NEUROGENIC ARTHRITIS

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J. Donald Smiley, M. D.

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Patients with musculoskeletal diseases utilize about 10% of the practice time of physicians in the United States(1). The causes of illness in perhaps as many as one-third of these patients may be considered as "neurogenic" (2). The basis for the complaints in these patients range all the way from major psychiatric illness with musculoskeletal conversion reactions to nerve root compression by herniated intervertebral discs or osteoarthritic spurs. Pain, often associated with minimal evidence of objective inflammation, is the most frequent reason that these patients seek medical help. A much smaller group have neurological defects in deep pain recognition or proprioception. All types of neurogenic arthritis may cause physicians problems in diagnosis and management. This important area of rheumatology will be discussed as outlined below.

I. Anatomy and Physiology of Musculoskeletal Pain

- A. Central nervous system "pain centers"
- B. Role of the autonomic nervous system in pain recognition and production
- C. Superficial pain fibers in peripheral and segmental nerves
- D. Deep pain and proprioception in joint tissues

II. Psychogenic Rheumatism

- A. Stress-tension headaches and neck myalgias
- B. Morning stiffness
- C. Fibromyalgia or myofascial pain syndromes
- D. Hysterical conversion reactions

III. Autonomic Dysfunction in Rheumatic Diseases - Reflex Sympathetic Dystrophy

- A. Shoulder-hand syndrome
- B. Sudeck's atrophy, causalgia and minor causalgia
- C. Painful idiopathic migratory osteoporosis
- D. Therapy of reflex sympathetic dystrophy
- E. Relationship to Raynaud's phenomenon, if any?

IV. Peripheral and Segmental Nerve Compression Syndromes

- A. Carpal tunnel, tarsal tunnel and ulnar neuropathies
- B. Thoracic outlet
- C. Painful shoulder
- D. Low back pain and sciatica

V. Deep Pain and Proprioceptive Defects - Neuropathic Arthropathy

- A. Tabes dorsalis (syphilis or diabetes mellitus)
- B. Syringomyelia
- C. Meningomyelocele, spina bifida and dysraphism
- D. Rare causes (pernicious anemia, leprosy, nerve trauma, congenital nerve defects, excess intraarticular steroids)
- E. Relationship to chondrocalcinosis and osteoarthritis

Four rheumatologists located in Boston, Miami, Seattle and La Jolla kept a log of patient diagnoses for new and return visits for two months (Ref. 2). Table I summarizes the distribution seen in 159 new and 577 follow-up patient visits. The impressive finding was the large fraction comprising "neurogenic" arthritis with 38% of new patients and 16% of return patients in this category.

TABLE I. A DESCRIPTION OF RHEUMATOLOGY PRACTICE

	New Visits		Return Visits	
Diagnosis	Number	Per Cent	Number	Per Cent
Rheumatoid arthritis	20	13	306	54
Osteoarthritis	19	12	61	10
Gout	8	5	8	2
Systemic lupus erythematosus	3	2	17	4
Scleroderma	1	-	2	-
Polymyositis	0	0	4	-
Raynaud's phenomenon	3	2	2	-
Polymyalgia rheumatica	6	4	18	3
Ankylosing spondylitis	0	-	6	1
Psoriatic arthritis	1	-	13	2
Reiter's syndrome	1	-	2	-
Neck pains	7		12	
Fibromyalgia (fibrositis)	10		21	
Capsulitis of shoulder	5		18	
Other myofascial pain syndromes	4		7	
Carpal-tunnel syndrome	4	(60) 38	12	(95) 16
Back pain syndromes	30		25	
Bursitis of shoulder	6	4	5	1
Tendonitis other than shoulder	5	3	1	-
Other rheumatic diseases	11	7	28	6
? Arthritis	15	9	9	1
Total	159		577	

Modified from Healey, LA, et al, Arth & Rheum 20:1278, 1977 (Ref. 2)

I. THE ANATOMY AND PHYSIOLOGY OF MUSCULOSKELETAL PAIN (Refs. 3,4,5,6,7)

Muscle, cartilage, tendon or bone can be cut in a normal conscious person with no pain response. However, skin, blood vessels, joint capsules, tendon sheaths and insertions of muscles or ligaments contain stretch and deep pain receptors which signal propioception. If these receptors are excessively distended, deep pain results. Other fine, non-myelinated pain fibers are sensitive to chemical mediators, such as bradykinin, released by inflammation or physical injury. These transmit the signals of sharp pain (pin-prick or knife-like), usually with recruitment of the rest of the nervous system to withdraw, or immobilize and increase blood flow to the injured area. Muscle splinting, erythema, edema and visceral deep pain of a completely different quality then follow. This last phase of the reaction to injury requires the active participation of the autonomic nervous system. It is believed that autonomic functions modulate recognition of pain at three different levels in the nervous system. At the *local site*, autonomic mediators such as epinephrine, norepinephrine and acetyl choline intensify the responses of local pain fibers, creating hyperesthesia. Light touch or pressure, slight cold or minimal movement that would otherwise go unnoticed now become painful.

At the level of the *paraspinal sympathetic ganglia*, autonomic fibers communicate with segments above and below the affected site to cause increased blood flow and muscle spasm which may be painful. Alteration of sweating, blood flow and piloerection in the involved segments emphasize the autonomic component in accentuating the response to painful stimuli. And finally, autonomic fibers communicate with *centers in the hypothalamus* to affect areas even on the opposite side of the body, often at a similar segmental level. The examples of sympathetic ophthalmia or bilateral shoulder-hand syndrome following a myocardial infarction illustrate the potential of the autonomic nervous reflexes, probably working through connections in the hypothalamus to produce serious bilateral inflammatory disease at an anatomical site at some distance from the original injury. In the presence of an intact nervous system both deep (visceral) and superficial pain recognition are monitored by "pain centers" in the hypothalamus and relayed through the thalamus to the sensory cortex.

Sensitivity to pain stimuli is highly variable from one person to another. At one extreme are those patients with the neurological defect of *congenital insensitivity to pain* who may develop neuropathic arthropathy (Charcot joints). Charcot joints also may develop in patients with the complete absence of autonomic function which is found in *familial dysautonomia* (Riley-Day syndrome). These rare experiments of Nature serve to emphasize the protective aspects of pain recognition and the critical role of the autonomic nervous system in amplifying minimal pain or proprioceptive signals.

On the other extreme of pain recognition are patients with *fibromyalgia (fibrositis)*, the bundle-of-nerves-type of patient with myalgias, arthralgias, painful skin and insomnia, all in the face of entirely normal laboratory tests, who overreacts to minor stimuli with such a vengence that the patient, her family and her doctor are made miserable.

Fig. 1
CENTRAL AUTONOMIC PATHWAYS (Ref. 4)

On the right, the course of the sympathetic pathways from the hypothalamus to the cells of the intermediolateral columns of the thoracic spinal cord from which arise the preganglionic sympathetic fibers.
On the left, the origin of parasympathetic fibers in the third and tenth cranial nerves.

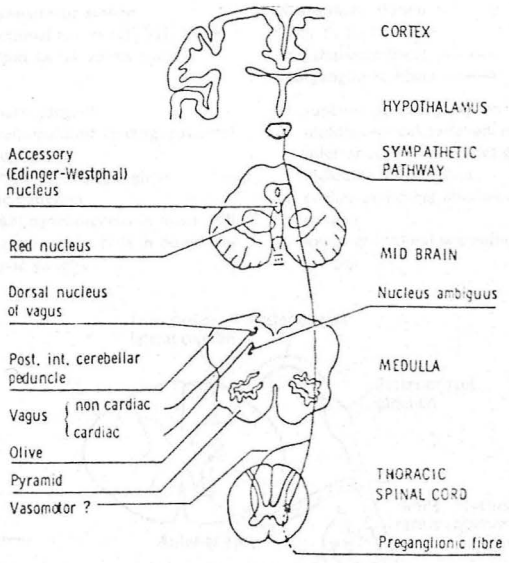
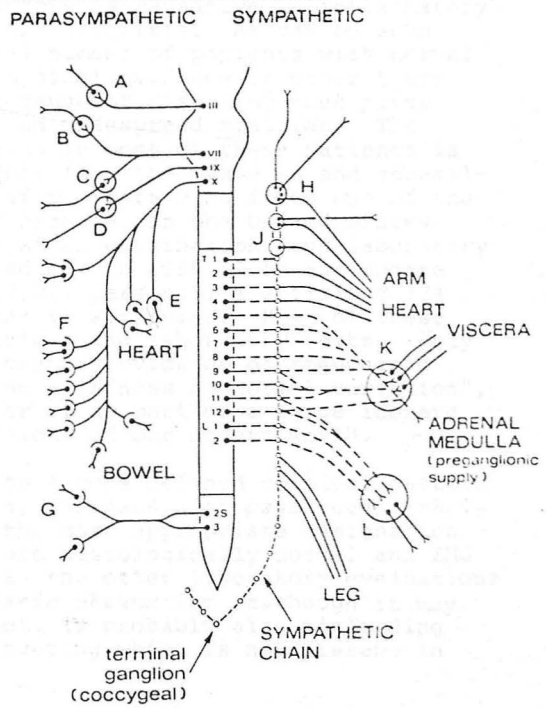


Fig. 2
PERIPHERAL DISTRIBUTION OF THE AUTONOMIC NERVOUS SYSTEM (Ref. 4)

Cell bodies in the intermediolateral cell column have myelinated (preganglionic) axons which pass out in the anterior roots (Fig. 3) to reach the sympathetic chain. This chain of ganglia extends from the base of the skull to the coccyx. Some preganglionic fibers synapse in the nearest ganglia, some pass up or down the sympathetic chain to synapse in other ganglia of the chain and others pass on to synapse in more peripheral ganglia, notably those in the splanchnic area. The ganglia contain cell bodies whose unmyelinated (post-ganglionic) fibers innervate the effector organ. Sympathetic ganglia, unlike the parasympathetic, are not usually immediately adjacent to their effector organ. In the limbs sympathetic fibers normally accompany the major peripheral nerves and are then distributed distally with the arterial supply.

