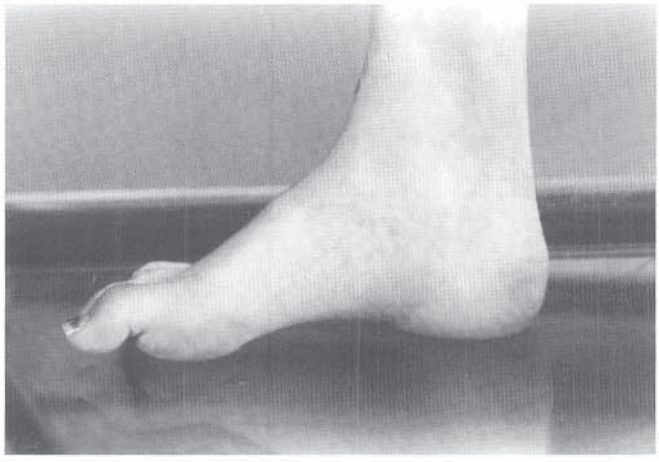
TABLE 27–2 **Classification of Hereditary Peripheral Neuropathies**

HMSN I	Charcot-Marie-Tooth disease (hypertrophic demyelinating type)
HMSN II	Charcot-Marie-Tooth disease (axonal type)
HMSN III	Dejerine-Sottas disease
HMSN IV	Refsum's disease
HMSN V	Spastic paraplegia
HMSN VI	Similar to type I, with optic atrophy
HMSN VII	Similar to type I, with retinitis pigmentosa



Seg #	Dist (mm)	Lat (ms)	CV (m/s)	NPamp (mV)	NParea (mVms)	PPamp (mV)	Scale (mV/d)	Stim1 (mA)	Stim2 (mA)	LowF (Hz)	HighF (kHz)	Temp (°C)
1		7.3	N/A	1.07	0.40	2.71	1.0	0	99	5	5	
2	331	25.0	18.7	1.35	7.11	1.90	1.0	0	99	5	5	

FIGURE 27–2 Nerve conduction velocity (NCV) measured for the deep peroneal nerve in a patient with Charcot-Marie-Tooth disease. The normal NCV is greater than 41.4 m/s. The NCV for the motor response of the deep peroneal nerve in the patient is 18.7 m/s, indicating slowing of conduction.



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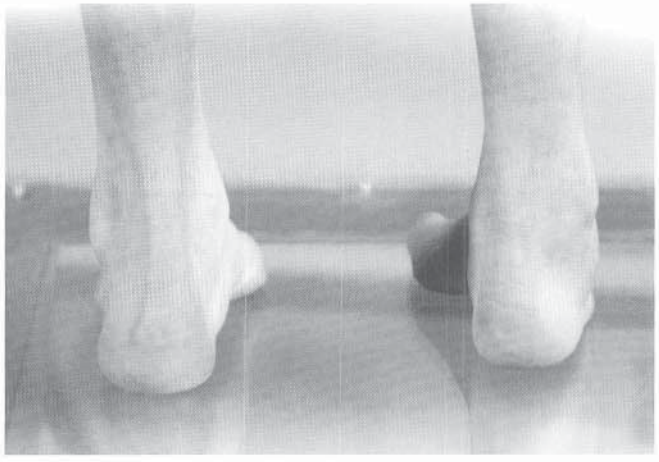

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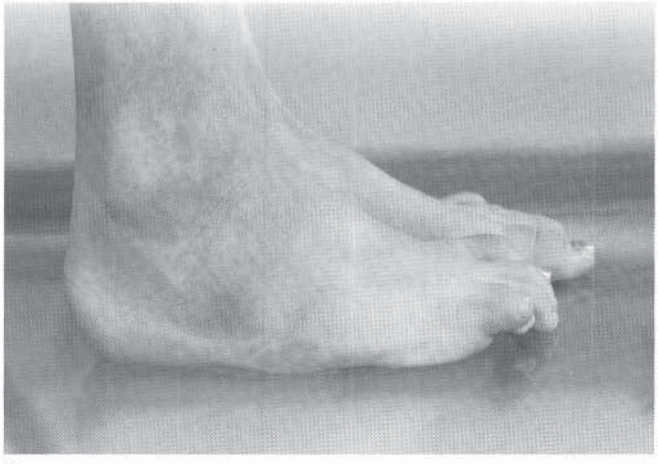

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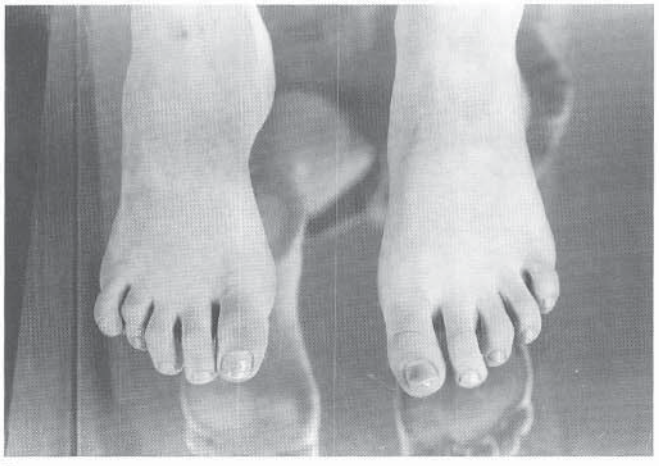

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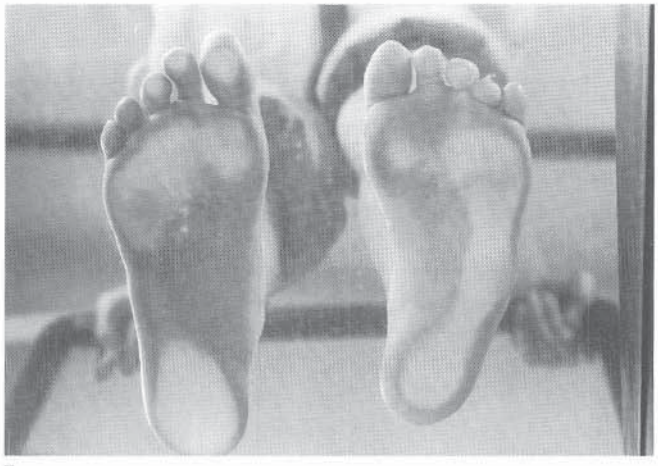

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FIGURE 27–3 Pes cavovarus in a 12-year-old girl with Charcot-Marie-Tooth disease. **A,** The longitudinal arch of the foot is elevated, and there is clawing of the great toe (hyperextension of the metatarsophalangeal joint and flexion of the interphalangeal joint). **B,** Hindfoot varus of the right foot is apparent. **C,** A callus is present over the base of the fifth metatarsal. **D,** Clawing of the lesser toes is present bilaterally. **E,** Pressure is abnormally distributed, with excess loading along the lateral border of the foot, on the first metatarsal head, and on the tips of the claw toes.

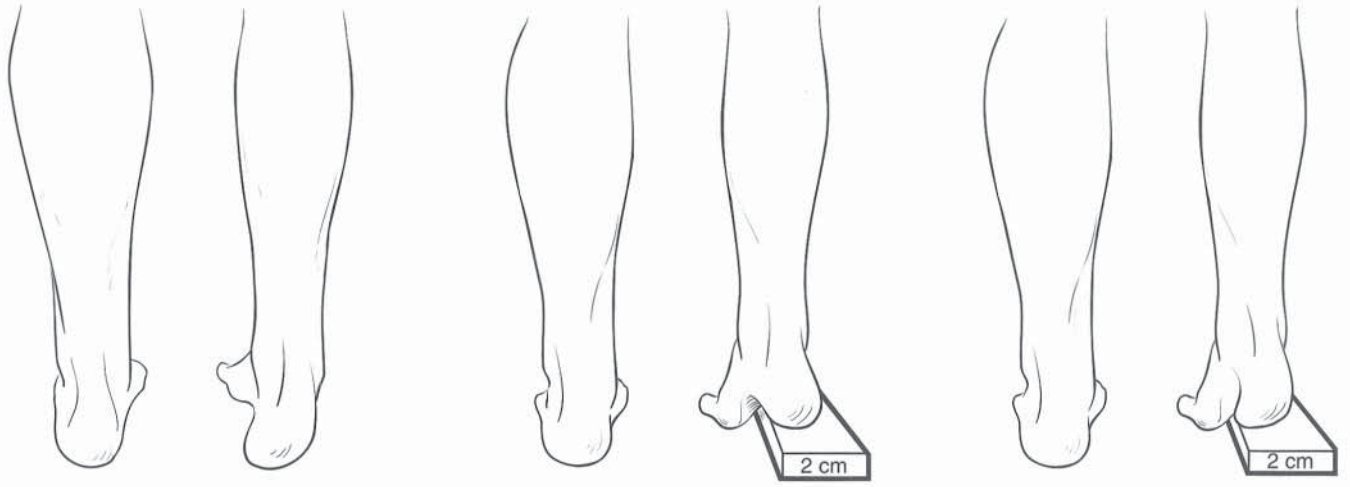
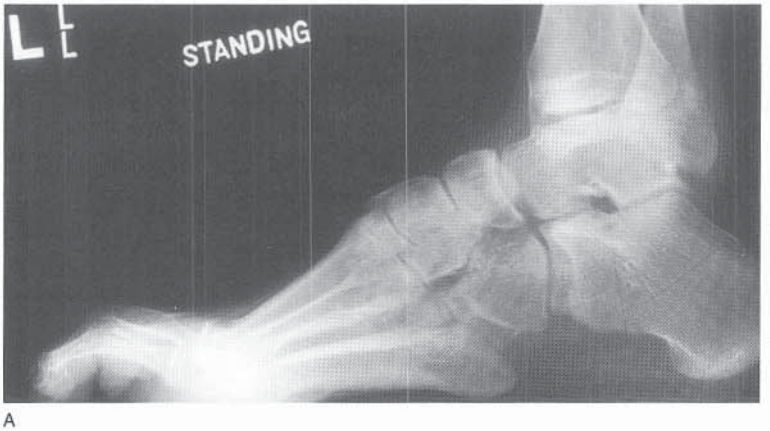


FIGURE 27–4 The Coleman block test. **A** to **C,** The heel of the foot and lateral border are placed on a wooden block, allowing the head of the first metatarsal to drop into plantar flexion. **B,** If the hindfoot varus is secondary to the tripod effect of the plantar flexed first ray, the hindfoot will correct to neutral or valgus alignment. **C,** If the hindfoot varus is rigid, it will not correct.



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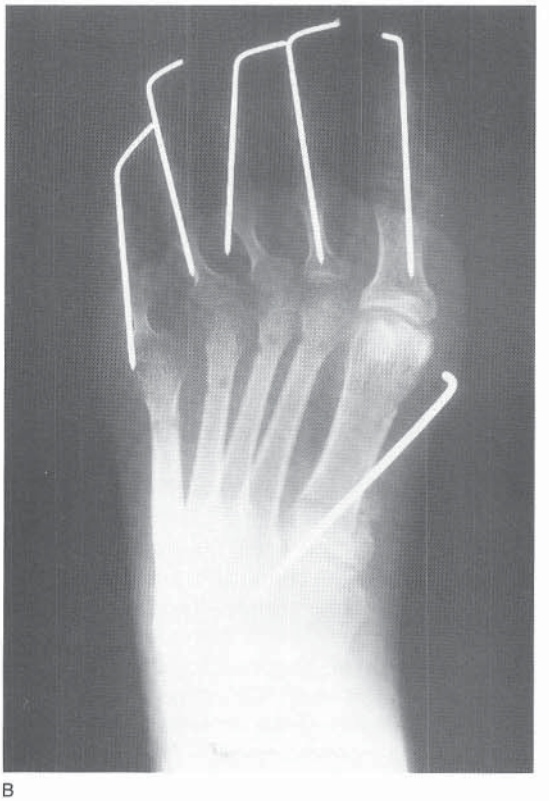

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FIGURE 27–5 **A,** Preoperative lateral radiograph of the foot of a 16-year-old boy with Charcot-Marie-Tooth disease. The calcaneus was not in equinus, although the patient walked on his toes. Note parallelism of the talus and calcaneus and plantar flexion of the first metatarsal. Clawing of all five toes was present. **B,** Postoperative radiograph. Surgery consisted of a proximal first metatarsal extension osteotomy, plantar fascia release, posterior tibialis lengthening, and Jones transfers of the long toe extensors back into the necks of the metatarsals with proximal interphalangeal joint fusions.