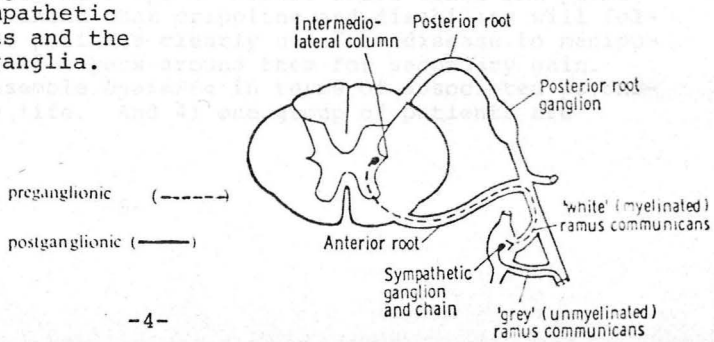


Parasympathetic system
from cranial nerves III, VII, IX, X and from sacral nerves 2 and 3

Sympathetic system
from T1 to L2
preganglionic fibers ------
postganglionic fibers ——

A ciliary ganglion
B sphenopalatine (pterygopalatine) ganglion
C submandibular ganglion
D otic ganglion
E vagal ganglion cells in heart wall
F vagal ganglion cells in bowel wall
G pelvic ganglia
H superior cervical ganglion
J middle cervical ganglion and inferior cervical (stellate) ganglion including T1 ganglion
K coeliac and other abdominal ganglia
L lower abdominal sympathetic ganglia

Fig. 3
Relationship of preganglionic and postganglionic sympathetic fibers with nerve roots and the sympathetic chain of ganglia. (Ref. 4)



II. PSYCHOGENIC RHEUMATISM (Ref. 8,9)

For the most part, the passage of time has markedly diminished the earlier emphasis on psychic factors as causative in inflammatory forms of arthritis such as rheumatoid arthritis. As can be seen from Table I, however, a substantial number of patients with normal laboratory findings, and without physical evidence of other types of arthritis, consult physicians because of disabling *neck pains* often linked to *tension headaches* and widespread myalgias. The cause of the myalgias and arthralgias in most of these patients is poorly understood, yet in its mildest form the myalgias and generalized stiffness seen in this group of patients constitute one of the most common adult complaints. For example, in the United States Public Health Service survey of physical examinations and laboratory tests for rheumatic diseases carried out in 1959-60 on the entire population of Tecumseh, Michigan (7,027 persons), a startling 17% of all adults reported frequent *morning stiffness*. Most of these people had normal physical examinations and laboratory tests. Only about 1.5% showed clinical and laboratory evidence of rheumatoid arthritis. Rather than call morning stiffness a "normal variation", it seems more reasonable to consider it as part of a large iceberg of mild disease related to the tensions of our modern world.

The tips of this iceberg take on a more defined clinical pattern which have been called *fibromyalgia, fibrositis* or *psychogenic rheumatism*. The term *fibromyalgia* is the most appropriate designation since biopsies of painful muscles are histologically normal and EMG and muscle enzyme studies as well as the other laboratory evaluations are also normal. The term *psychogenic rheumatism*, although it may turn out to be etiologically correct, is probably also misleading because it infers hysteria or malingering which is not present in most patients.

Fibromyalgia may be defined as a syndrome of persistent pain in the muscles of the neck, upper back and shoulders with a normal sedimentation rate and without features of other rheumatic diseases. The myalgias are worsened after physical exercise. Fibromyalgia may be associated with arthralgias of large joints and bone and skin tenderness to pressure. The absence of joint changes of disabling arthritis and a disconcerting intensity of pain complaints are also characteristic. The link to an emotional cause for fibromyalgia is based on the reasons: 1) Most patients have a job or home situation which causes chronic emotional distress. 2) Most also have perfectionistic personalities which result in magnification of minimal complaints that most other persons would ignore. They also have a lower pain threshold than most, being more apt to notice small aches and pains and becoming easily convinced that crippling and disability will follow. 3) Another group of patients clearly uses the disease to manipulate their environment and others around them for secondary gain. Their pain responses resemble *hysteria* in terms of associated psychological trauma in daily life. And 4) one group of patients are conscious *malingerers*.

For nearly all patients, *fibromyalgia* results in (or is caused by ?) a cycle of pain, muscle spasm, more pain, often associated with alterations in sleep, bowel habits, and diet which resemble those in non-fibromyalgic depressed patients.

Search for "Trigger Areas" in Myofascial Pain Syndromes

The excellent review by Berges (Ref.8) ties *fibromyalgia* (fibrositis) to a group of *myofascial pain syndromes* which results from acute or subacute muscle trauma related to work or recreational activities. These pain syndromes demonstrate a *trigger area* (sometimes called myalgic spot or myalgic area) identifiable on physical examination and susceptible to treatment by injections of local anesthetic. The trigger area is usually in muscular connective tissue or in a muscle, and is associated with a predictable pattern of pain at a more distant site. Pain, muscle spasm, tenderness, stiffness, limitation of motion, weakness and occasionally autonomic dysfunction occur in the distant site.

Although the neurophysiologic mechanisms are unclear in these myofascial pain syndromes, the treatment with local anesthetic is designed to interrupt the pain-muscle spasm-more pain cycle. Work or recreational patterns of muscle use or abnormal posture may then be altered to eliminate predisposing or precipitating factors and to prevent recurrence of similar attacks.

The diagrams reproduced on the following pages in Fig. 4,5,6, 7,8, and 9 are designed to illustrate the more common varieties of these myofascial pain syndromes, more than one of which may coexist and their treatment with local anesthetic injections. The injection is made with a 25 gauge 5 cm needle. Usually a 10 to 15 ml volume of a solution of 0.5% lidocaine and 0.1% tetracaine with epinephrine 1:200,000 is used. The incidence of toxic reactions has been negligible since the amount injected is relatively small. An additional 25 mg of hydrocortisone is occasionally included in the anesthetic solution. A fan-like approach is made by inserting the needle at the trigger area at different angles as illustrated in Fig. 8 (Ref. 8). Three or four such injections may be necessary to obliterate the referred pain if the condition has been present for some time, but in acute cases, a single injection given soon after an injury may be all that is required.

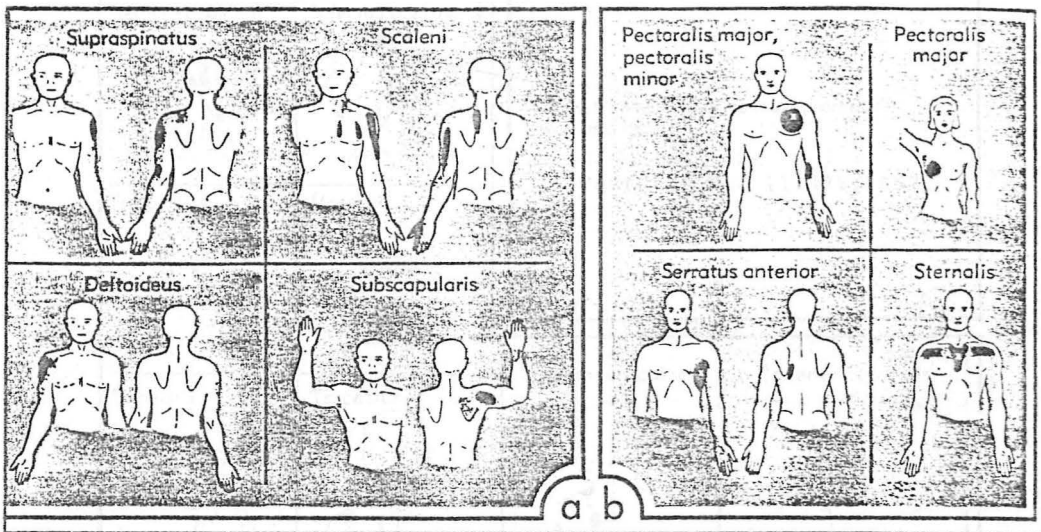


Figure 4. Myofascial pain syndromes of shoulder and arm (**a**) and chest (**b**). X, trigger area; solid black, essential reference area of pain; stippling, spillover reference area of pain.

From Travell and Rinzler. Postgrad Med 11:425,1952

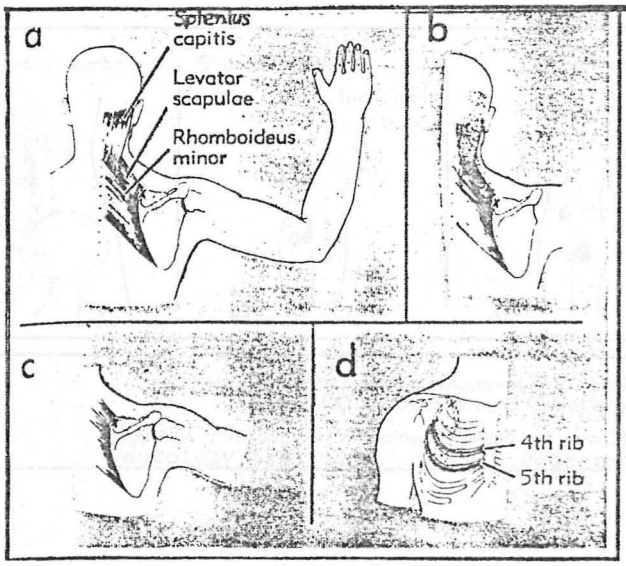


Figure 5. Scapulocostal syndrome radiating toward medial side of extremity and simulating ulnar neuralgia (**a**), in occipital region of posterior part of neck and simulating occipital neuralgia (**b**), in shoulder girdle (**c**), and in chest (**d**).