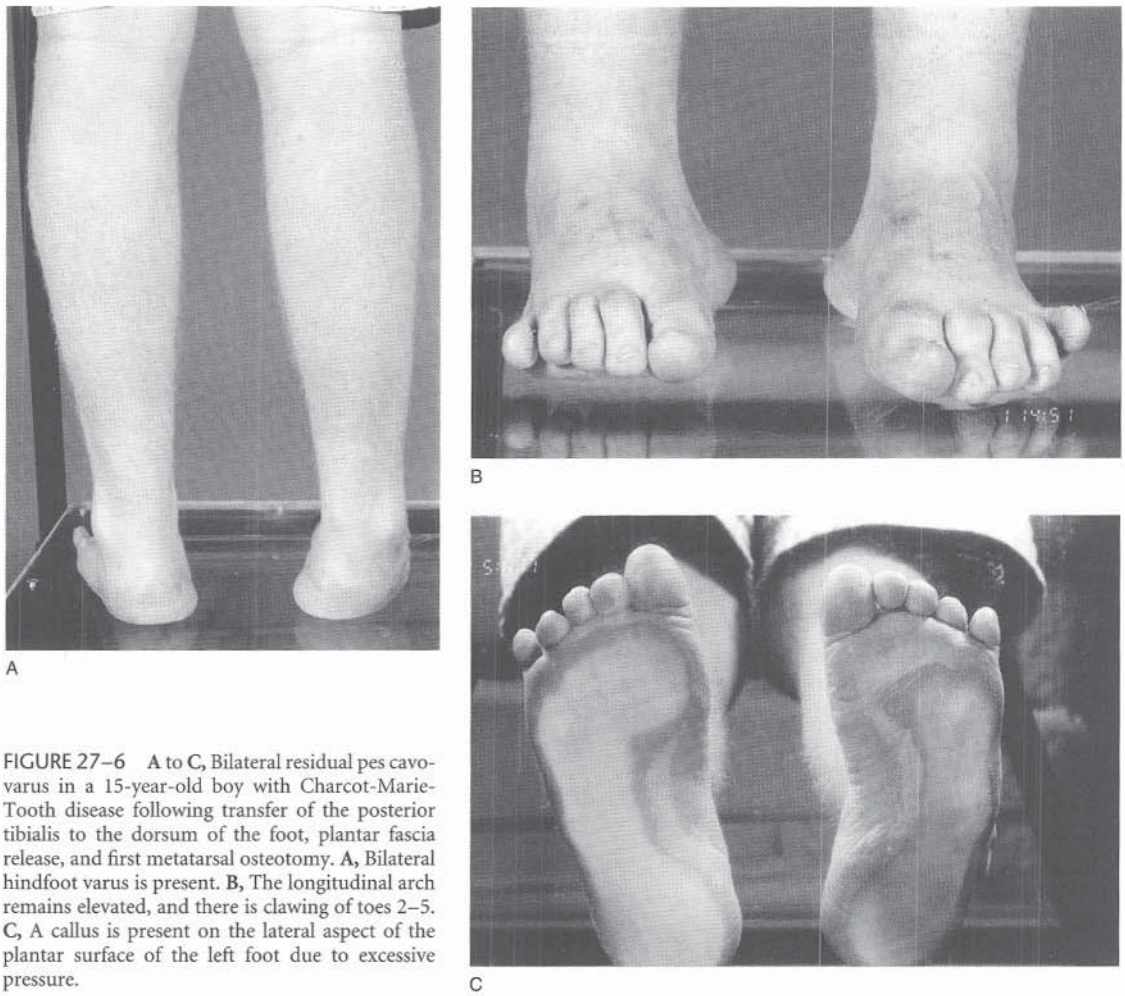


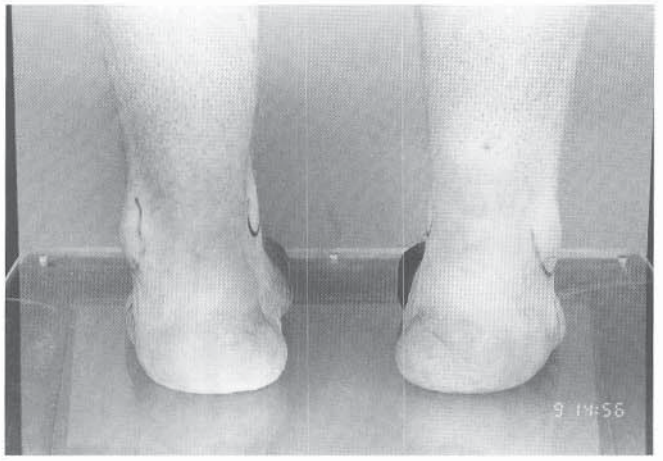
FIGURE 27–6 **A** to **C,** Bilateral residual pes cavovarus in a 15-year-old boy with Charcot-Marie-Tooth disease following transfer of the posterior tibialis to the dorsum of the foot, plantar fascia release, and first metatarsal osteotomy. **A,** Bilateral hindfoot varus is present. **B,** The longitudinal arch remains elevated, and there is clawing of toes 2–5. **C,** A callus is present on the lateral aspect of the plantar surface of the left foot due to excessive pressure.

patient, as the open physis is located proximally. When fixed deformities are present, bony surgery such as calcaneal osteotomy, midfoot dorsal closing wedge or dome osteotomy,[249] or triple arthrodesis is necessary to restore a plantigrade foot (Figs. 27–6 and 27–7).[83] Careful planning of wedges to be resected during the triple arthrodesis is necessary to correct the complex hindfoot and midfoot deformities.

Intermediate follow-up results of triple arthrodesis in patients with Charcot-Marie-Tooth disease have been reported by Mann and Chu. Despite some patients having fibrous unions of the talonavicular joint, only those feet that were fused in a nonplantigrade position were symptomatic 7 years after surgery.[144] Another study found that although only 32 percent of 22 patients with Charcot-Marie-Tooth disease who underwent triple arthrodeses had good objective results, 86 percent of the patients were satisfied with the results of the procedure at 10-year follow-up.[252] Wetmore and Drennan found less satisfactory results at 21-year follow-up, with about half of those treated with triple arthrodesis having a poor result.[248] They and others found that deterioration in results may be due to progressive weakness and to degenerative changes occurring in neighboring joints, especially the ankle joint.[153,248] They concluded that triple arthrodesis should only be used as a salvage procedure in patients with Charcot-Marie-Tooth disease (Fig. 27–8).[248] Alexander and Johnson stated that cavus feet in Charcot-Marie-Tooth disease are the most difficult to treat, as the progressive neuropathy leads to a significant rate of recurrence of deformity after all forms of surgery.[3]

Patients with Charcot-Marie-Tooth disease often walk on their toes, and it is tempting to perform an Achilles tendon lengthening procedure in these patients. It is important to note that the forefoot is in equinus in Charcot-Marie-Tooth disease, and usually not the calcaneus, and therefore lengthening of the Achilles tendon is not advised. Additionally, when a plantar release is performed, a cast is used to maintain dorsiflexion of the forefoot. Manipulating the foot into dorsiflexion in the presence of a surgically lengthened Achilles tendon usually leads to overlengthening of the Achilles tendon and losing correction of the forefoot equinus.

Weakness in the ankle dorsiflexors also leads to the development of claw toes, as the intrinsic muscles are paralyzed and contracted and the toe extensors are recruited to help dorsiflex the ankle. When the condition is symptomatic, Jones transfers of the extensor tendons of the great and lesser toes can help relieve pain on the dorsum of the toes. The long toe extensors are inserted through bone into the necks of the metatarsals so that they help dorsiflex the ankle rather than clawing the toes.[73] Fusion of the interphalangeal joint of the great toe and of the proximal interphalangeal



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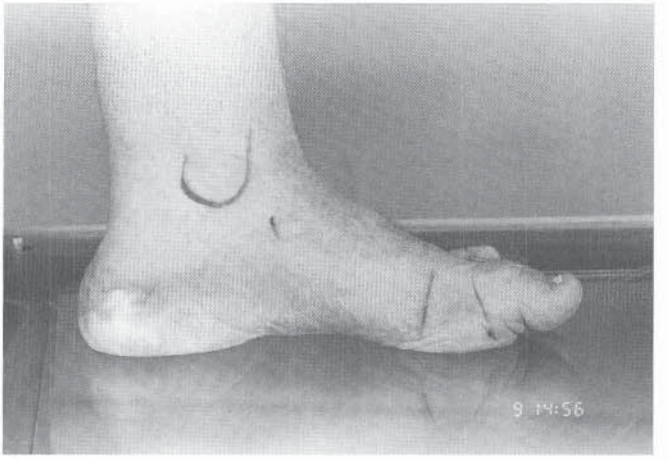

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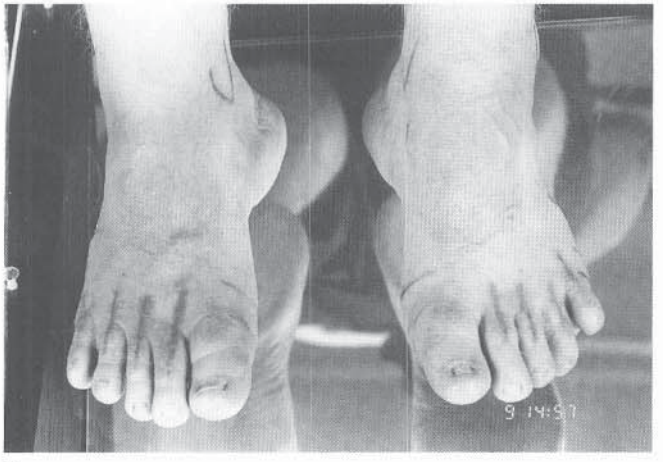

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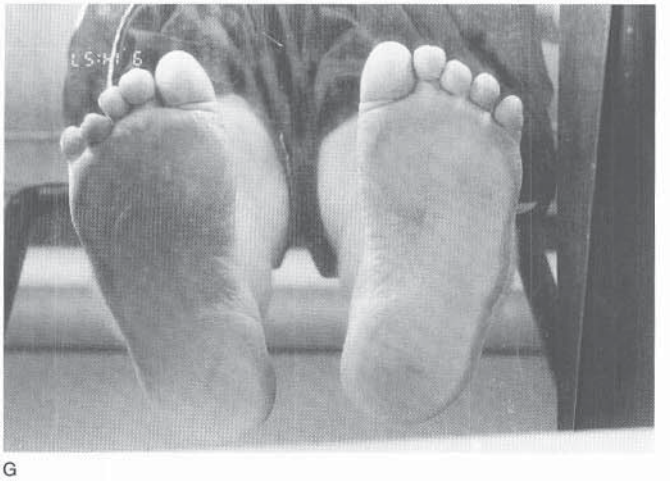

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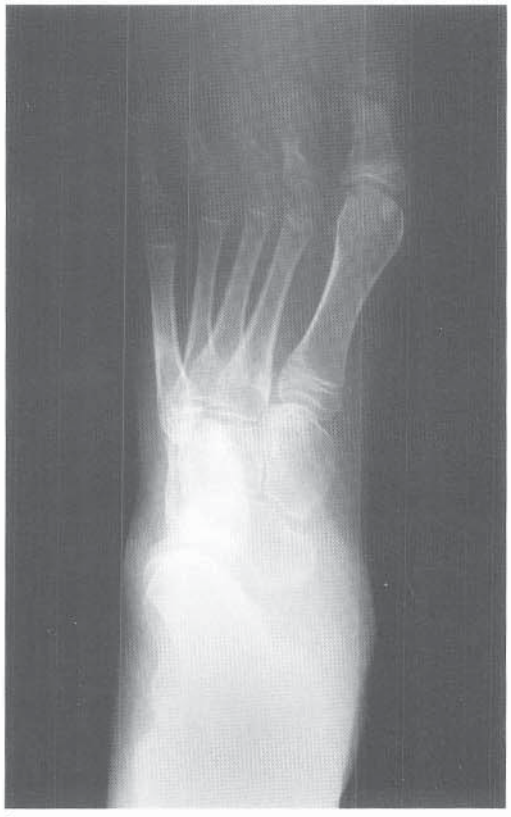
FIGURE 27–6 *Continued.* **D** to **G,** Clinical appearance of the foot at age 18, following calcaneal osteotomies and Jones transfers. **D,** Varus has been improved, but is not obliterated. **E,** The longitudinal arch is restored to normal. **F,** The toes lie in neutral alignment following Jones transfers and proximal interphalangeal joint fusions. **G,** Distribution of weight across the sole of the foot has improved.

joints of the lesser toes helps to prevent deformity of the foot and toes and should be done concomitantly with extensor tendon transfer (see Fig. 27–5).

Weakness of the tibialis anterior leads to a steppage gait and foot drop during swing phase in patients with Charcot-Marie-Tooth disease. Transfer of the posterior tibialis through the interosseous membrane to the dorsum of the foot has been performed in this patient population.[157] This weakens the varus-producing forces on the foot and augments dorsiflexion during swing phase (see Plate 28–1).

A second orthopaedic problem that is seen in patients with Charcot-Marie-Tooth disease is hip dysplasia.[67,170,240] It has been proposed that subtle weakness in the proximal musculature leads to progressive dysplasia of the hip. Although there are rare cases of hip instability in newborns who have Charcot-Marie-Tooth disease, subluxation and acetabular dysplasia are usually asymptomatic until adolescence.[124,170] Surgical treatment consisting of varus osteotomy of the femur with an acetabular redirectional osteotomy such as the Steele osteotomy has been useful in these patients in our practice. The treatment of teens with Charcot-Marie-Tooth disease is similar to the treatment of adolescent idiopathic hip dysplasia outlined in Chapter 15, Developmental Dysplasia of the Hip (Fig. 27–9). Scoliosis is seen in up to 37 percent of adolescents with Charcot-Marie-Tooth disease.[241] Curves resemble idiopathic curves in location but may have increased kyphosis, unlike idiopathic scoliosis, which is typically lordotic (Fig. 27–10).[43] Patients at highest risk for scoliosis are females and those with CMT-1 disease.[241] Posterior spinal fusion surgery may be needed if orthotic management fails and the curves are progressive (Fig. 27–11).[91] Spinal cord monitoring of somatosensory-evoked potentials (SSEPs) may be impossible owing to the peripheral neuropathy, so an intraoperative wake-up test may be necessary.[123]

Hand involvement also occurs in patients with Charcot-Marie-Tooth disease, but intrinsic muscle atrophy and weakness usually become symptomatic later in the course of the disease.[158] The onset of hand symptoms can occur in the first decade or as late as age 30. Brown and colleagues found that the appearance of hand involvement lagged behind the appearance of lower extremity symptoms by 8 years.[28]



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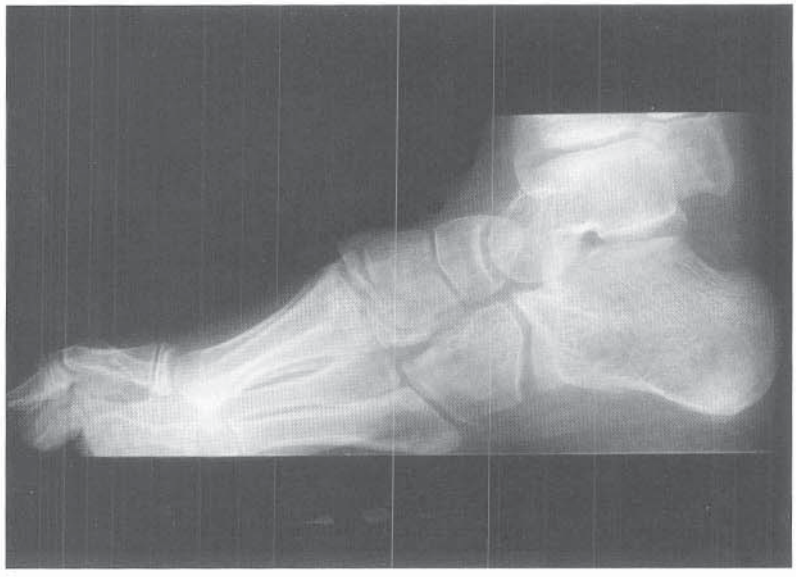

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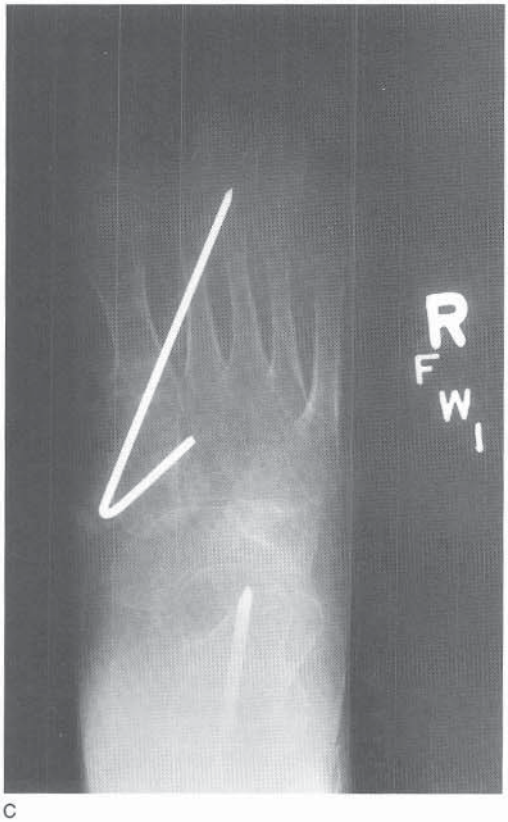

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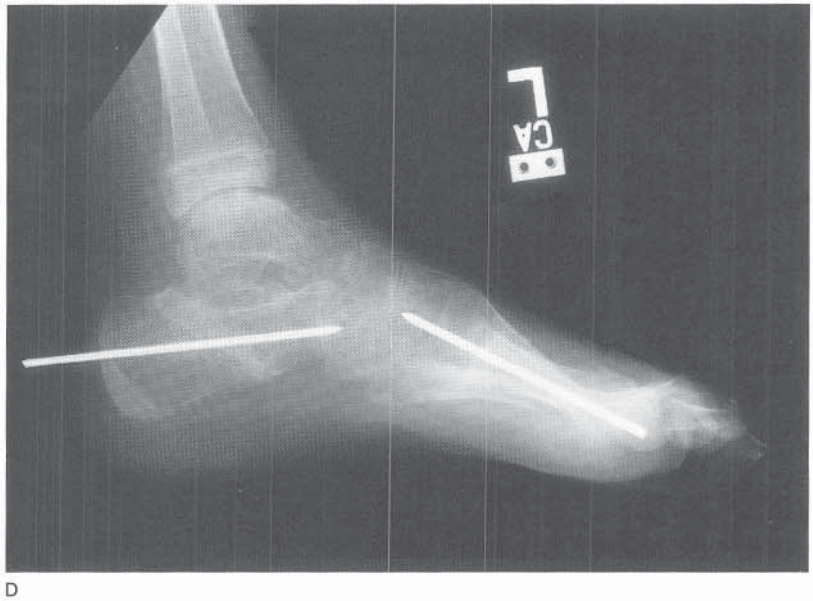

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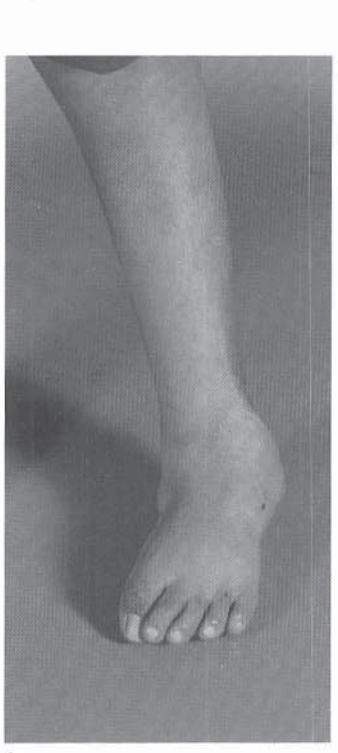
FIGURE 27–7 **A** and **B,** Radiographs of an 11-year-old child with cavovarus feet secondary to Charcot-Marie-Tooth disease. The hindfoot varus was inflexible. **C** and **D,** Postoperative radiographic appearance. Surgery consisted of a calcaneal osteotomy, first metatarsal osteotomy, plantar fascia release, and peroneus longus to brevis transfer.



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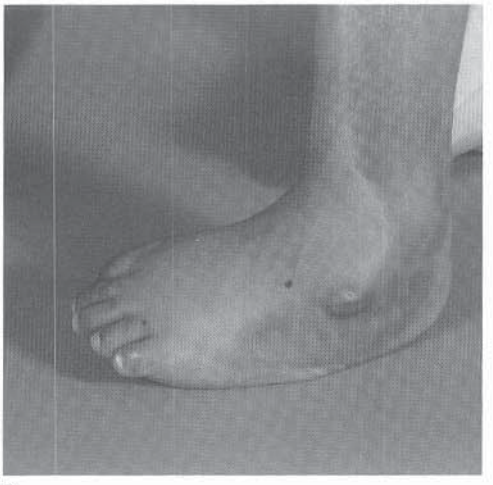

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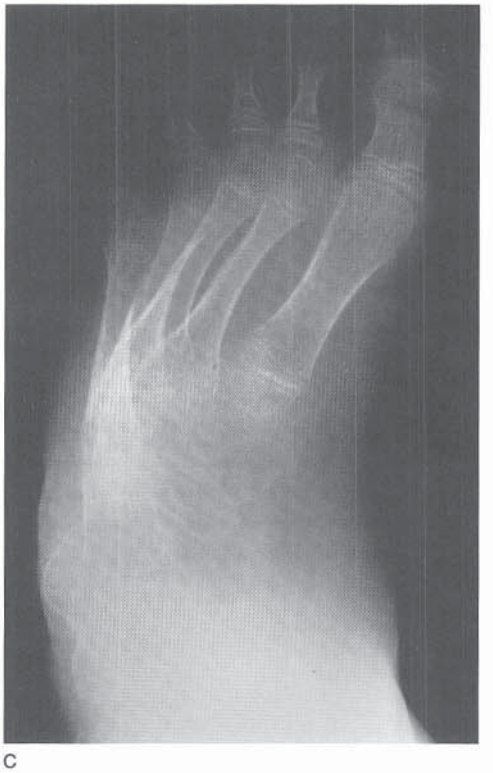

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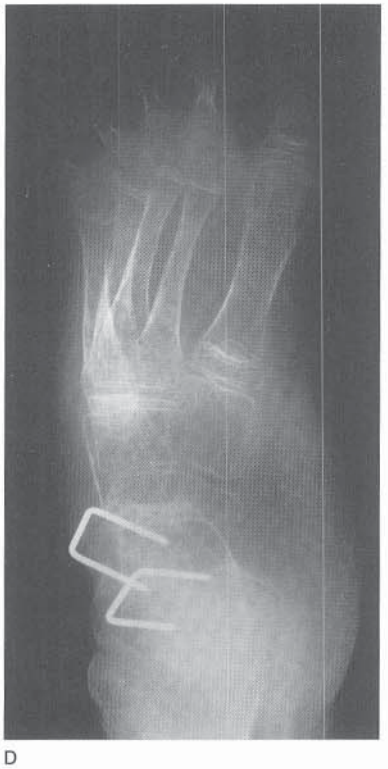

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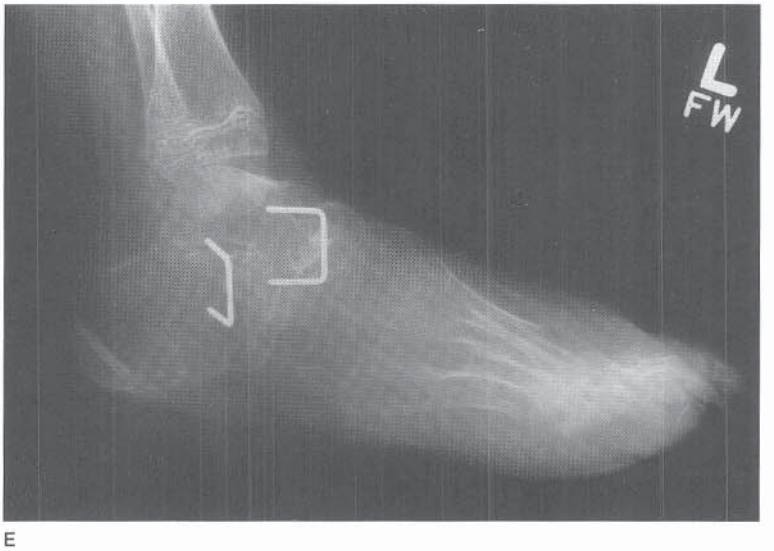

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FIGURE 27–8 **A** and **B,** Preoperative clinical appearance of an 11-year-old boy with severe rigid cavovarus feet secondary to Charcot-Marie-Tooth disease. Bracing could not be performed because of the deformity. **C,** Preoperative radiograph showing severe varus and supination of the forefoot. **D** and **E,** AP and lateral radiographs after triple arthrodesis.