From Michele AA, Davies JJ, Krueger FJ, et al: Scapulocostal syndrome (fatigue-postural paradox). NY State J Med 50:1353, 1950.

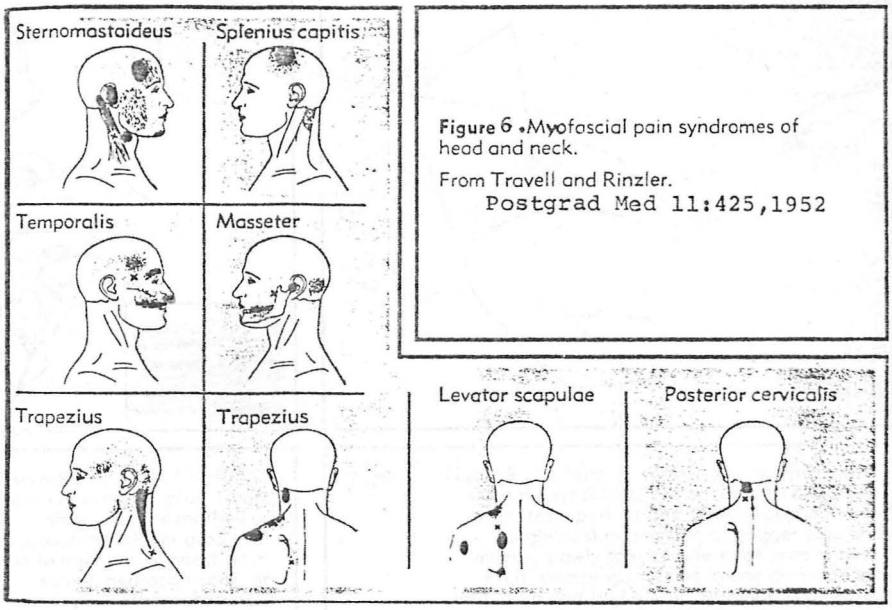


Figure 6. Myofascial pain syndromes of head and neck.

From Travell and Rinzler.
Postgrad Med 11:425,1952

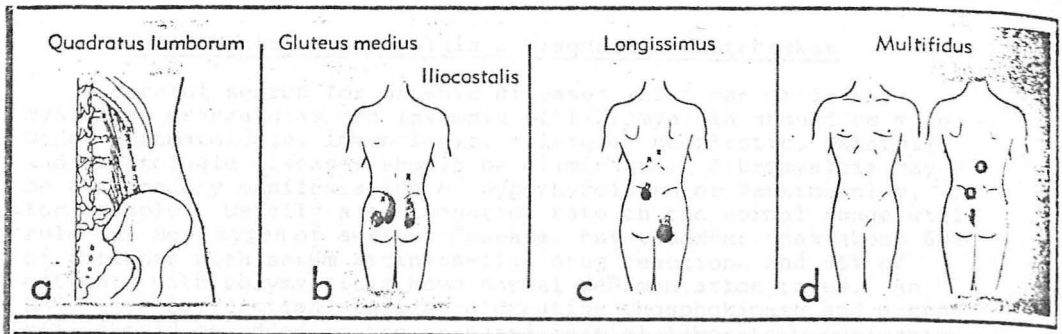


Figure 7. Myofascial pain syndromes of low back. Note location of trigger areas (X) on insertions and lateral edge of quadratus lumborum.

Figure 7a from Sola and Williams; figures 7b, c, and d from Travell and Rinzler.
Neurology 6:91,1956 Postgrad Med 11:425,1952

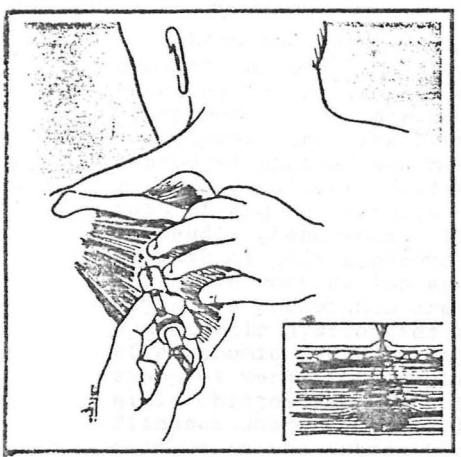


Figure 8. Technic of injecting trigger area in infraspinatus. Insert shows fanlike method of approaching trigger area with needle to inject local anesthetic, saline, hydrocortisone, or other substance.

From Bonica. The Management of Pain. Lea & Febiger, Philadelphia, 1953.

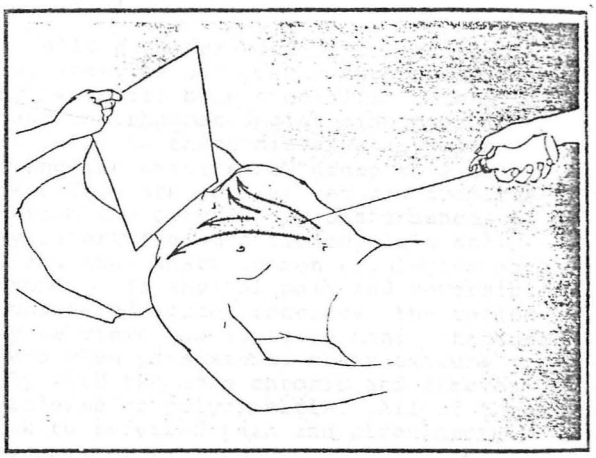


Figure 9. Technic for spraying ethyl chloride for sternalis syndrome. Bottle is held 12 to 18 in. away from patient and spray is applied at an angle to skin, starting at trigger area and moving slowly toward reference area of pain. Even, sweeping motions in one direction are used, as in painting a wall. Spraying is repeated at intervals of a few seconds until entire reference area has been sprayed.

From Travell and Rinzler. Postgrad Med 11:425, 1952

Avoid Making Fibromyalgia a Diagnostic Wastebasket

A careful search for organic diseases which can mimic the myalgias, arthralgias and insomnia of fibromyalgia should be made. Other rheumatologic, immunologic, allergic, neoplastic, metabolic and hematologic diseases should be eliminated. Fibromyalgia may be a secondary manifestation of hypothyroidism or Parkinsonism, for example. Usually a sedimenation rate in the normal range will rule out most types of serious disease, but remember that about 60% of patients with serum sickness-like drug reactions and 65% of patients with polymyositis have normal sedimentation rates. An EMG, thyroid function studies, a creatine phosphokinase and a bone scan should be added to the standard initial laboratory evaluation (CBC, ESR, Urinanalysis, SMA-12, stool guaiac and Chest x-ray) and the usual arthritis tests (RA latex, antinuclear antibody, anti-streptolysin 0, serum protein electrophoresis) to avoid misdiagnosis dangerous to the patient and embarassing to the physician.

III. REFLEX SYMPATHETIC DYSTROPHY

What the cardiologist calls *shoulder-hand syndrome*, the general surgeon labels *causalgia*, the orthopedic surgeon designates *Sudeck's atrophy*, the metabolic bone specialist refers to as *migratory osteoporosis* and the rheumatologist diagnoses as *polycapsulitis*. The French refer to these diseases as "algo-neurodystrophies" and most English writers now group them as *reflex sympathetic dystrophy*. They are not far removed from the pain of angina pectoris or from the circulatory disturbances of Raynaud's phenomenon. They intertwine with fibromyalgia and myofascial pain syndromes, and they share common etiologies with the nerve compression syndromes. If anginal pain and reversible Raynaud's phenomenon are considered acute processes, the reflex sympathetic dystrophies may be viewed as subacute manifestations of autonomic dysfunction, and when persistent, their extreme examples merge imperceptibly with the more chronic and irreversible changes seen in scleroderma or polymyositis. All of these diseases share a common link to referred pain and circulatory changes in the extremities, neck or face potentiated by the autonomic nervous system.