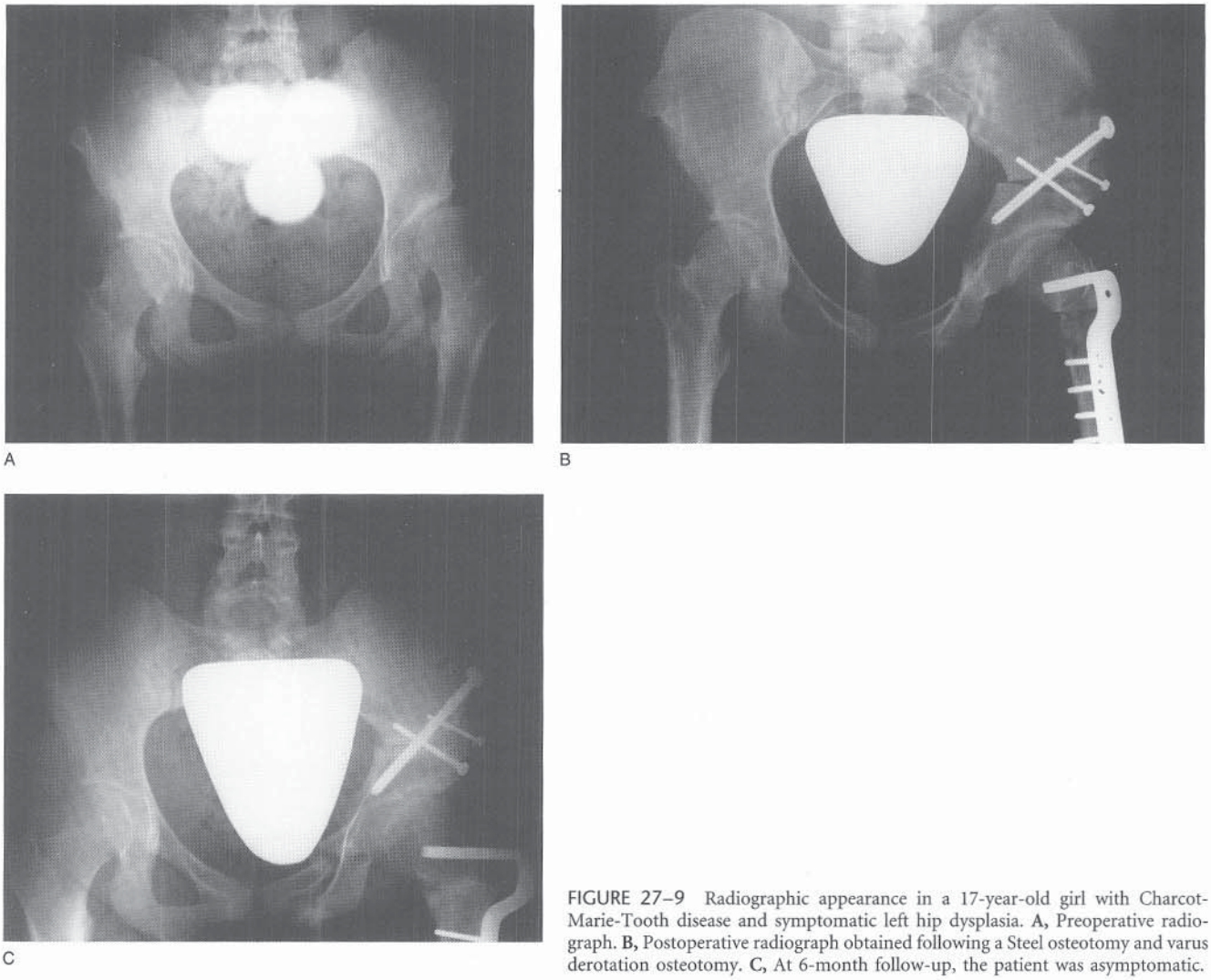


FIGURE 27–9 Radiographic appearance in a 17-year-old girl with Charcot-Marie-Tooth disease and symptomatic left hip dysplasia. **A,** Preoperative radiograph. **B,** Postoperative radiograph obtained following a Steel osteotomy and varus derotation osteotomy. **C,** At 6-month follow-up, the patient was asymptomatic.

Patients with significant upper extremity weakness are at risk for weakness of the respiratory muscles as well.[161]

Intrinsic weakness with clawing of the ring and small digits occurs first. Intrinsic paralysis of muscles innervated by ulnar and median nerves is common, whereas muscles innervated by the radial nerve are usually spared. Weakness of the forearm musculature innervated by median and ulnar nerves also occurs.[140]

Treatment to augment upper limb function in patients with Charcot-Marie-Tooth disease has not been widely published. Although nerve conduction velocities are typically slowed, this appears to be a problem intrinsic to the nerve and not caused by the compressive neuropathy. Thenar muscle wasting and increased median motor and sensory nerve latencies in this diagnosis are not indicative of carpal tunnel syndrome. A carpal tunnel release therefore may not relieve symptoms.

The specific functional problems related to the intrinsic weakness of the hands include loss of opposition of the thumb, loss of side-to-side pinch, and clawing of the fingers (Fig. 27–12). Surgical procedures to augment function are available to take advantage of tendon donors that are unlikely to deteriorate with time, or to use bony procedures to correct deformity. Electrodiagnostic evaluation of potential donor muscles for tendon transfers can help select the best motor. Opponensplasty using the extensor carpi ulnaris or extensor indicis proprius can greatly increase prehension.[175] Transfers to augment side pinch use the radially innervated extensor pollicis brevis, abductor pollicis longus, or the extensor indicis proprius routed either to the first dorsal interosseous or to the adductor pollicis. Transfers that do not require pulleys are preferred, and where a pulley is necessary, it should be static and not another tendon or tendon loop because of the potential for deterioration.[251]

Arthrodesis of the thumb metacarpophalangeal (MCP) joint or the carpometacarpal joint can predictably stabilize one of the unstable motion segments.

Intrinsic transfer procedures build in flexion at the MCP joint to help balance the extrinsic metacarpal extensors. Flexor digitorum superficialis looped around the A1 pulley, as described by Zancolli, or metacarpal capsulodesis restores a more useful posture to the hand.[260]

Selection of upper extremity tendon transfer procedures in young patients should be done cautiously. Because hand deformities are likely to progress and because aftercare for the tendon transfers requires protection from excessive

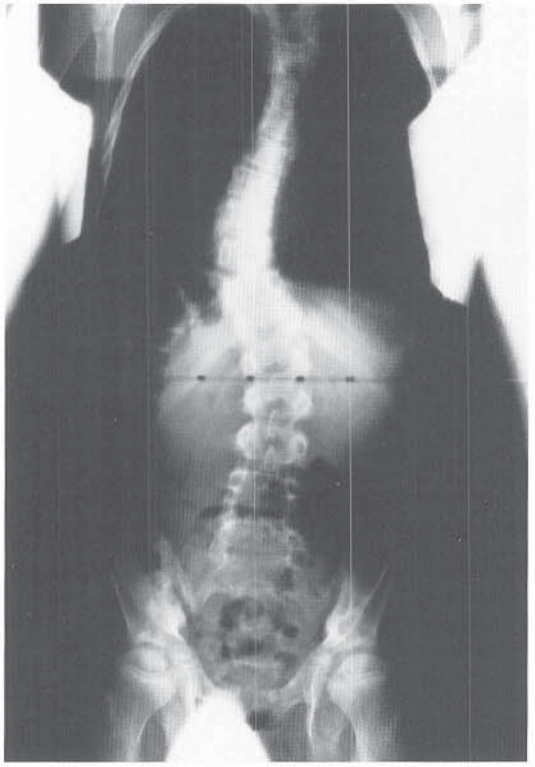


FIGURE 27–10 Scoliosis in an 11-year-old child with Charcot-Marie-Tooth disease.

abuse, it may be best to wait until the patient reaches an age to understand the limitations of what can be done and what is expected of him or her afterward.

Neuropathic pain is a significant problem for many people with Charcot-Marie-Tooth disease. In a recent study, 71 percent of patients who participated stated that they had neuropathic pain, most frequently in the lower back, the knees, and the feet.[32]

Central nervous system involvement such as sensorineural deafness has been described in a few patients with the X-linked dominant form of the disease.[221]

CHARCOT-MARIE-TOOTH DISEASE TYPE 2

Charcot-Marie-Tooth disease type 2 (CMT-2) is a peripheral neuropathy that is inherited as an autosomal dominant disorder. It is characterized by older age at onset (usually in the third decade) and normal to only slightly diminished nerve conduction velocities. Deep tendon reflexes are preserved.

CMT-2 is pathologically and genetically distinct from CMT-1.[15,34] One form of CMT-2 maps to chromosome 1p36, which encodes for myelin protein zero (CMT-2A), another maps to chromosome 3p (CMT-2B), and another maps to chromosome 7p (CMT-2D).[102,116,148] Unlike in CMT-1, there is no enlargement of the peripheral nerves, and sensory changes are infrequent.[202] Nerve biopsy does not show hypertrophy; rather, axonal degeneration is seen.

The orthopaedic manifestations of the disease resemble those seen in CMT-1.

HYPERTROPHIC INTERSTITIAL NEURITIS (DEJERINE-SOTTAS DISEASE)

Dejerine-Sottas disease, also known as HMSN III, is a severe, infantile-onset, demyelinating polyneuropathy. Dejerine and Sottas described this chronic familial polyneuropathy in 1893.[48] It belongs in the family of hereditary motor and sensory neuropathies and is related to but more severe than Charcot-Marie-Tooth disease.[34]

Dejerine-Sottas disease is traditionally thought to be inherited in an autosomal recessive pattern,[171,220] but new molecular genetic research has shown autosomal dominant inheritance in many patients.[192,229,238] Mutations in the genes coding for the P0 myelin protein (MPZ) on chromosome 1 and peripheral myelin protein 22 (PMP 22) on chromosome 17 have been demonstrated in patients with this disease.[90,147,168,237,245] P0 myelin protein is the major structural membrane protein expressed in Schwann cells of peripheral nerves,[244] while PMP 22 plays a critical role in the formation and maintenance of myelin in the peripheral nervous system.[222]

Pathology. Peripheral nerves are enlarged as a result of the proliferation of perineural and endoneural connective tissue. Classic onion bulb formation is seen on cross section of a nerve biopsy specimen and represents proliferation of the Schwann cells.[258] There is a lower density of myelinated fibers.[169] Muscle biopsy reveals atrophy.

Clinical Features. The usual presenting complaint is poor gait.[8] There is a history of delayed walking. The child is unsteady, falls frequently, has difficulty climbing stairs, and cannot run. Sensory disturbances such as paresthesias may occur.

Physical examination reveals weak, floppy feet. Deep tendon reflexes are either absent or markedly reduced. Sensory loss involves all modalities of sensation and occurs in a stocking-and-glove pattern. Proprioception is disturbed, and Romberg's sign is positive. Nystagmus and slurred speech occur in some patients.

The gait is similar to a steppage gait. Muscle weakness is seen distally, and pes cavus occurs at an early age. Paralysis of the intrinsic muscles of the hand appears later. Flexion contractures of the wrist and fingers occur in late childhood. Scoliosis develops in early adolescence.

Diagnosis. The diagnosis is made by electrodiagnostic studies. The nerve conduction velocity will be markedly prolonged, even more so than in Charcot-Marie-Tooth disease.[17,56,237] EMG shows fibrillation within the stimulated muscle due to denervation.

Cerebrospinal fluid (CSF) shows an elevation in total protein. Cell counts are within normal range. Laboratory measurements of serum aldolase and creatine phosphokinase are normal.

MRI of the spine is performed to rule out an intraspinal tumor. Enlargement of the spinal nerves, the cauda equina, and the sciatic nerve can be seen in older patients with Dejerine-Sottas disease.[143,149,224]

Nerve biopsy and muscle biopsy are usually needed to confirm the diagnosis.

Prognosis and Treatment. The disease progresses slowly. In mild cases, the neuropathy may plateau and life expectancy may be normal.

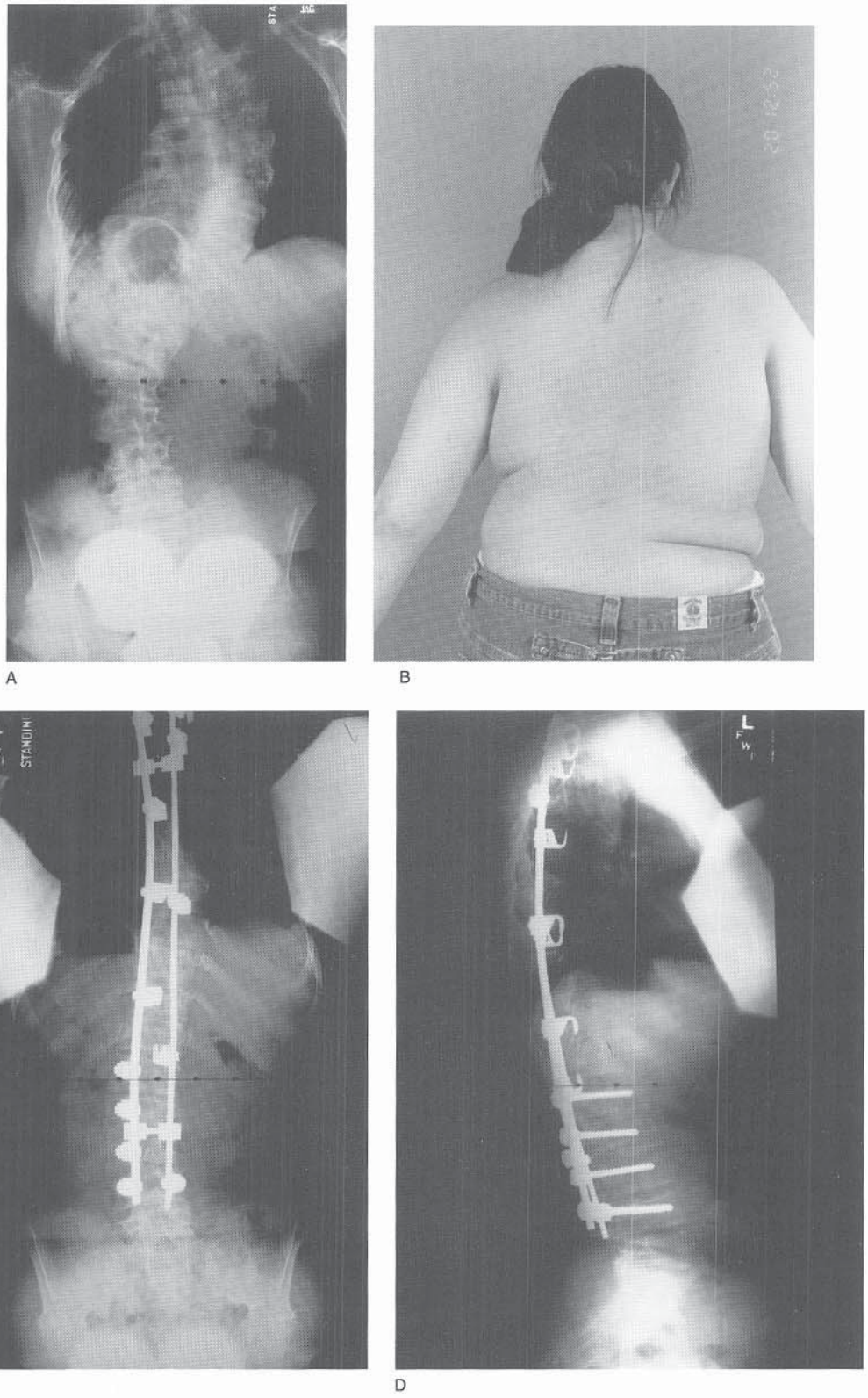
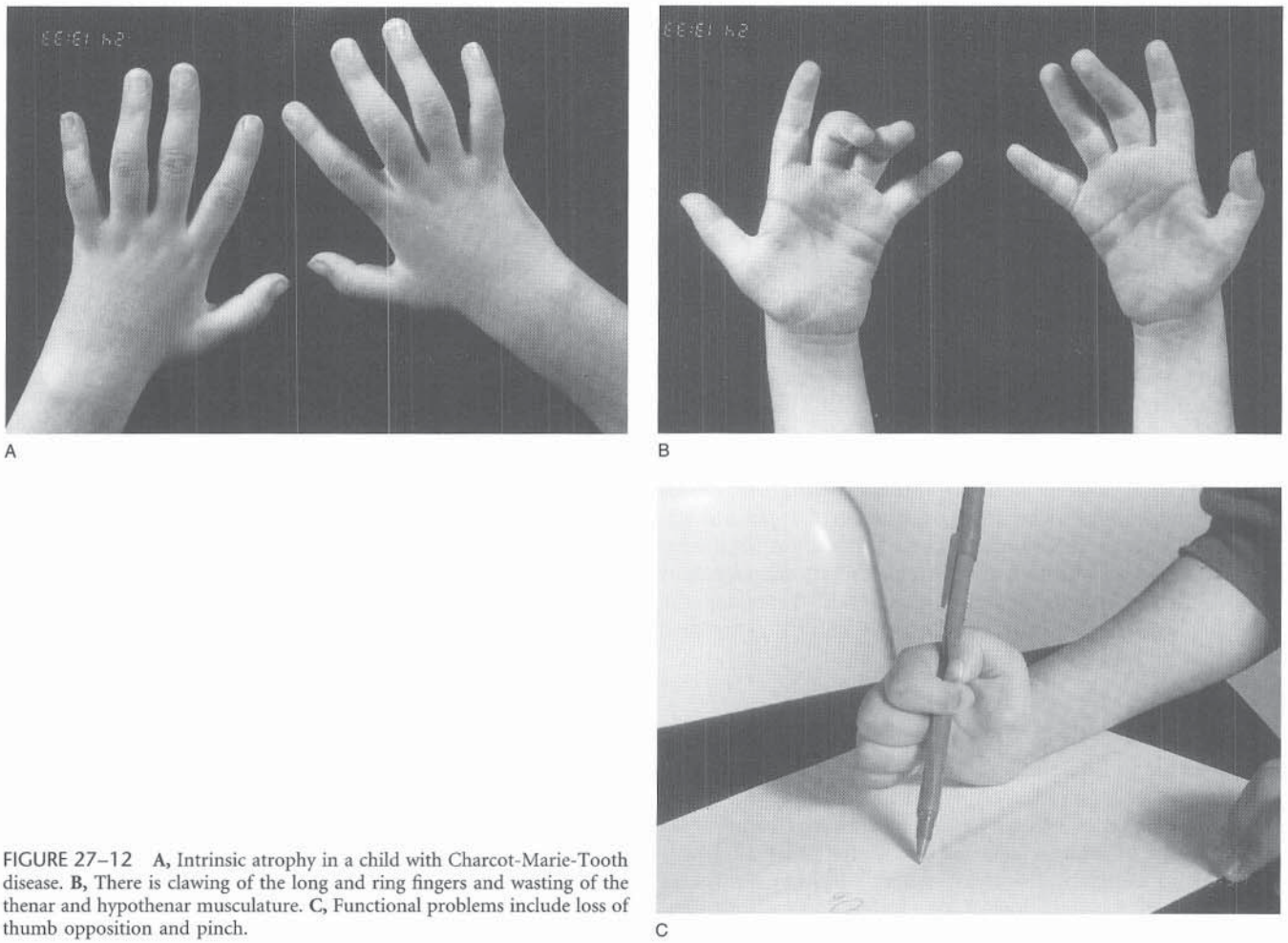


FIGURE 27–11 **A,** Idiopathic-appearing scoliosis in an 11-year-old girl with Charcot-Marie-Tooth disease. The curve progressed despite bracing. **B,** Clinical appearance. **C** and **D,** PA and lateral radiographs obtained following posterior spinal fusion with TSRH instrumentation.



A B C

FIGURE 27–12 **A,** Intrinsic atrophy in a child with Charcot-Marie-Tooth disease. **B,** There is clawing of the long and ring fingers and wasting of the thenar and hypothenar musculature. **C,** Functional problems include loss of thumb opposition and pinch.

There is no specific treatment. Corticosteroids are reported to improve the condition and may be tried in severe cases or during acute exacerbations. Orthopaedic management usually consists of prescribing orthoses to improve gait. Pes cavus may require surgical reconstruction. Scoliosis may progress and require orthotic management or surgery. Spinal cord compression has been reported in adults with Dejerine-Sottas disease as a result of hypertrophy of the nerve roots.[31,45]

REFSUM'S DISEASE

Refsum's disease (HMSN IV), also known as heredopathia atactica polyneuritiformis, is a rare disorder of lipid metabolism that is characterized by peripheral neuropathy, retinitis pigmentosa, ataxia, and increased protein in the CSF.[187,218] Other clinical findings may include cataracts[38] and cardiac arrhythmias. The condition is caused by a defect in phytanoyl-CoA hydroxylase, the enzyme responsible for the degradation of phytanic acid.[107,108,217] This results in an accumulation of phytanic acid in the blood and tissues. As is the case with the vast majority of enzyme deficiencies, the disease is inherited in an autosomal recessive pattern. The gene responsible for Refsum's disease has been mapped to chromosome 10.[156]

There are two clinical presentations of the disease. In the infantile form, hypotonia and developmental delay are first noted. Growth retardation, mental retardation, hepatosplenomegaly, and retinitis pigmentosa then develop.[207] Abnormalities in peroxisomal function are present in the infantile type.[180,197,243] Peroxisomes are organelles involved in the metabolism of lipids critical to the functioning of the nervous system.[27]

In the classic form of Refsum's disease, symptoms develop between 4 and 7 years of age. The gait becomes unsteady and the limbs weaken as the distal musculature atrophies. Deep tendon reflexes are absent, and there is no spasticity. Babinski's reflex is negative, but Romberg's sign may be present. Vibration and position sense in the legs may be disturbed. Ophthalmologic changes may be present, and deafness is seen in some patients. Hepatosplenomegaly occurs due to the fatty accumulation.

The skeletal changes in Refsum's disease include osteopenia, mild epiphyseal dysplasia (especially in the knees and elbows), and shortening and deformity of the tubular bones in the hands and feet.[179,242] Pes cavus may result from the peripheral neuropathy.

The diagnosis is made by documenting increased serum phytanic acid levels. Carriers can be detected by a phytol loading test.[92] Nerve biopsy shows onion bulb formation, with increased endomesium and fatty deposits. Motor nerve conduction velocities are slow. CSF protein levels are increased.

Conditions from which Refsum's disease must be distinguished include Freidreich's ataxia and the other rare inherited ataxias, and peroneal muscular atrophy. Retinitis pigmentosa is seen only in Refsum's disease.

Treatment of both forms of Refsum's disease is first dietary, with avoidance of foods that contain phytanic acid.[194] Low phytanic acid intake is achieved by restricting fat while allowing free amounts of fruit and green vegetables.[52] Medical treatment by plasmapheresis can lower the phytanic acid levels.[9,70,99] Cascade filtration, a procedure resembling plasmapheresis, similarly lowers the serum phytanic acid level while avoiding loss of albumin and decreasing the loss of immunoglobulins.[81] The main indication for plasma exchange is a severe deterioration in the patient's clinical condition. A lesser indication is failure of dietary management to reduce the plasma phytanic acid level.[84] Lowering the serum phytanic acid level can improve clinical symptoms of ataxia and weakness.

CONGENITAL ANALGIA

In children, indifference to pain, termed analgia, may be congenital or acquired. Congenital analgia may be one of the following types: (1) congenital insensitivity to pain, (2) familial dysautonomia, also known as the Riley-Day syndrome, (3) congenital sensory neuropathy, (4) hereditary sensory radicular neuropathy, or (5) familial sensory neuropathy with anhidrosis. Acquired indifference to pain may be due to syringomyelia, spinal cord tumor, or diabetes mellitis. The differential diagnosis of absent pain perception in a child is given in Table 27–3.

Physical examination should assess the different sensory modalities. The physician should assess for temperature sensation with cold and warm items, for light touch sensation, and for deep pain sensation. Deep pain may be tested by applying firm pressure to the bones or muscles and by assessing the response to insertion of needles. It may be difficult to assess small children accurately, but if pain is felt, the pulse rate, respiratory rate, and blood pressure will rise, and the pupils will dilate. It is important to try to determine whether a painful stimulus is not felt at all or whether the stimulus is felt but not perceived as painful.

Radiographic evaluation is rarely diagnostic, but MRI of the brain and spinal cord should be done to rule out pathologic processes such as syringomyelia or tumor.

Finally, nerve conduction studies of the motor and sensory nerves should be performed. Often, a nerve and muscle biopsy will be necessary to confirm the diagnosis. Skin biopsy may be helpful in cases with anhidrosis and to assess for dermal innervation.

CONGENITAL INSENSITIVITY TO PAIN

This rare disorder is characterized by the absence of subjective and objective responses to noxious stimuli in patients with intact central and peripheral nervous systems.[47,228] Temperature and touch sensation are preserved.[95] Onset of disease is at or shortly after birth. The etiology is unknown. The cutaneous nerve endings in the skin and periosteum are normal in congenital insensitivity to pain.[138] Nerve biopsies in childhood are normal, although it is suspected that the condition may be due to a sensory neuropathy and that pathologic changes may be seen in adulthood.[130] Substance P, a nociceptive cytokine protein, is absent in the synovial fluid in individuals with congenital insensitivity to pain.[50] The disease may be inherited in an autosomal recessive pattern,[64] but it is usually sporadic.[128]

Clinical Features. As soon as the teeth erupt, the condition becomes evident from the child's biting the tongue, lips, and fingers. Burns and bruises do not elicit crying. Corneal damage can be caused by trauma and foreign bodies in the eye. Intelligence is normal.