TABLE II. PRECIPITATING CAUSES FOR REFLEX SYMPATHETIC DYSTROPHY

Clinical Syndrome	Frequency %	Probable Causes	(References)
Shoulder-Hand (80% over age 50)	20-27	Myocardial infarction	(12,15,16,17,26)
	20	Cervical osteoarthritis or intervertebral disk	(11,26) (18)
	20	Trauma or surgery	(11)
	5-7	Cerebral vascular accident	(20)
	6-10	Cancer	(25,26)
	rare	I-131 therapy, barbiturates, isonicotinic acid hydrazide	(10,22,24,25)
	rare	Amyotrophic lateral sclerosis, H.zoster	(25)
	10-20	Unknown cause	(11,26)

TABLE II. (Continued) CAUSES OF REFLEX SYMPATHETIC DYSTROPHY

Clinical Syndrome	Frequency %	Probable Causes	(References)
Sudeck's atrophy or Causalgia (50% under age 50)	40	Soft tissue trauma including nerve injury	(11,27,28) (45,46,47)
	25	Fracture	(44)
	20	Post-surgery	(11,23,45)
	rare	Post-myelography	(19)
	15	Unknown	(11)

TABLE III. A LIST OF THE MANY TERMS APPLIED TO REFLEX SYMPATHETIC DYSTROPHY (Ref 10)

Term	Source
Causalgia	Mitchell, 1864, 1872
Sudeck's acute atrophy of bone	Sudeck 1900
Leriche syndrome	Leriche 1914
Peripheral acute trophoneurosis	Zur Verth, 1929
Traumatic angiospasm	Morton and Scott, 1931
Post-traumatic osteoporosis	Fontaine and Herrmann, 1933
Traumatic vasospasm	Lehman, 1934
Reflex dystrophy of the extremities	deTakats, 1937
Minor causalgia	Homans, 1940
Post-infarctional sclerodactyly	Johnson, 1943
Shoulder-Hand syndrome	Steinbrocker, 1947
Neurotrophic rheumatism	Ravault, 1945
Reflex neurovascular dystrophy	Steinbrocker et al, 1947
Algodystrophie	DeSèze, 1954
Reflex sympathetic dystrophy	Evans, 1947
Dystrophic pseudoarthritis	Shilling, 1973

The multiple causes of reflex sympathetic dystrophy range from direct nerve trauma to remote injuries of heart muscle, brain, lungs or thyroid (Table II). These injured tissues may directly inflame adjacent components of the autonomic nervous system, branches of the brachial plexus or peripheral nerves, activating reflexes which pathologically produce pain responses.

Three stages (Ref. 33, 58) in the development of reflex sympathetic dystrophy have been identified. An early *first stage* is associated with localized pain which is aggravated by movement and potentiated by emotional upset, visual or auditory stimuli. The skin is super sensitive, may show intradermal edema, warmth and swelling, or occasionally is dry. Adjacent muscle groups show increased tone and involved joints have decreased range of motion due to periarticular swelling. At this first stage, there is no evidence of osteoporosis by x-ray examination. The first stage of reflex sympathetic dystrophy usually responds promptly after either nerve blocks or vigorous physical therapy. The *second stage* of reflex sympathetic dystrophy is associated with osteoporosis in the involved extremities with more atrophy of the skin which becomes slightly cyanotic, shiny, and waxy in appearance. There is a greater muscle stiffness, restricted range of motion and some degree of atrophy may be present. More extensive involvement of the entire extremity with edema and increased pain are present. Even at this stage of involvement, sympathetic blocks, steroids, and/or sympathectomy are usually effective in promptly relieving the pain and the rest of the syndrome. Recalcification of the bone may require many months. The *third stage* occurs after many months of involvement without treatment, and is associated with atrophy of the skin, loss of muscle mass, and usually fibrous contractures of the involved joints. The skin is quite tight and bound down, very similar to the appearance of scleroderma. Osteoporosis is diffuse and the pain may be extremely severe and more widespread. This third stage responds poorly to nerve blocks or sympathectomy.

TABLE IV. CLASSIC SIGNS AND SYMPTOMS OF REFLEX SYMPATHETIC DYSTROPHY (Ref. 25)

1. Pain and swelling in an extremity
2. Trophic skin changes in the same extremity, including
   a. skin atrophy or pigmentary changes
   b. hypertrichosis
   c. hyperhidrosis
   d. nail changes
3. Signs and symptoms of vasomotor instability
4. Pain and/or limited motion of the ipsilateral (Shoulder-Hand syndrome) extremity

Pathophysiology of Reflex Sympathetic Dystrophy

A debate exists about the cause of reflex sympathetic dystrophy, particularly the Shoulder-Hand syndrome. Moberg (Ref. 13) suggested a pumping action by the shoulder to maintain normal venous and lymphatic flow from the arm. This received widespread support from the orthopedic community (Ref. 14) who pointed out that immobilization in a cast or with bedrest increased the frequency of Shoulder-Hand

syndrome. Myocardial infarction followed by Shoulder-Hand syndrome may also be closely tied to bedrest and immobilization. It was pointed out that immobilization of the shoulder with tendinitis or impaired venous drainage (Ref. 21) with thrombosis of veins around the shoulder can lead to reflex sympathetic dystrophy.

Most studies of reflex sympathetic dystrophy have shown increased blood circulation to the extremities involved (Ref. 29) although later in the course of the disease some impairment of peripheral blood flow may supervene.

Clinically the joint areas are most affected by the disease process. There is greater tenderness in the articular as compared to the interarticular areas. Joints also show the greatest roentgenographic and scintigraphic changes. Both Mitchell (Ref. 46) and Sudeck (Ref. 44) recognized the prominence of the articular changes. Describing patients affected with reflex sympathetic dystrophy as a result of wounds incurred during the American Civil War, Mitchell stated that: "...a painful swelling of the joints... may attack any or all articulations of a member. It is distinct from the early swelling due to the inflammation about the (gunshot) wound itself, although it may be masked by it for a time; nor is it merely a part of the general edema...Once fully established, it keeps the joint stiff and sore for weeks or months. When the acute stage has departed, the tissues become hard and partial ankylosis results...Were we asked to state in what essential respect these lesions differ from subacute rheumatid disease...we should certainly be at some loss to discern a difference."

Synovial biopsy specimens from the more severely affected hand show a unique histologic appearance, characterized by proliferation and disarray of synovial lining cells and by increased numbers of small blood vessels. A mild chronic perivascular inflammatory infiltrate is occasionally noted (Table V, Fig.10,11). Skin, subcutaneous and muscle tissues appear normal or exhibit minor, nonspecific changes and the fascia of affected hands resemble that in *Dupuytren's contracture*. Affected bone is characterized by increased vascularity and prominent osteoclastic activity.

Similar histologic changes have been induced in animals after immobilization of a limb (Ref.30) or by direct irritation of the stellate ganglion (Ref.31). In one such study, histologic synovial changes remarkably similar to those described in reflex sympathetic dystrophy were seen and were associated with local hyperemia (Ref.30). These histological studies, the blood flow measurements (Ref.28,29) and the venous oxygen saturation studies (Ref.29) in patients with reflex sympathetic dystrophy suggest a prominent pathogenetic role of local hyperemia. Such increased blood flow offers an explanation for the severe regional osteoporosis of the entire extremity and for the accentuation of signs of activity in the periarticular areas which are richly vascularized (Ref.32). The involvement of the opposite extremity may then be attributed to a "reflex circulatory" mechanism comparable to that producing osteoporosis in contralateral intact bones of patients with fractures (Ref.32).

Table V. Histologic Changes in the Synovial Tissues*

Case No.	Joint	Synoviocyte Proliferation	Vascular Proliferation	Subsynovial Fibrosis	Synovial Edema	Inflammatory Infiltrate
2	Wrist	1+	0	3+	0	1+
	MCP	1+	0	1+	0	0
4	Wrist	1+	1+	1+	1+	0
	PIP	2+	2+	1+	0	0
5	Wrist	1+	1+/2+	1+	0	3+
	MCP	3+	3+	0	3+	1+
8	MCP	1+	2+	3+	1+	1+
Frequency	Wrists	3/3	2/3	3/3	1/3	2/3
	MCP/PIP	4/4	3/4	3/4	2/4	2/4

* Scale: 1+ Minimal–Mild (Focal); 2+ Mild (Diffuse); 3+ Moderately Severe; 4+ Severe. (Ref. 25)

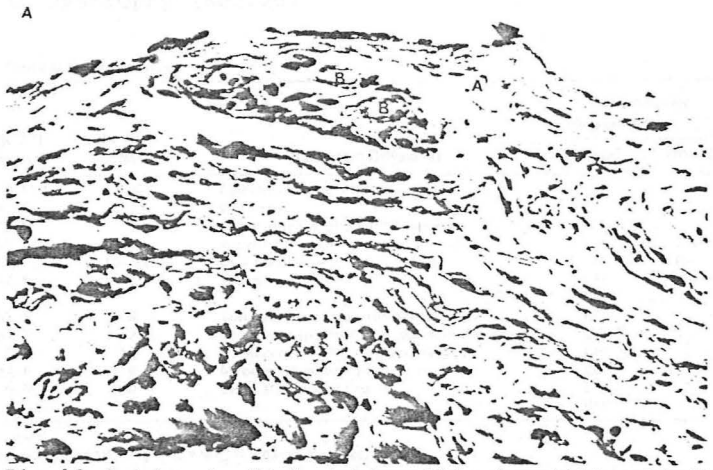


Fig. 10 *Control synovium. Note the single layer of flattened synovial lining cells (**solid arrow**), the loose subsynovial connective tissue layer (A), the number and distribution of synovial capillary blood vessels (B), and the absence of inflammatory cell infiltrate. Mallory trichrome stain, original magnification × 100.* (Ref. 25)

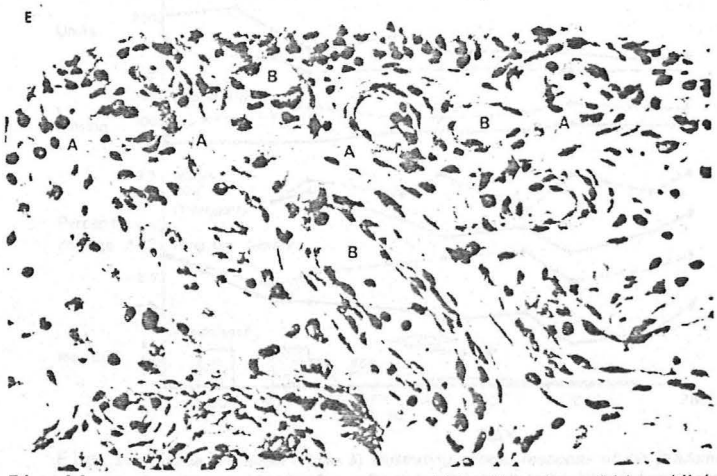


Fig. 11 *Involved synovium, metacarpophalangeal joint. The subsynovial layer (A) is edematous and contains increased numbers of capillaries (B), as well as a few lymphocytes (**solid arrows**). Mallory trichrome stain, original magnification × 100.* (Ref. 25)

"Eleven consecutive patients fulfilling criteria for reflex sympathetic dystrophy were studied by quantitative clinical methods, providing measurements of swelling (ring size), tenderness (dolorimeter) and functional capacity (grip strength). The predominately affected extremity was clearly identified by these technics and its serial progress determined in six patients. Corticosteroid therapy predictably resulted in improvement of all treated patients. Greater tenderness was found in the joints than in the interjoint areas, indicating a possible accentuation of the disease process in juxta-articular tissues. Synovial biopsy specimens in four patients were abnormal, and the histology was presented in detail for the first time. All patients showed bilateral involvement during the study, providing evidence of a central neural mechanism in the reflex sympathetic dystrophy"(Ref.25).

Table VI Clinical Characteristics

Case No.	Age (yr) and Sex	Duration (wk)	Associated Disease (s)	Predominantly Involved Extremity*		Subsequent Evidence of Bilateral Involvement§
				Criteria†	Other‡	
1	69, M	4–6	Carcinoma (bladder) Parkinsonism	RH	...	+
2	44, F	52	Uncertain	LH	...	+
3	66, M	2	Carcinoma (esophagus) hemiplegia	LH	...	+
4	60 F	52	Amyotrophic lateral sclerosis (mild)	RH	LH¶	+
5	58, F	10–12	Cervical osteoarthritis	LH	RH	+
6	47, F	4	Trauma	RH	...	+
				LF		+
7	53, F	8	Tuberculosis of hip, isoniazid therapy	LF	...	+
8	64, M	2	Carcinoma (pulmonary), isoniazid therapy	LH	...	+
9	36, F	12	Cervical osteoarthritis (minimal)	LH	...	+
10	64, F	4	Myocardial infarction	LH	...	+
11	59, M	60	Cervical osteoarthritis	LH	...	+
				RH	...	+

*At initial assessment.
†Criteria in Table II fulfilled (R = right; L = left; H = hand; F = foot).
‡Usually pain.
§Clinical or roentgenologic evidence.
¶In Case 4 apparent bilateral disease developed during study.

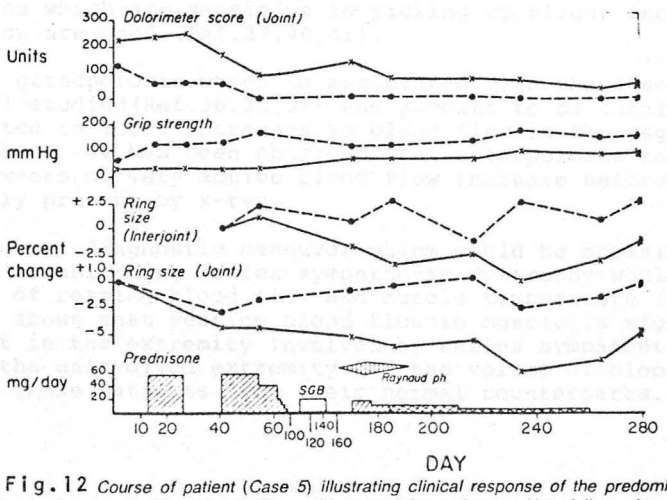


Fig. 12 *Course of patient (Case 5) illustrating clinical response of the predominantly affected (x — x) and contralateral hands (● - - - ●) to prednisone therapy. Note failure of response to serial stellate ganglion blockade (SGB).*

(Ref.25)

"Patchy osteoporosis is the primary roentgenologic manifestation of reflex sympathetic dystrophy. As recent clinical and histologic data suggested articular changes in reflex sympathetic dystrophy, fine-detailed roentgenograms were obtained in eight consecutive patients. Juxta-articular and soft-tissue swelling, osteoporosis and erosions of the subchondral bone were found. $^{99m}TcO_4$ and ^{99m}Tc-EHDP scintigraphy showed localization of nuclide predominately in the juxta-articular tissues.

Serial roentgenographic, scintigraphic and quantitative bone densitometric measurements showed changes that reflected the clinical course of the disease (Ref.35)".

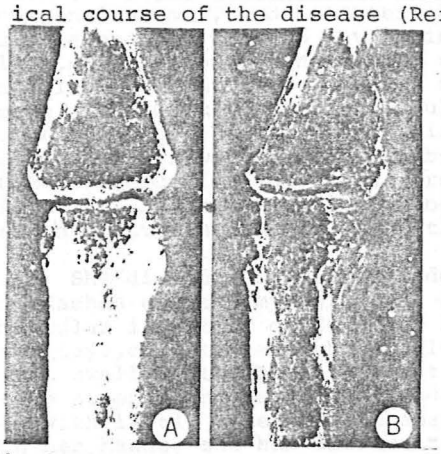


Fig.13 *Sequential roentgenograms in patient before (A) and six months after (B) the development of the RSDS in the left hand (see text). Note the development of reactive new bone and a "crumbling" appearance along with resorption of bone in the endosteal, intracortical and subperiosteal areas*

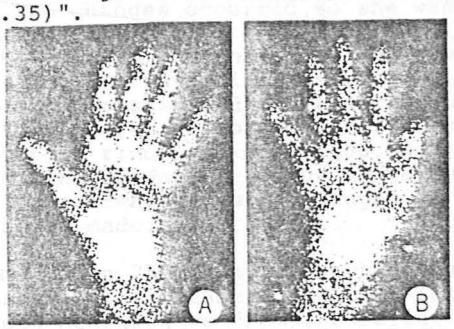


Fig.14 *^{99m}Tc-EHDP scan showing increased activity in all joints of the predominantly affected side (A) compared with the normal contralateral hand (B).*

Reflex sympathetic dystrophy is not limited to the upper extremities but may occur in lower extremities (Ref.33,34) and may also be present bilaterally (Ref.35) although frequently the "uninvolved" extremity shows significant involvement when bone scan procedures which are sensitive in picking up slight increases in blood flow are used (Ref.37,40,41).

The osteoporosis which is associated with the disease has also been well studied(Ref.36,38,39) and appears to be focal in nature and related to local increases in blood flow in the region where bone is absorbed. It has been observed that osteoporosis requires between 4 and 8 weeks of very active blood flow increase before loss of bone is visibly present by x-ray.

A recent diagnostic maneuver which would be occasionally of value in establishing reflex sympathetic dystrophy would be the measurement of resting blood flow and muscle temperature (Ref.79). It has been shown that resting blood flow in muscle is significantly different in the extremity involved by reflex sympathetic dystrophy than in the uninvolved extremity and the volume of blood flow can separate those patients from their normal counterparts.

PATIENT I. SHOULDER-HAND SYNDROME AFTER SILENT MYOCARDIAL INFARCTION

M.T. is a 72 WF whose illness began sometime before July 1976 when she developed exercise related mid-chest pains without radiation which lasted a few minutes and were associated with shortness of breath. An electrocardiogram at St. Paul Hospital was taken which showed "an anterolateral subendocardial myocardial infarction of unknown age". An entirely normal EKG had been previously taken during a physical examination in December 1975. Muscle enzymes, ESR remained normal, and no interval EKG changes occurred, so she was discharged and went on a vacation to California. About August 1, 1976, she developed generalized stiffness and soreness of her arms and legs without fever or skin rash. Her physician observed bilateral pain with movement in both shoulders, wrists, and the small joints of the hands. He obtained a history of severe morning stiffness. Elbows were always normal. Laboratory findings: WBC=7,100, Hgb=11.3, ESR=45, serum iron=34, total iron binding capacity=320, RA latex= negative, LE prep=negative, stool guaiac=negative. A diagnosis of seronegative rheumatoid arthritis was made.

She did not do well on indomethacin 75 mg/day. She had severe headaches and the myalgias and arthralgias became worse. An intramuscular injection of 80 mg of Depo-Medral gave dramatic relief for two days, only to have the shoulder and hand pain return, this time with swelling to the point that she could not make a fist. She then stopped indomethacin (headaches) and took Empirin #3 or Tylenol #3 with little benefit. Because of shoulder stiffness and aching in her hands, she had difficulty sleeping at night and was referred to Southwestern Medical School.

On 10/21/76, she was a thin, intelligent woman with pain in both shoulders associated with spasm of the shoulder girdle muscles. Even with assistance, her arms could not be raised laterally above a 60° angle with the body because of pain and restriction. Compression of the MCP, PIP and wrist joints produced pain. She could not make a good fist and had a weak grip. The backs of her hands were slightly swollen. The creases over the hand joints were less than would be expected for a person of her age. After direct pressure from the examiner, a fingerprint could be seen in the skin between the PIP and the DIP joints compatible with intradermal edema of the skin of the fingers. The elbows and neck motion were normal. Remaining physical examination was normal.

She was diagnosed as having, "shoulder-hand syndrome precipitated by a silent myocardial infarction suffered sometime prior to July 1976", and begun on prednisone 5 mg tid. She also received ferrous gluconate 325 mg tid and ascorbic acid 500 mg tid for her anemia. She was scheduled for an active program of physical therapy for both shoulders.

Within 4 days after starting prednisone, she experienced dramatic improvement in shoulder and hand pain, was able to initiate active physical therapy and to start reducing her prednisone dosage one mg less every three days in daily dosage. By early December 1976, she was completely asymptomatic. She has been able to discontinue steroid therapy without recurrence of her musculoskeletal complaints.