The orthopaedic manifestations of the disease vary among patients.[76] Traumatic fractures are common and, because of the lack of pain, may go unrecognized for prolonged periods of time, resulting in malunions or pseudarthroses (Fig. 27–13). Multiple neglected fractures in patients with burns and bruises may lead to confusion of this condition with child abuse.[216] Epiphyseal separations may occur in infancy and may resemble rickets radiographically. Avascular necrosis of the talus, femoral head, or femoral condyles may occur. Recurrent dislocation of the hip that is refractory to cast management has also been described in patients with congenital indifference to pain.[193]

Repetitive trauma to the joints can lead to effusion, hemarthrosis, synovial hypertrophy, and ligamentous laxity. A Charcot joint may be the end result, particularly in the weightbearing joints such as the ankle and knee (Fig. 27–14).[80] Increasing laxity can lead over time to dislocation of the involved joint.[138] Surgical treatment is rarely successful, and conservative treatment with protective orthoses is advised (Fig. 27–15).[76] Septic arthritis is also seen with increased frequency in these patients. Some patients with congenital insensitivity to pain have required amputation for treatment of their Charcot or septic joints.[77] It is very important to anticipate and prevent neuropathic joints in these children. Patient and parent education in joint protection and surveillance for injury is the most important component of the treatment plan for these children.[138]

Spinal manifestations of congenital insensitivity to pain include instability due to the development of Charcot-like changes from neuropathic arthropathy of the spine, and scoliosis.[100,176] Radiographs initially show disk space narrowing, facet arthropathy, and hypertrophic spurs. With time, osteopenia, fragmentation, large osteophytes, and subluxation can be seen.[176] Flexion-extension lateral radiographs can demonstrate the instability. Patients may present with neurologic deficits, and surgical fusion (either posterior or combined anterior-posterior) has been successfully performed in small numbers of patients with congenital insensitivity to pain.[51,100]

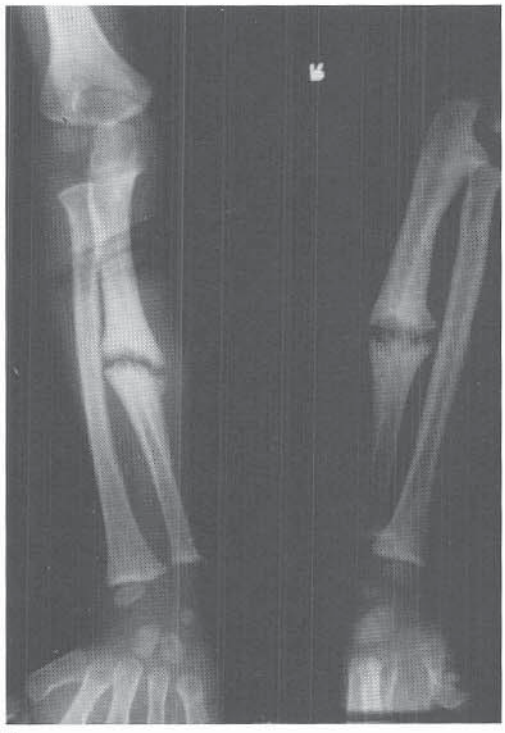
Osteomyelitis is seen more frequently than in the general population, probably as a result of neglected foci of infection such as dental abscesses and bitten fingers. The most frequent sites are the fingers and toes. Osteomyelitis is most commonly indolent and chronic rather than acute in presentation.

Text continued on page 1453

TABLE 27–3 **Differential Diagnosis of Congenital Insensitivity to Pain**

Parameter	Congenital Indifference	Familial Dysautonomia	Congenital Sensory Neuropathy	Hereditary Sensory Radicular Neuropathy	Familial Sensory Neuropathy with Anhidrosis	Acquired Sensory Neuropathy (Toxic, Infectious)	Syringomyelia
Hereditary	None	Recessive	None, occasionally dominant	Dominant	Recessive	None	None
Age at onset	Birth	Birth	Birth	Early adolescence	Birth	Adult	Young adult
Physiologic pain reactions	Present	Absent	Absent	Absent	Absent	Absent	Absent
Touch perception	Normal	Normal	Lost	Lost	Normal	Normal	Normal
Temperature perception	Normal	Diminished	Lost	Lost	Diminished	Normal	Normal
Distribution of sensory loss	Universal	Incomplete	Islands of normal sensation	Legs and feet, occasionally hands	Islands of normal sensation	Legs and feet, occasionally hands	Arms and hands
Axon reflex	Normal	Absent	Absent	Absent	Absent	Absent	Normal
Nerve conduction	Normal	Normal	Sensory absent Motor present	Sensory absent Motor normal	Sensory absent Motor normal	Motor and sensory abnormal	Normal or slightly reduced
Motor strength	Normal	Normal	Normal	Normal	Normal	Weak (atrophied)	Weak (atrophied)
Sensory nerve biopsy	Normal	Absence of fungiform papillae on tongue	No myelinated fibers	No myelinated fibers	Myelinated fibers present	Loss of myelinated fibers	Normal
Skin biopsy	Normal	Normal	No nerve endings No cholinesterase	—	Normal	Degeneration of nerve, normal cholinesterase	Normal
Brain and other	Normal	Normal *Autonomic N.S.* Lack of lacrimation Excessive perspiration Poor temperature control	Normal	Normal	Normal Absence of Lissauer's tract and small dorsal root axon	Normal	Normal
Intelligence	Normal	Dull to average	Dull to average	Normal	Defective	Normal	Normal

Modified from Winkelmann RK, Lambert EH, Hayles AB: Congenital absence of pain: report of a case and experimental studies. Arch Dermatol 1962;85:334. Copyrighted 1962, American Medical Association.



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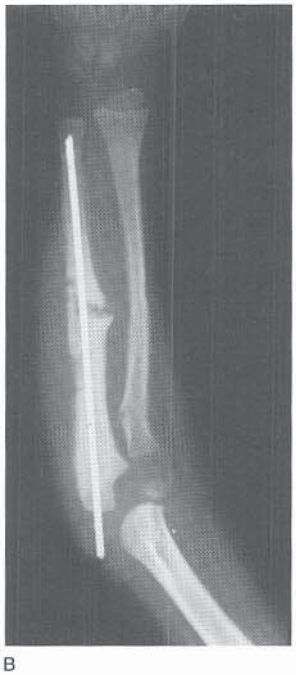
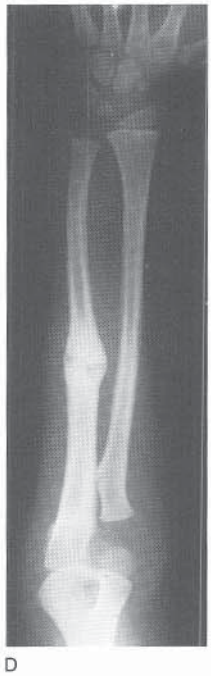


B

C



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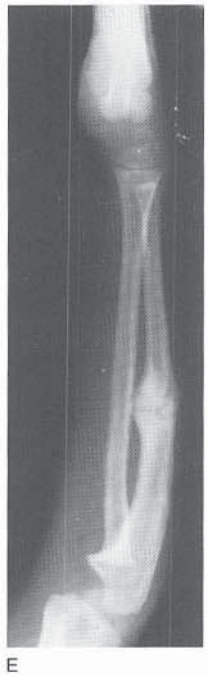

E

FIGURE 27–13 **A,** Radiographs of right forearm showing nonunion of fracture in the middle third of the ulna in a 4-year-old child with congenital indifference to pain. After immobilization in an above-elbow cast for 3 months there was no evidence of healing. Thus, an open reduction, intramedullary fixation with a Steinmann pin, and onlay bone grafting was performed. **B** and **C,** Radiographs of the forearm obtained 3 months after surgery. **D** and **E,** Radiographs obtained 1 year later showing healing of the fracture.

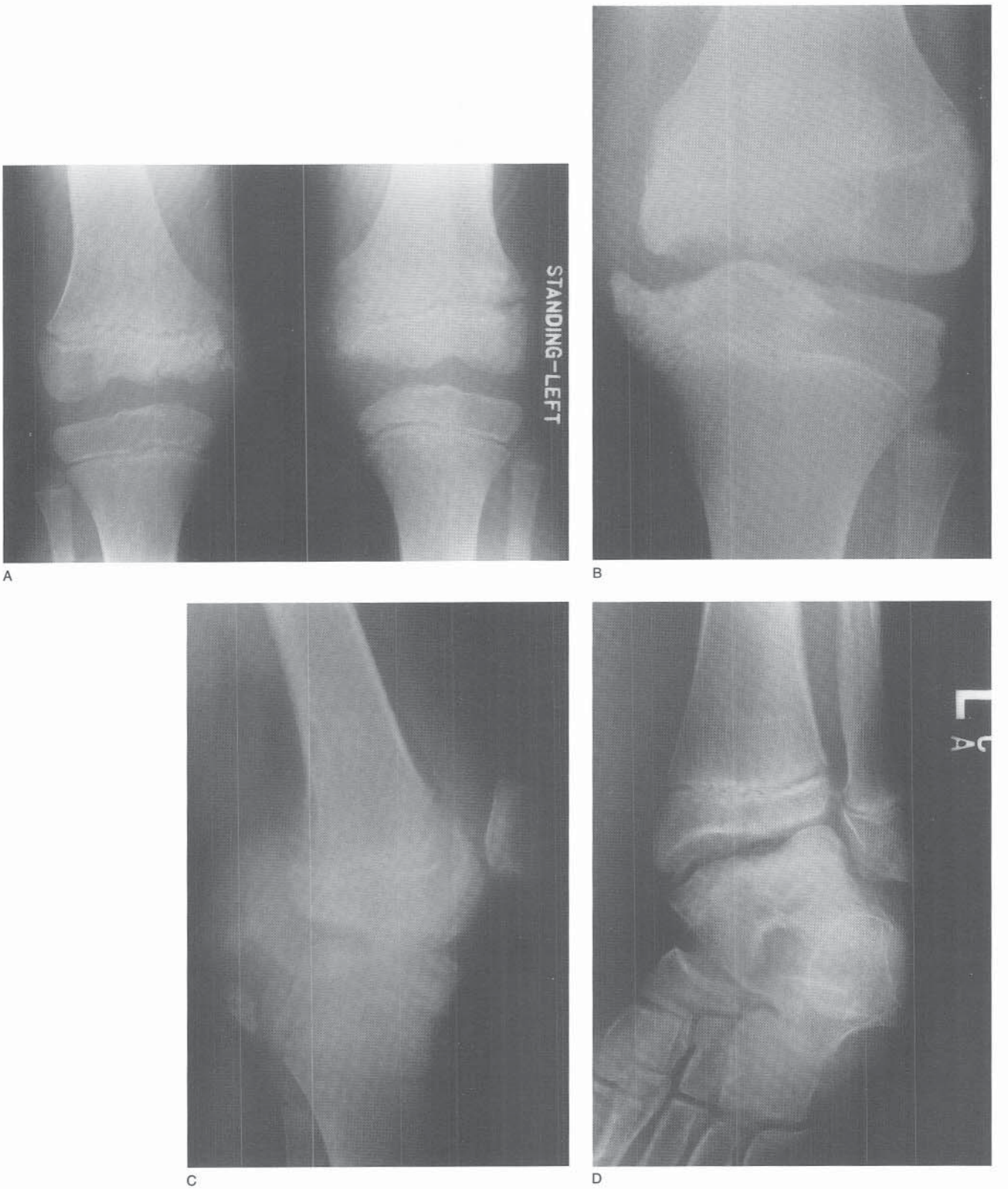

FIGURE 27–14 **A,** Charcot knees in an 8-year-old boy with congenital indifference to pain. **B** and **C,** AP and lateral radiographs obtained at age 16 show destruction of joint with multiple loose bodies. **D,** Charcot changes at the ankle are also present at age 16.