TREATMENT OF REFLEX SYMPATHETIC DYSTROPHY

The initial enthusiasm for physical therapy alone (Ref.42, 62,64,65,66,67,68) has been tempered by a number of failures in management of patients and has led to the addition of steroids to the physical therapy regimen.

Recently, the use of steroids in the treatment of reflex sympathetic dystrophy has gained increasing popularity. This was first suggested by Rosen and Graham who used cortisone in conjunction with active physical therapy with better results than physical therapy alone (Can Med Assn J 77:86,1957) in Shoulder-Hand syndrome. Later, others (Ref.25,26,60,61,62) illustrated the effectiveness of steroids when other measures have been unsuccesful. The selective use of sympathetic blocks (Ref.63,72,74) and occasionally sympathectomy (Ref.48,71) may be beneficial in some refractory patients. Other procedures such as the use of transcutaneous nerve stimulation (Ref.69,70) and the use of local sympathetic blocking agents such as propranolol (Ref.75), guanethidine (Ref.76,77) have been tried with reported success. In addition, recent reports of the use of pig calcitonin (Ref.78) in restoring bone calcium in localized osteoporosis has been described.

PAINFUL IDIOPATHIC MIGRATORY OSTEOPOROSIS

A recently discovered variant of reflex sympathetic dystrophy is painful transitory osteoporosis often with no well-defined cause (Ref.51-59). The initial description of this clinical syndrome was made by Curtis and Kincaid in 1959 (Ref.49) and was more completely described by Duncan and his co-workers in 1967 (Ref.50) as migratory osteolysis of the lower extremities. This variant would appear to be predominately seen in the hip joint, more likely to occur during pregnancy in females but also commonly seen in male patients and associated not infrequently with the loss of bone associated with pain but without bone anatomy deformation. This transitory demineralization is then restored only to reappear often at some other location in the foot or knee. The appearance of transient osteoporosis is associated with normal serum calcium levels and in most published series is associated with normal alkaline phosphatase levels (unlike patient II). However, there have been reports of elevated urinary hydroxyproline and increased urinary calcium excretion at the time of active demineralization in these patients (Ref.55-56), as was true for urinary calcium excretion in Patient II.

PATIENT II. PAINFUL MIGRATORY OSTEOPOROSIS

E.M. This 54 year old WM developed pain in the right hip in December 1976, which progressively increased, particularly with weight bearing. He consulted an orthopedic surgeon who found intrinsic hip disease, an x-ray showing slight osteoporosis, and an elevated alkaline phosphatase of 167 (normal=<85). A bone scan showed increased uptake over the right femoral head. An exploration of the right hip with bone biopsy of the femoral head taken from below, outside of the joint space showed a few plasma cells not compatible with multiple myeloma and slight changes of osteoarthritis. He did not do well following the hip biopsy, and continued to have hip pain for about six weeks. This hip pain gradually decreased, but on February 11, 1977,he began to have pain in his right knee. He then consulted a rheumatologist. All laboratory tests were normal except for a sedimentation rate of 50 and an alkaline phosphatase of 130 (nl=<85). The knee pain continued and a significant right knee effusion developed. This was aspirated and found to be thick viscous fluid, yellowish in color containing 60 WBC/mm^3. He was then given 40 mg of prednisolone tertiary butylacetate into the right knee joint without benefit. Because of the viscous synovial fluid and the osteoporosis in the right hip, ? hyperparathyroidism was raised and metabolic bone studies done, including calcium=9.1, phosphorus=3.7, alkaline phosphatase 110,120, (nl=<85), T3, T4,= normal, urinary calcium excretion on a 400 mg calcium diet=252 mg/24 hrs. (normal=<150), urinary hydroxyproline=48 mg/24 hrs.(mean value for normal adults=32, upper limits of normal=77). He continued to complain bitterly of knee pain. The knee effusion recurred with pain at night even when not weight-bearing. The pain was "like a toothache and affected the whole leg". His knees were again x-rayed and an area of marked demineralization in the medial femoral condyle was found at the site of maximum bone pain. On 4/1/77, a bone biopsy was taken from the right femur at the site of the x-ray bone loss. At surgery, the femur showed extremely soft bone that could be cut with very little resistance. Histology showed "vascular proliferation and scattered mononuclear inflammatory cells in soft tissue portions of trabecular bone". A few fragments of synovium were also seen and showed "chronic lymphocytic infiltration without evidence of tumor". Diagnosis: "Chronic synovitis and chronic inflammation involving adjacent fibrous tissue". "No diagnosis" was attached to the bone biopsy. It was concluded that the patient did not have hyperparathyroidism, that he had a "migratory painful osteoporosis" similar to that described by Dr. Gene Hunder of the Mayo Clinic (Ref.51)

The patient was then referred to Dr. Charles Pak and his colleagues at Southwestern Medical School for further evaluation of the possible hypercalciuria. Their conclusion was that the patient "did not have any identifiable bone disease or hormonal abnormality". He was then treated with high doses of aspirin and progressively improved. He described his pain as "suddenly stopping" on December 11, 1977.

IV. PERIPHERAL AND SEGMENTAL NERVE COMPRESSION SYNDROMES

Carpal tunnel, tarsal tunnel and ulnar (Ref.98,99) neuropathies

Carpal tunnel syndrome is the most frequently encountered peripheral nerve compression syndrome. The most common cause for this, by far, is rheumatoid arthritis (Ref.157). The patient has numbness, dull aching pain, or pins-and-needles tingling in the hand, often radiating proximally up the arm toward the shoulder (Ref.94,95). Almost invariably, the pain will occur at night when the patient lies on his arm during sleep or when driving a car or performing activities requiring slight flexion of the wrist. About 40% of the time, the median nerve compression is bilateral. Physical maneuvers (Tinel's or Phalen's (Ref.83) tests) will usually suggest the diagnosis of nerve compression, but nerve conduction studies (Ref.99) may be necessary if the above tests are equivocal or for quantitation of the degree and permanency of the block. A wide variety of metabolic, hormonal or other disorders may also be associated with carpal-tunnel compression of the median nerve. These include osteoarthritis (Ref.85), physical trauma to the tunnel (Ref.82), amyloidosis (Ref.83), hypertriglyceridemia (Ref.84), pregnancy (Ref.83), median nerve enlargement (Ref.88), osteoid osteoma (Ref.89), thrombophlebitis (Ref.90) myxedema (Ref.91), acromegaly (Ref.92) and abnormal hand muscles (Ref.86,87). Both the median and the ulnar nerve may be damaged by compression simultaneously (Ref.93,96,157). Early carpal-tunnel compression may respond to local steroid injections into the nerve sheath (Ref.83). Treatment of long-standing carpal-tunnel compression may require more than simple surgical incision of the carpal-tunnel. Long-standing or refractory median nerve impairment may respond to *neurolysis* of intraneural adhesions under a dissecting microscope (Ref.97). Isolated ulnar nerve palsy may also be seen in rheumatoid arthritis (Ref.157), scleroderma, or following trauma (Ref.98,99,100). Tarsal-tunnel compression of the sural nerve can also be caused by rheumatoid synovial proliferation or similar pathological processes to those compressing the median and ulnar nerves (Ref.101,157).

Thoracic outlet syndrome

Two excellent reviews of thoracic outlet syndrome have appeared (Ref.102,103). In a series of 40 operated cases of thoracic outlet syndrome (Ref.102) the following diagnostic studies were recommended and carried out in nearly all cases prior to surgery: chest roentgenography to rule out pulmonary disease, sulcus tumor and cervical ribs: cervical spine films to rule out arthritis, fracture, and anomalies: electromyography to locate the level of nerve involvement and to determine if central nervous system disease is present: myelography to establish that cervical disk, cord lesions, and cervical spine deformity are absent: and arteriography to locate the level of arterial compression and to eliminate the possibility of other arterial diseases. The operative treatment consisted of resection of the first rib. The overall results in this series were good. In four cases the results were poor, and no improvement resulted from surgery. The remainder were free of symptoms or sufficiently asymptomatic to allow resumption of activities without limitations.

Because neurologic symptoms are more frequent than vascular ones in the early stage of this condition, nerve conduction velocity studies should be routine in every case (Ref.103). Fifty-nine patients underwent 81 electrodiagnostic conduction studies and Doppler frequency shift evaluations of neurovascular compression through the costroclavicular space (Ref.104). There was a highly significant statistical correlation between normal and abnormal conduction velocities and obstructive changes found with the Doppler unit. Both studies provided significant data in the clinical diagnosis of costoclavicular neurovascular compression disorders. Doppler frequency shift units are relatively inexpensive and may provide a simple, painless, and uncomplicated method of evaluation or screening for costoclavicular neurovascular compression syndromes.

The vascular manifestations of thoracic outlet compression syndrome are rarer than the neurologic manifestations but more serious because they may be progressive and ultimately lead to loss of the limb. The arterial lesion of the thoracic outlet compression syndrome usually begins with the clinical manifestations of peripheral embolization to the digital vessels of the fingers. The sudden, late onset of unilateral Raynaud's phenomenon is typical. Coldness, clumsiness, weakness and color change phenomena may occur, followed by gangrene and intermittent claudication. The technique of choice for angiography is arch aortography by femoral percutaneous catheterization followed by selective catheterization of the right or left subclavian artery. The angiographic appearance in seven cases of thoracic outlet compression revealed complete obstruction from the distal axillary artery onward as the most common finding. Slight fusiform dilitation beyond the bony abnormality was seen frequently without evidence of frank constriction of the artery itself.

Conventional arteriography in the supine position at times may not confirm subclavian compression in patients with unequivocal physical findings of thoracic outlet syndrome. The erect position and weight of the shoulder girdle are important factors in producing the clinical symptoms and findings. Arteriography performed with the patient in erect sitting position should result in positive arteriographic changes in cases in which conventional views have not demonstrated subclavian compression.

Painful shoulder

Painful shoulder is frequently a seriously disabling problem which is misdiagnosed and mistreated. Because the shoulder hurts and is held immobilized, it becomes "frozen" or markedly restricted in range of movement. Often the patient is told that he has "bursitis, tendinitis, or osteoarthritis" and x-rays taken of the shoulder show minimal or normal bone findings (Ref.107,108). It would now appear that *most* of the patients who develop a painful shoulder in the absence of direct trauma have a variant of reflex sympathetic dystrophy which manifests itself as *capsulitis* or have nerve root compression of C5-6 by osteoarthritic spurs or a herniated intervertebral disk. The superimposition of some autonomic nerve component to enhance the secondary pain causes the entire shoulder girdle musculature and arm to ache in many of these patients.

PATIENT III. NERVE ROOT COMPRESSION DUE TO CERVICAL OSTEOARTHRITIS

S.E. This 59 WM was aware of occasional neck pains for approximately eight years, and had had cervical spine x-rays which showed numerous osteoarthritic spurs some of which narrowed the foramina of Luschka. However, he had no significant difficulty until the summer of 1977 at which time he took a trip to Europe, carried heavy baggage, and visited several art museums in which he had to hyperextend his neck to see artwork hung above his head. He began to develop pain in his right arm, particularly noticeable on the volar aspect of the right forearm. This was made worse by looking upwards. Upon returning to Dallas, an attempt at cervical spine traction initially accentuated his pain. He consulted a neurosurgeon who sent him home to rest, gave him a soft cervical collar, and suggested over-the-head traction in bed with a seven pound weight. He also took low doses of aspirin and occasional Valium. However, the neck and arm pain persisted. Cervical spine x-rays, including oblique projections, showed marked narrowing of the nerve foramen at C5-6 and C6-7 bilaterally - worse on the right.

After about four weeks an electromyogram of the right upper extremity was done which showed no positive sharp waves, fibrillations or fasiculations in the right deltoid, biceps brachii, triceps, bracheoradialis, wrist extensors, or the first dorsal interosseous muscles of the right hand. Voluntary motor action unit potentials did show a "marked increase in tall polyphasic voluntaries in the right triceps, bracheoradialis, wrist extensors and first dorsal interosseous muscles" representing a chronic neuropathic pattern consistent with cervical spondylosis causing C6-7 nerve root compression with some involvement also in the C5-6 segment.

Since he had no carotid bruit, cervical traction was continued increasing the weight applied to stretch the cervical muscles more. The traction was applied in a slightly more flexed position. He was also fitted with a Philadelphia-type hard plastic collar to restrict flexion-extension to 29% of the normal range and rotation to 44% of the normal range. He was instructed to use the soft collar at night only. The switch to the soft collar at night was recommended to avoid compression on the suprascapular nerve at the suprascapular notch which would occur if the hard collar were used 24 hrs/day. He was cautioned to discontinue use of the traction if he had vertigo representing impingement on the vertebro-basilar arteries by osteophytes.

He returned on 12/3/77 after using the neck traction having made considerable improvement in the amount of right arm pain. However, he now reported discomfort in the ulnar aspect of the right hand associated with tingling paraesthesias, and hypersensitivity to light touch. Range of motion of the neck remained limited about 20%. Neither thickening of the ulnar nerve at the right elbow nor significant Tinel's sign on tapping over the ulnar nerve at the elbow were found. Nerve conduction study of the right ulnar nerve revealed "a mildly slowed elbow velocity of 48 millisecond". To check for a possible *thoracic outlet syndrome*, a Doppler evaluation of the right axillary artery and vein were done which showed normal arterial and venous sounds in all head positions (See Ref. 104). Interpretation of the ulnar nerve slowing at the elbow was, "either a direct pressure from leaning on the elbow which can occur,

or possible entrapment in the heads of the flexor carpae ulnaris". It was suggested that the patient avoid heavy gripping activity which might cause the carpae ulnaris muscle to increase pressure on the ulnar nerve and accentuate the problem.

This patient is an excellent example of possible multiple levels of peripheral nerve compression beginning in the neck with osteoarthritis as the primary site, but perhaps also involving other mechanisms for peripheral nerve compression of the ulnar nerve.

Back pain syndromes

Backache poses both health and economic problems for a large sector of the general population. Workers engaged in occupations that allow them to sit and to stand for brief periods of time had a low incidence of low back pain, whereas workers sitting or standing for prolonged periods of time had a high incidence (Ref.110). Although they are not helpful in predicting injury, preplacement radiologic examinations of the low back helped to place workers and therefore reduced lost job time and disability payments.

There are a number of pitfalls in the diagnosis of low back and leg pain (Ref.109). Differential diagnosis of low back pain should include cord tumor, spondylosis, Leriche syndrome, and inflammatory lesions.

A psychological profile of patients with low back pain included latent or masked depression, a life-style of invalidism, and repeated challenges to various physicians to diagnose the cause of pain (Ref.111,112,113). Antidepressants and sleep medications are useful in treating these patients (Ref.111). The late results of laminectomy for lumbar disk prolapse appears promising (Ref.114).

V. NEUROPATHIC JOINT DISEASE (Ref. 115, 116, 117)

Etiology and pathogenesis

The diabetic patient with peripheral neuropathy(Ref.126) can stand without discomfort in one position for so long that he causes a pressure necrosis of the skin of the foot leading to deep ulceration and indolent infection. The same defect in deep pain or position sense can affect joints by producing cartilaginous damage (Ref.120,121). Chondrocytes in the deeper cartilage layers then proliferate in an attempt to repair the cartilage injury, and degenerative joint changes which resemble osteoarthritis develop (Ref.156). A small fraction of patients with diabetes-about one out of 600-go on to develop a rapidly destructive arthritis of the involved joint (Ref.122,123). Diabetic neuropathic arthropathy is clinically similar to that described by Jean Martin Charcot in patients with neurosyphilis (Ref.119) in 1868 except for differences in joint distribution.

Since most diabetic or syphilitic patients with severe neuropathy do *not* develop the destructive arthritis, other contributing factors must be necessary. Recently, McCarty and his co-workers (Ref.153,154) have observed that chondrocalcinosis caused by the deposition of calcium pyrophosphate dihydrate (CPPD) in cartilage is an almost universal accompaniment of neuropathic arthropathy. Chondrocalcinosis is many times more frequent in diabetic patients (Ref.155) than in non-diabetic controls, and is usually associated with roentgenological and histological changes of osteoarthritis (Ref.155). It is reasonable to suggest, therefore, that the neuropathy of diabetes predisposes the joints of the foot to cartilage injury, that the injured, now-dividing chondrocytes release inorganic pyrophosphate, and that this leads to CPPD deposition. The CPPD further alters the physical properties of cartilage and degenerative changes result. The remarkable similarity of the early histopathology in cartilage and synovial tissue of neuropathic arthropathy to that found in osteoarthritis emphasizes cartilage degeneration as a common initiating event in both conditions (Ref.155,156). Thus, it is suggested that Charcot joints occur in those occasional patients whose CPPD deposition exceeds a critical level. Since pain recognition is impaired, the patient continues to use the affected joint, cartilage surface is lost, shedding CPPD crystals into the joint space and generating inflammation and synovitis. With absent cartilage the non-cushioned bone then develops microfractures, joint surface destruction and fragmentation (Ref.124,125,127). Intraarticular hemorrhages (Ref.147) follow and the *destructive phase* of the Charcot joint is seen. The degree and location of sensory loss, the relative intensity of physical use of the desensitized joint, the level of cartilage injury and repair and probably other variables in cartilage metabolism all influence the development of neuropathic arthropathy. Very rare patients without demonstrable neuropathology (Ref.129) have been described in whom destructive arthritis indistinguishable from

Charcot joints has developed. Perhaps other genetic or metabolic disorders which predispose cartilage to CPPD deposition could explain the joint pathology found in these otherwise normal patients.

Charcot joints may develop in patients with almost any cause of significant sensory loss except those associated with increased spastic muscle tone. Table I lists the more common causes in the order of their relative frequency in the United States. The rapid decline in the incidence of syphilis will eventually make diabetes the leading cause of neuropathic arthropathy.

TABLE I - CAUSES OF NEUROPATHIC ARTHROPATHY (REF.)

Syphilitic tabes dorsalis (119)	*Familial dysautonomia Riley-Day (130)
Diabetic polyneuropathy (122,123,128)	*Other hereditary neuropathies (117,130)
Syringomyelia (117)	*Thalidomide-induced injury (142)
*Spinal bifida with meningomyelocele (131)	Pernicious anemia (118)
Alcoholic neuropathy (141)	Hemiplegia (134)
Trauma to or surgery of the spinal cord (132,133)	Arachnoiditis after tuberculosis or spinal anesthesia (135,136)
Tumors of the spinal cord (133)	Amyloidosis, paramyloidosis (139,140)
Leprosy (138)	Acromegaly (143)
*Peroneal muscle atrophy (Charcot-Marie-Tooth) (137)	Intraarticular steroid therapy (152)

*More common in children

PATIENT IV. NEUROPATHIC ARTHROPATHY: SYPHILITIC TABES DORSALIS

L.K. (PMH #27 23 51): This 66 WM was admitted on 4/2/71 with a 10-day history of a warm, swollen, tender, left thigh which had become progressively more uncomfortable two days prior to admission. The patient had been followed at Parkland since 1964 with a diagnosis of "neuritis and rheumatism". In 1964, his knee, which was quite unstable, showed bony swelling with spur formation. A VDRL was positive but a lumbar puncture produced spinal fluid which showed a negative Wasserman, no cells and no increase in protein. Neurology diagnosed "tabes dorsalis which was *burned out*" and he was given a brace to stabilize his right knee. Past history included an infectious arthritis of the left knee at age 19, possibly gonococcal arthritis,followed by two years of stiffness and pain in the left knee. In 1955, he fell injuring his left hip without a fracture,following which he had intermittent pain in the left hip when weight bearing. He has also had chronic obstructive pulmonary disease.