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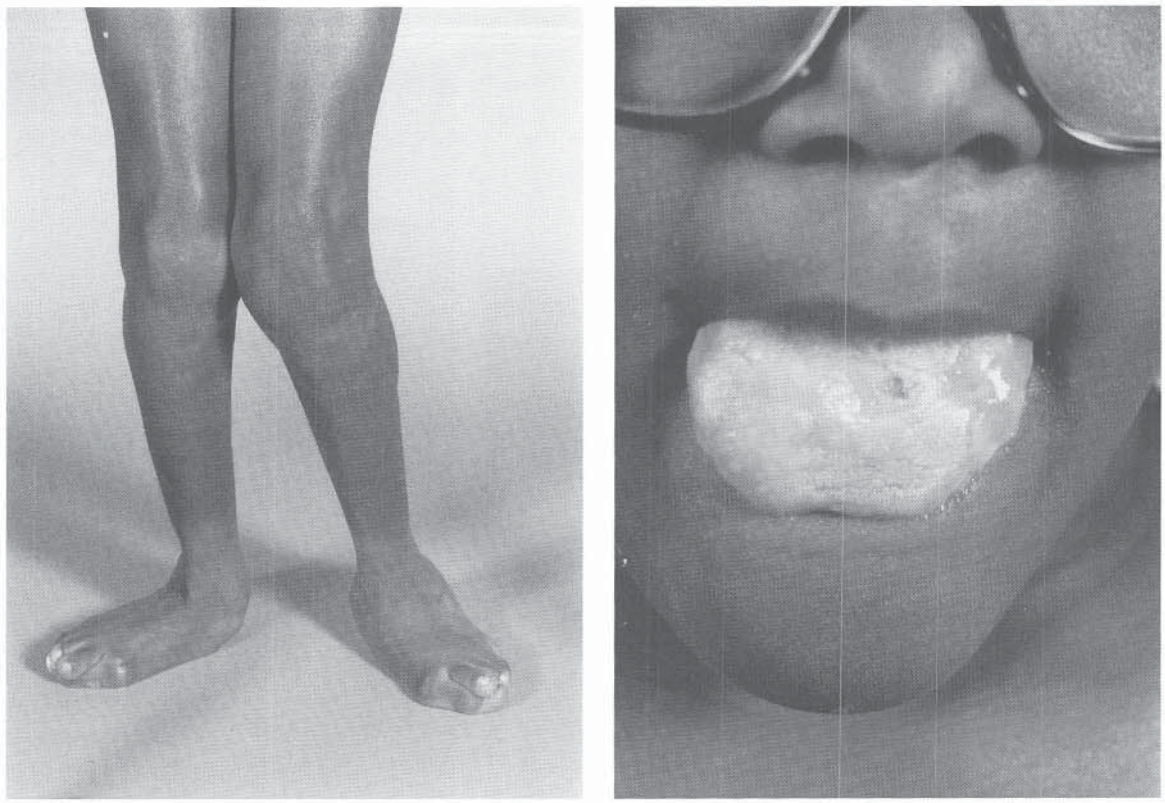
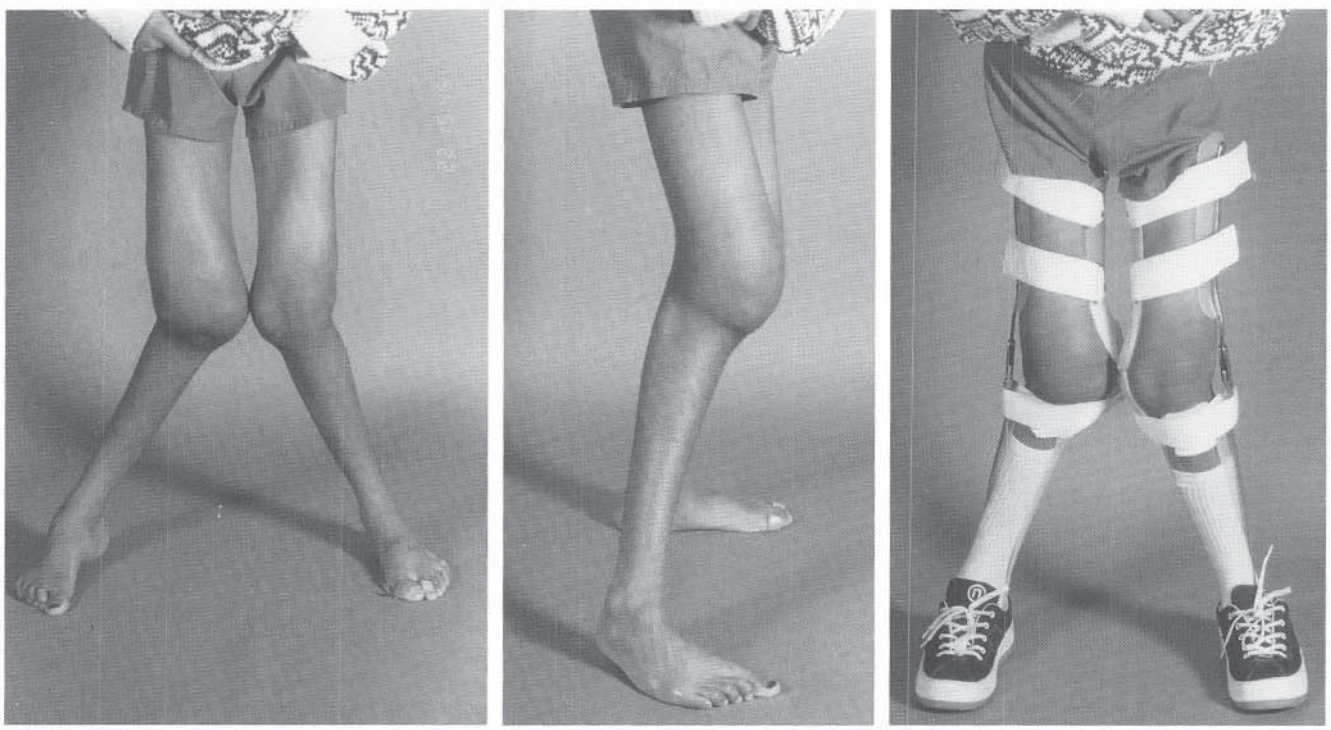


E F

FIGURE 27–14 *Continued.* **E,** Clinical appearance of the lower extremities. **F,** Self-inflicted ulcerations of the tongue.



A B C

FIGURE 27–15 **A** and **B,** Clinical appearance of a 15-year-old boy with congenital insensitivity to pain, bilateral Charcot knees, and insensate wounds on his feet. **C,** Treatment consisted of a knee-ankle-foot orthosis to protect the knees.

FAMILIAL DYSAUTONOMIA (RILEY-DAY SYNDROME)

This disturbance in pain perception is the result of an autosomal recessive trait and is most commonly seen in patients of Ashkenazi Jewish descent.[191] The genetic locus has been mapped to chromosome 9.[115] Babies present with lack of tears, excessive perspiration, labile blood pressure, abnormal gastrointestinal motility, and poor temperature control. There is a characteristic lack of fungiform papillae on the tongue. Speech development is frequently delayed, and the patients usually are of subnormal intelligence.

Neurologically, patients with familial dysautonomia have diminished temperature sensation but preserved touch perception. They have a lack of objective response to painful stimuli. Deep tendon reflexes are absent.

Orthopaedic manifestations are the same as in congenital insensitivity to pain and include fractures, Charcot joints, and osteomyelitis. Scoliosis is seen in up to 90 percent of children with Riley-Day syndrome and can be extremely difficult to manage.[115] Curves tend to be rigid and may exhibit significant kyphosis as well, unlike the deformity seen in idiopathic scoliosis. When orthotic management fails, spinal fusion may be necessary. A preoperative nutritional evaluation should be performed to rule out malnutrition and reflux with aspiration. Combined anterior and posterior spinal fusion with instrumentation is recommended in patients with kyphoscoliosis.[199] Patients are prone to autonomic dysfunction while anesthetized, with wide swings in blood pressure.[195] Intraoperative fatal cardiac arrest has been described in these patients.[257] Postoperatively, monitoring in an intensive care setting is necessary. Immobilization should be done postoperatively, and a TLSO is preferred over a cast owing to the tendency for unrecognized skin breakdown beneath the irremovable cast.[91,199] Treatment complications are very common in this patient population and range from infection to wound breakdown to failure of fixation.[2] The patients do not notice loss of fixation due to hook pull-out because of the lack of painful sensation.

Life expectancy is decreased, with many patients succumbing to pulmonary infections.[257] In a study by Axelrod and Abularrage, the probability that a child born after 1982 would reach the age of 30 was 50 percent.[11]

CONGENITAL SENSORY NEUROPATHY

Congenital sensory neuropathy is a very rare, nonprogressive disease that is usually inherited as an autosomal recessive trait. In this disorder, touch, temperature, and pain sensation are all absent.[10,13] Motor nerve conduction is normal, but sensory nerve conduction is absent. Nerve biopsy shows absence of myelinated nerve fibers and dermal nerve networks. The brain and spinal cord are normal.

Deep tendon reflexes are diminished or absent. Retinitis pigmentosa may be present. There is an association with mental retardation and deafness.

HEREDITARY SENSORY RADICULAR NEUROPATHY

This autosomal dominant disorder is characterized by a primary degenerative neuropathy of the dorsal root ganglia.[49,235] All sensory modalities are lost, but there is no disturbance of sweating. Deep tendon reflexes in the lower extremities are absent. This disorder becomes evident late in childhood, unlike the previously discussed disorders, which manifest in infancy. The sensory changes begin distally in the lower extremities and progress proximally. Rarely does the neuropathy extend proximal to the knees. Owing to the lack of all sensation, neuropathic foot ulcers are frequently seen in these patients.[210]

CONGENITAL INSENSITIVITY TO PAIN WITH ANHIDROSIS

This neuropathy, also known as familial sensory neuropathy with anhidrosis and as hereditary sensory and autonomic neuropathy type IV, is characterized by absence of temperature and pain sensation but intact touch perception.[178] Sweating is absent, owing to lack of eccrine sweat gland innervation.[103] The inability to sweat leads to problems with body temperature regulation and hyperpyrexia. The disease is present from birth and affects the entire body.[151]

The disease is inherited as an autosomal recessive trait. Molecular genetic research has suggested that the gene responsible for congenital insensitivity to pain with anhidrosis encodes for a tyrosine kinase receptor for nerve growth factor.[101]

Electron microscopy has recently revealed mitochondrial abnormalities in muscle biopsy specimens of patients with congenital insensitivity to pain with anhidrosis.[57] Nerve histopathology shows a loss of the small myelinated and unmyelinated fibers.[225] EMG and nerve conduction velocity studies show slow conduction and decreased amplitudes, especially in the sensory nerves.

Systemic findings include mental retardation, and self-mutilating behavior is frequently a problem.[19] Patients bite their tongues and extract their own teeth.[7] Corneal ulcerations occur as a result of lack of protective sensation.[253] Orthopaedic manifestations are the same as in the other sensory neuropathies, with fracture, nonunions, deformity, Charcot joints, and osteomyelitis seen.[79,122,125,151,223] Recurrent hip dislocation has been described in this patient population and was refractory to conservative treatment with a Pavlik harness. Open reduction with femoral osteotomy failed to prevent redislocation.[86,121] The merit of operative reduction in these patients is questionable.

LESCH-NYHAN SYNDROME

Lesch-Nyhan syndrome is a rare congenital disorder of purine synthesis characterized by self-mutilating and aggressive behavior, mental retardation, choreoathetosis, and hyperuricemia.[134] The syndrome is caused by the absence of hypoxanthine guanine phosphoribosyltransferase (HPRT). It is inherited as an X-linked recessive trait, and therefore is seen in boys.[60] The gene locus on the X chromosome has been identified.[44,208,227]

The diagnosis is made by determining the blood uric acid level, which is elevated in Lesch-Nyhan syndrome. The blood uric acid level should be determined in the diagnostic evaluation of all children with suspected congenital insensitivity to pain. Uric acid crystals are also seen in the urine

of affected patients.[165] Prenatal diagnosis by measurement of HPRT or by molecular genetic testing is possible.[5,75,150,254]

Recently, sural nerve biopsy showed that there was a decrease in large myelinated fibers in a patient with Lesch-Nyhan syndrome.[167]

There is no treatment for this disease at present, but research is currently directed at bone marrow transplantation and potential gene therapy.[58,137] A case report of atlantoaxial instability in two brothers with Lesch-Nyhan syndrome has been published.[214]

SYRINGOMYELIA

Syringomyelia, defined as a CSF-filled dilation of the central canal of the spinal cord, is the most common spinal cord anomaly that can lead to an acquired sensory neuropathy. Presenting symptoms in children with syringomyelia are most commonly scoliosis, with or without back pain, and sensory disturbances, usually in the upper extremities. Decreased pain sensation may be present in the arms and hands, but temperature sensation is usually normal. Unlike in most of the congenital forms of insensitivity to pain, motor weakness in the upper extremities may accompany the sensory changes seen in patients with syringomyelia.[76]

Although Charcot neuropathic joints do not commonly occur in the upper extremities, when a Charcot joint is present, it is usually the result of syringomyelia. There is a predilection for destruction of the shoulder.[80,87,113] Neuropathic joint changes are rarely seen in the hands, but diminished sensation in the hands may result in self-injurious behavior such as multiple burns. Diminished sensation on the trunk in a bandlike dermatomal distribution may be seen. Motor findings are present, and clawing of the hand may be noted on physical examination. Asymmetry of the abdominal reflexes may support the diagnosis of syringomyelia.

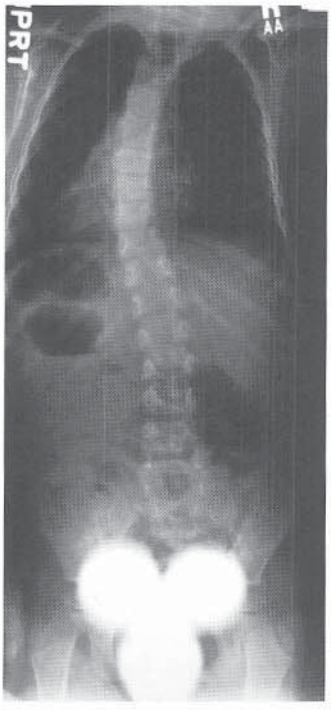
Radiographic findings include scoliosis, which may be upper thoracic in location, lack the typical apical lordosis seen in idiopathic curves, or be convex to the left. The diagnosis of syringomyelia is established by spinal MRI (Fig. 27–16).

Symptomatic syringomyelia is treated either by neurosurgical foramen magnum decompression or by shunting.[93] Sensory changes usually resolve,[231] while the scoliosis may persist, progress, and require treatment in up to 50 percent of cases.[35,63] Treatment of asymptomatic small syringomyelias is usually by neurosurgical observation at our center.