On physical examination, he was slightly overweight. He moved his left leg cautiously. The pupils did not react to either light or accommodation and there was irregularity of the right pupil. The patient had a varus deformity of the right knee and a valgus deformity of the left knee. The right knee showed striking bony enlargement, marked crepitance on movement, but was not painful on movement. He resisted movement of the left knee and hip. His left thigh was swollen and had a large hematoma in the upper medial portion of the leg. The skin in the upper leg was tense, tender, and warm. The left hip caused discomfort when fully abducted and internal rotation was resisted. There was a bilateral hallux valgus of both great toes, Heberden's and Bouchard's nodes were noted on the hands. None of the hand or foot joints were tender.

X-rays showed disorganization and fragmentation of the left hip joint with demineralization and multiple loose bodies in the joint. Severe osteoarthritic changes were present in adjacent bone. Propioception was reasonably intact in the upper leg.

Because of the fragmentation of the hip joint in association with marked hypertrophic changes in the right knee and the past history of a definitely positive serum VDRL, this patient is believed to represent an example of syphilitic tabes dorsalis with two Charcot joints. The different time of appearance caused the hip joint to be in the *destructive phase* and the right knee joint to be in *hypertrophic phase* of the disease. The lack of a positive spinal fluid Wasserman in this patient does not rule out syphilitic tabes dorsalis with Charcot joints since penicillin treatment may cause the spinal fluid to revert to negative, but does not alter the progression of the neuropathic arthropathy (Ref.149). Only 80% of patients with Charcot joints related to syphilis show positive spinal fluid Wasserman at the time of their clinically active joint disease.

Pathology

The underlying disease processes responsible for neuropathic arthritis are often present a number of years prior to the onset of the joint disease. For example, diabetes and syphilis usually require fifteen to twenty years before sufficient neuropathy develops to cause Charcot joints to appear. The location of the greatest sensory loss determines the site of the joint destruction. In patients with syphilitic tabes dorsalis, the knee is the most frequent joint involved, but 40% of patients show multiple joint involvement reflecting the wide-spread nature of the sensory loss. Ankle, foot, and hip involvement are common and 6% of patients develop axial spine arthropathy (Ref.116).

Diabetic patients tend to develop Charcot joints primarily in the forefoot (Ref.124,125) in the metatarsal-phalangeal and tarsal-metatarsal joints, with only 12% of patients showing ankle involvement (Ref.127). Only an occasional diabetic patient develops a Charcot joint in the knee, hip or spine. Syringomyelia, which creates sensory loss primarily in the upper extremities, selects the shoulder joint most frequently, followed by the elbow (Ref.146) and the wrist, altogether accounting for 80% of affected joints. Cervical spine involvement is the next most frequent location and multiple joint involvement is also common in syringomyelia (Ref.117) In leprosy, (Ref.118) the joints involved most frequently are the small joints of the hands and feet including the tarsus and wrist joints, again emphasizing the selective nature of the neuropathy in various conditions.

Syringomyelia and leprosy have a high frequency (25% to 29% of patients) of Charcot joint development (Ref.117). Between 4% and 10% of patients with syphilitic tabes dorsalis develop Charcot joints. In diabetes, a wide range (0.11% to 6.8%) of estimates of the frequency of neuropathic arthropathy have been reported (Ref.122,123). Because many of the joints involved in the diabetic foot coexist with adjacent infectious ulcers, a number of series have excluded these patients thereby underestimating the true incidence of Charcot joints in diabetic subjects. Neuropathic arthropathy probably occurs in about 0.2% of adult diabetic patients. Congenital abnormalities of the spine associated with spina bifida and meningomyelocele are the most frequent causes of Charcot joints in children (Ref.131). These defects, even when surgically repaired, often produce damage to nerves serving the lower extremities and predispose these children to neuropathic arthropathy.

The histopathology of the different types of neuropathic arthropathy is similar (Ref.118). Early the features resemble that of osteoarthritis. However, the *destructive phase* rapidly creates such fragmentation of the joint surface and surrounding bone tissue that particles of calcium are implanted in the synovium even at some distance from the major joint surface. An "auto-arthrogram" is occasionally generated in the suprapatellar space or in bursae surrounding the joint (Ref.154).

The synovium proliferates and becomes invasive with large numbers of capillaries in the deeper layers. The macrophages lining the synovial membrane pick up fragments of cartilage and bone, and in some areas these cartilage fragments calcify or even ossify. During the *hypertrophic phase* osteophytes develop and can be fractured to generate large loose bodies which may be numerous. This phase represents an effort to repair the instability generated during the destructive phase. Once the patient has passed through the hypertrophic phase, the joint gradually becomes more stable and rarely reverts to the destructive phase of the disease. At this point, essentially all cartilage surface has been lost and further generation of calcium pyrophosphate dihydrate is lessened.

Clinical Aspects

An unexpected dislocation of a weight-bearing joint (Ref.145) should strongly suggest the diagnosis of neuropathic arthropathy. After a thorough neurological examination which demonstrates the loss of sensation, the diagnosis of Charcot joints involves evaluation of laboratory parameters related to the causes of the disease (Ref.144). Laboratory studies should include VDRL, spinal tap with spinal fluid Wasserman, blood sugar determination, glucose tolerance curves, serum B12 determinations, skull x-rays, and myelograms if syringomyelia is suspected, nerve conduction studies in the peroneal nerve area for Charcot-Marie-Tooth disease and nerve biopsies if Djerine-Sottas disease is suspected. Since the fluid from the neuropathic joint is often present in large amounts and reaccumulates rapidly after arthrocentesis, this may be useful in suggesting the diagnosis. Initially, it resembles the fluid obtained from an osteoarthritic joint with high viscosity and little tendency to clot. This joint fluid usually has a low white blood cell count ranging from a few hundred to 2,000 per cubic millimeter although rare effusions have been described that resemble sterile pus (Ref.116,117). Fragments of cartilage and collagen fibers are often present and CPPD crystals can usually be demonstrated by careful examination under polarized light. As time progresses, there is a greater tendency to bleed into the damaged joint producing an inflammatory reaction similar to that seen in hemophilia (Ref.147). The blood flow to the joint, and indeed the entire extremity may be significantly increased and tense swelling and erythema may appear. The pain is much less than would be expected from the amount of the swelling and inflammation present. In some patients, the joint hemorrhage and bony destruction occur in the complete absence of pain (Ref.147).

Involvement of the spine is particularly likely to occur without symptoms until spinal cord compression supervenes (Ref.132,133). Excessive doses and/or too frequent use of intraarticular steroids may produce joint changes closely resembling Charcot joints (Ref.152). The pain relief provided by steroids, when followed by overexercise of injured joints, may mimic a neuropathic process.

Because the large synovial effusion which occurs in a neuropathic joint may dissect into the adjacent soft tissues, causing

inflammation, this condition may also resemble acute thrombophlebitis in an occasional patient.

Those conditions that mimic neuropathic arthropathy include coagulation disorders which cause bleeding into the joint space, infections with tuberculosis or staphylococci, and neoplasms such as osteogenic sarcoma or chondrosarcoma which may cause extensive bone destruction and also produce hemorrhage into the joint space (Ref.115). Less commonly, gout, pseudogout, rheumatoid arthritis, or psoriatic arthritis may be so severe that they cause rapid joint destruction in a weight-bearing joint (Ref.115)

Treatment

Treatment of the patient with a Charcot joint should be primarily directed at stabilization of the joint involved and thorough instruction of the patient to avoid joint trauma. Sometimes this is very difficult because the patient has relatively little pain in the area of the joint involvement. Reduction in the amount of walking, use of protective shoes, special boots or splints, or even a hip spica to stabilize disintegrating joints allows healing of the numerous microfractures that are present.

Control of the underlying disease in syringomyelia by surgical decompression of the syrinx may allow improvement in the arthropathy. Also, careful management of the diabetes may be beneficial in some patients (Ref.148). Treatment of syphilis with high doses of penicillin does not reverse the progression of destructive Charcot joint changes (Ref.149). Careful treatment of skin ulceration with eradication of local infection is necessary to care for the diabetic foot which develops a neuropathic joint. In patients who have gross anatomical dislocations of joints, transplantation of peripheral nerves or decompression of the spinal cord may be necessary. In occasional patients, the judicious removal of large loose bodies may allow the involved joints to become more stable. Rarely, more extensive surgery may be necessary. Arthrodesis using Charnley's compression clamps or prolonged immobilization in a cast can be very beneficial (Ref.151). The use of gleno-humeral joint replacement has been evaluated in the shoulder of syringomyelia patients and may be helpful (Ref.150). Weight-bearing prostheses in the lower extremity for hip, knee or ankle joint replacement are of doubtful usefulness because of the tendency of these patients to traumatize and fragment bone adjacent to the artificial joint because of their loss of deep pain sensation.

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