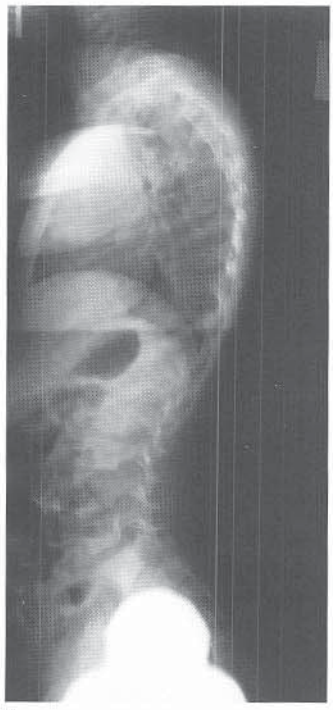
GUILLAIN-BARRÉ SYNDROME (ACUTE POLYRADICULONEURITIS)

Now that poliomyelitis is approaching eradication in most of the world, acute inflammatory demyelinating polyneuropathy, or Guillain-Barré syndrome, is the most common cause of acute flaccid paralysis in children.[12,166] This rare disease is characterized by symmetric motor and sensory paresis of the limbs and, at times, the trunk. The paralysis ascends rapidly and may involve the muscles of respiration and the cranial nerves. The disease was first described by Landry in 1859[129] but was further described by Guillain, Barré, and Strohl in 1916.[78] Guillain-Barré syndrome is quite rare, with an incidence of 0.38 to 1.5 cases per 100,000 population age 15 years or less.[181,186] It is more common in the elderly adult population.

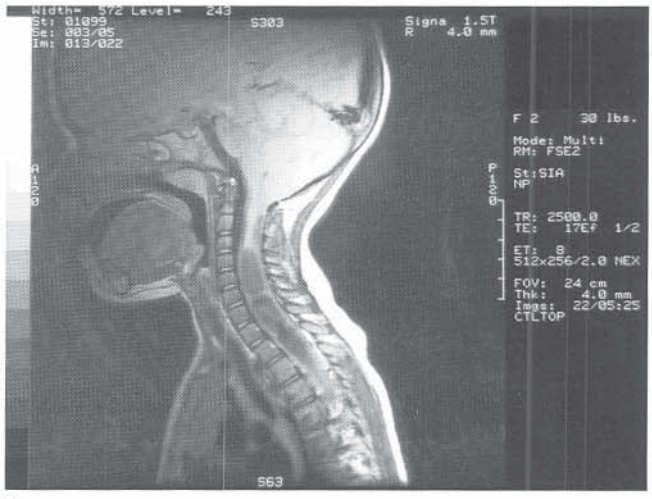
The etiology of the disease is autoimmune and directed against the peripheral nervous system myelin, axon, or both.[61] The disease is triggered by a preceding bacterial or viral illness.[36,71,82] The most frequently identified cause of



A



B



C

FIGURE 27–16 **A,** Left thoracic scoliosis in a 3-year-old girl. **B,** Lateral radiograph showing normal thoracic kyphosis. **C,** MRI was diagnostic for syringomyelia.

Guillain-Barré syndrome is *Campylobacter jejuni* infection.[98] The possibility of vaccinations leading to Guillain-Barré syndrome has been investigated, but no cause-and-effect relationship has been proved.[117,131,184,236] The pathophysiology is an acute demyelinating process. The posterior nerve roots and ganglia, the proximal portion of the peripheral nerves, and the anterior nerve roots are involved. The initial pathologic changes consist of edema, followed by degeneration of axons and myelin with lymphocytic infiltration. In severe cases the peripheral nerves undergo wallerian degeneration.

Diagnosis. The CSF shows a characteristic increase in protein, with a normal cell count. The increase in CSF protein levels peaks at 2 to 4 weeks, then declines.

Nerve conduction is delayed in both the motor and sensory nerve fibers. Sensory-evoked potentials are absent or decreased.[26] Subtypes of the disease have been described based on electrical diagnostic studies.[232]

MRI of the spine shows thickening of the cauda equina and nerve roots. There is enhancement of the intrathecal spinal nerve roots with gadolinium.[42,105] Enhancement of only the anterior spinal nerve roots is strongly suggestive of Guillain-Barré syndrome.[29]

The differential diagnosis includes acute poliomyelitis, transverse myelitis, tick paralysis, and toxic neuropathy.[255]

Clinical Features. There is variation in the mode of onset, the severity of motor and sensory involvement, and the distribution of paresis. Patients may be seen in the emergency room or by a pediatric orthopaedist with acute deterioration in gait or inability to walk. They may also complain of acute severe leg or back pain, and so may be referred to the orthopaedic surgeon.[106,146] Because the child may initially present with inability to walk, and because the paralysis can rapidly ascend, leading to death, it is imperative for the pediatric orthopaedic surgeon to be aware of this rare disease.

Paralysis is usually symmetric and more marked distally than proximally. The deep tendon reflexes are diminished or absent. Motor weakness is accompanied by some sensory disturbance, which varies widely. Bowel and bladder involvement may be seen in severe cases. Cranial nerve involvement is most frequently seen in the facial and accessory nerves. Occasionally, papilledema may be present. Tachycardia and hypertension may be seen.[40] Intelligence is usually preserved.

The clinical course varies with the severity of disease.[85,104] In patients with mild involvement, complete recovery may occur within a few months. In severe forms, recovery may take up to 2 years, and there may be residual paralysis. In very severe cases, all voluntary musculature may become paralyzed, and death may rarely occur from respiratory arrest or pneumonia, particularly in the elderly.[132] The need for mechanical ventilation has been correlated with high CSF protein levels and cranial nerve involvement.[185,203] Death from cardiac arrhythmias due to autonomic nervous system involvement has also been described.[25]

In a multicenter study of 175 patients between the ages of 11 months and 17.7 years, 26 percent of patients remained able to walk, but 16 percent had to be mechanically ventilated at the peak of neurologic involvement. The median time from onset of symptoms to the first sign of recovery was 17 days; to walk unaided, 37 days; and to complete resolution of symptoms, 66 days. There was a large group with a benign course and a smaller group with a more protracted course. At long-term follow-up, 98 of 106 patients were free of symptoms and the remainder were able to walk unaided.[120]

Treatment. Treatment is managed by the pediatric neurologist. Patients are immediately admitted to the hospital and monitored for autonomic and respiratory involvement.[111] Intubation and mechanical ventilation may be necessary in some patients.

Plasma exchange or intravenous immune globulin (IVIG) shortens the duration and severity of the disease significantly when started early in the course of the disease.[61,109,127,141,256] Repeated plasmapheresis works in Guillain-Barré syndrome by removing the pathogenic autoantibodies. The use of IVIG is based on the theory that it may inactivate specific antimyelin antibodies and indirectly inhibit their production.[206] The administration of IVIG has gained favor because of its simplicity and similar clinical results, with clinical improvement noted within 1 to 2.4 days in recent series.[1,5,163] The number of immune globulin infusions necessary to obtain the best results is unknown.[259] Treatment with combined selective plasmapheresis and IVIG administration has also been shown to be beneficial.[88] The efficacy of plasmapheresis or immune globulin therapy in established severe disease is debated.[74,188,209] Corticosteroids are less effective in the treatment of Guillain-Barré syndrome.[120]

The paralyzed limbs are exercised with physical therapy to maintain motion, and orthoses are used as needed to position the joints. When the child regains the ability to walk, orthoses may be helpful to provide support. Tendon transfer or arthrodesis may be useful in the treatment of the child with permanent neurologic deficits, but surgery should be delayed at least 2 years following the onset of the disease to allow for any return of function.[20,72]

SCIATIC AND PERONEAL NERVE PALSY

Etiology. A common cause of sciatic nerve injury in infants and children is intramuscular injections of antibiotics or other medications into the gluteal region. The medication is injected into or adjacent to the nerve as it exits from the sciatic notch and is crossed by the piriformis muscle. The child may be emaciated and have gluteal atrophy, or may be a well-nourished child who is kicking at the time of the inoculation.[21,41,126,239]

Parenteral administration of medications through the umbilical vessels in a newborn may also cause thrombosis of the inferior gluteal arteries and damage both sciatic nerves. The buttock skin may slough in this circumstance.[46,182,212]

Other causes of sciatic nerve palsy include trauma (such as posterior dislocation of the hip)[112] or stretch incurred during femoral lengthening or reduction of the developmental dislocation of the hip.[94,118] The sciatic nerve may also be injured during exposure of the sciatic notch during such pelvic osteotomies as the Salter innominate osteotomy or the Chiari osteotomy.[16,65] Sciatic nerve palsy has been described following intramedullary nailing of the femur and as a result of stretch incurred during hamstring lengthening in children with cerebral palsy and knee flexion contractures.[8] Lastly, the sciatic nerve may be injured during a difficult obstetric

delivery[62,110] or in penetrating missile injuries (gunshot wounds).[226]

Peroneal nerve palsy has been described following resection of proximal fibular osteochondromas,[30,135] after proximal tibial osteotomy for angular deformity,[177,215] and in patients with anorexia nervosa due to direct compression.[139] Patients undergoing application of external fixation for tibial lengthening may develop peroneal nerve palsy as well, and this may be discovered intraoperatively with the use of SSEP monitoring.[69,142] Peroneal nerve palsy has been documented in patients who had early spica cast application for the treatment of femoral shaft fractures[247] and in patients who underwent delayed nailing of shortened femur fractures.[190]

Pathologic Anatomy. The sciatic nerve is made up of the tibial and peroneal divisions. The peroneal division is most prone to palsy, owing to its more superficial anatomic location.

Histology. In sciatic nerve injury resulting from an injection, an acute inflammation of the intraneural and perineural tissues develops first. Destruction of the axons and disappearance of the myelin sheath follow, with eventual fibrosis of the nerve.

Grossly, the nerve appears withered and fibrotic. The nerve becomes adherent to the surrounding fatty and muscular tissues, and there is local hypervascularity.

Clinical Course. Loss of motor function and sensory disturbances occur immediately following injection of the nerve. Usually there is intense local and referred pain in the distribution of the nerve. There may be local gluteal tenderness.

If the peroneal nerve division of the sciatic nerve is selectively involved, dorsiflexion of the ankle and toes and eversion of the ankle are lost, and sensation over the lateral aspect of the calf and the dorsum of the foot is absent. If the tibial component of the nerve is injured as well, the entire foot will be anesthetic and the ankle will be flail. The neurologic injury is maximal immediately following injury, and the paresis will either remain static or slowly improve. Atrophic changes in the lower extremity mirror the severity of the nerve deficit. Muscle wasting, atrophic skin changes, and decreased bone growth with leg length inequality should be anticipated.

Imaging Studies. Routine radiographic studies should be performed to rule out fracture of the lesser trochanter, posterior hip dislocation, and heterotopic ossification when these entities are suspected. MRI of the sciatic nerve can show the inflammation.

Treatment. Thorough documentation of the neurologic deficit is imperative at initial presentation. The neurologic examination is repeated monthly. The prognosis for recovery is good when the paralysis is incomplete initially and when monthly examination reveals improvement in motor function.

Medical treatment usually begins with the prescription of pain medication (usually narcotics) to treat the dysesthesias and pain. Medications to stabilize the membrane of the injured nerve, such as Elavil and Neurontin, may be used under the supervision of a neurologist to decrease the hyperesthesia felt during nerve recovery.

If there is no improvement in motor or sensory function 3 months following injury, electrical studies should be performed to document the status of the nerve. Nerve conduction velocities may delineate early recovery from complete palsy.[66] Tachdjian recommended exploration of the sciatic nerve in children with complete palsy 3 months after injury and in children whose neurologic recovery remains incomplete and who have significant functional limitations due to the residual deficits 12 months after injury. When intraoperative nerve action potential recordings indicate distal transmission of signal, neurolysis may be helpful in regaining motor and sensory function. Grafting the damaged sciatic nerve by using the sural nerve has been studied in adult and pediatric populations with sciatic nerve injury. It was found that young pediatric patients have the best chance of recovering motor function after sural nerve grafts.[234] Protective sensation improves more than the motor strength in these patients, but half of the children were able to decrease their reliance on orthoses for ankle stability.[233] Recovery in the tibial division of the nerve occurs more often than recovery in the peroneal division following surgery.[119]

Similarly, if peroneal nerve function fails to recover by 3 to 6 months following the onset of the palsy, or if nerve severance is suspected from the etiology of the palsy, surgical exploration of the nerve is merited, with sural nerve grafting as needed.[250]

Supportive orthopaedic care consists of prescription of ankle-foot orthoses for treatment of the flail ankle or foot drop. In patients with permanent peroneal nerve palsy, anterior transfer of the posterior tibialis tendon through the interosseous membrane to the middorsum of the foot may restore some dorsiflexion, or at least serve as a tenodesis and improve the steppage gait from the foot drop.[189,196]

It is crucial to prevent sciatic nerve palsy due to gluteal injections. Tachdjian outlined the following preventative measures:

1. Intramuscular injections in the anterior and lateral portions of the midthigh should be made in the quadriceps muscle.
2. If multiple intramuscular injections must be given, rotate them from the right to left sides.
3. Inject into the upper outer quadrant of the buttock if the gluteal site is necessary.
4. Use an assistant to immobilize the kicking child, and observe the site of injection at all times.
5. Pick up the muscle with one hand and perform the injection with the other.
6. Control the depth of penetration and do not use long needles.
7. Double-check the site of injection before and after administering the medication.
8. If repeat injections are necessary, consider an intravenous route of administration.

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