

COMPLETE SET OF CASE HISTORIES TEXTBOOK: INTEGRATED NEUROSCIENCES
PART I CASES- PERIPHERAL NERVOUS SYSTEM, SPINAL CORD, EMBRYOLOGY

CHAPTER 2 :OVERVIEW OF LOCALIZATION OF FUNCTION AND DISEASES OF THE NERVOUS SYSTEM

Case 2-1: This 90 year old right handed white male awoke on the morning of admission with weakness of the left side, which was most marked in the leg. The initial admission examination indicated no motor function of the left leg, severe weakness of the left arm and minimal weakness of the left side of the face.

Past history indicated a previous minor “stroke” involving the left side of the body. Although, he had been briefly hospitalized, he had made a full functional recovery with only minimal left sided weakness. He had received treatment of elevated blood pressure for many years.

During the last year prior to admission, occasional periods of confusion had been present and progressive problems in memory had developed.

Neurological examination

1. Mental status:

- a. The patient was disoriented for time and place.
- b. He was however cooperative and able to follow all commands. He was fluent with no disturbance of language function.
- c. His remote memory was excellent. He could repeat the name of the examiner and of his primary physician but could recall neither name after five minutes.

2. Cranial Nerves: a minor left central facial weakness was present.

3. Motor System:

- a. He had no movement of the left leg. There was little function of the left shoulder and elbow, however handgrip was strong and independent finger movements were present.
- b. The patient was recumbent in bed with external rotation of the left leg into a hemiplegic posture.

4. Reflexes:

- a. Deep tendon stretch reflexes were absent in the lower extremities and the left upper extremity
- b. The plantar response was extensor bilaterally (bilateral sign of Babinski).

5. Sensation: pain and position sense were normal

6. Carotid pulses were normal.

Clinical Diagnosis: 1) Acute vascular lesion of the upper one third of the motor cortex, possible anterior cerebral artery occlusion or hemorrhage secondary to amyloid angiopathy. 2) Alzheimer's disease

Laboratory data: *CT scan (Fig. 2-29)* indicated hemorrhage upper Rolandic area probably secondary to amyloid angiopathy

Comment: This patient presents many of the neurological problems that occur in the elderly. The patient had a one-year history of progressive memory problems, which primarily involved the formation of new memories. At age 90 such memory problems occur in more than 50% of the population. Usually, this represents the development of those degenerative changes in the neurons of the cerebral cortex seen in the process defined as Alzheimer's senile dementia.

The patient had elevated blood pressure for many years and had already experienced one “stroke” affecting the left side 10-15 years previously

In the present episode, the sudden development of symptoms would suggest an additional vascular event. Compare this case to Case 1-1 in which the patient had a gradual development of weakness in the leg secondary to a meningioma.

As regards the localization, the marked involvement of leg and proximal arm with relative sparing of hand and face might suggest a process involving the upper half of the motor cortex (refer to **CHAPTER 1 AND CHAPTER 18**)

CHAPTER 4: NEUROEMBRYOLOGY.

Bilateral subcortical band heterotopias: double cortex

Case 4- 1: This 24 year old right handed mother of 2 children and home health aide was admitted to the neurology service after a recurrence of seizures with a flurry of 4 seizures on the day of admission. Seizures

had begun at age 11 and would occur every 2 months. She described the seizures as beginning with an involuntary driving of the head and eyes to the right “as though she was going to look over her right shoulder “. At this point she might experience a sensation of fear. She was aware that involuntary movements of both legs would then occur as well as clonic or tonic movements of the right upper extremity. On some occasions, she would then lose consciousness and a secondarily generalized tonic-clonic seizure would then be witnessed. She had been initially treated with anticonvulsants: phenytoin and phenobarbital, without control of seizures. Carbamazepine was then utilized but produced side effects. She had discontinued all medications 14 months prior to admission.

Family history: negative for neurological or seizure disorders.

Past history: head trauma right frontal with short period of unconsciousness at age 9 years. She had a tubal ligation and bilateral carpal tunnel surgery, 5 years prior to admission.

Neurological examination: mental status, cranial nerves, motor system, reflexes and sensory system were all normal.

Clinical diagnosis: Focal seizures (partial epilepsy) originating left frontal eye field with subsequent spread to left supplementary motor cortex and amygdala (or possibly cingulate gyrus).

Laboratory data:

1. Electroencephalogram: normal

2. **MRI:** bilateral triangular shaped foci of heterotopic gray matter were present in the frontal white matter extending from the superolateral aspect of the frontal horns to the gray white junction superiorly (**Fig.4-1**).

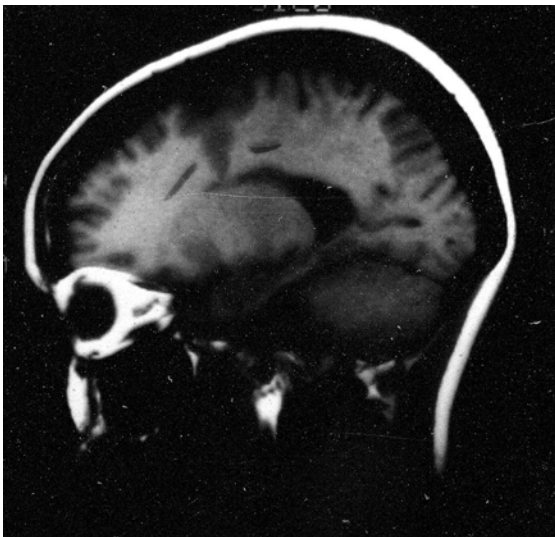


Fig 4-1. Heterotopic Gray Matter;Case 4-1.

Subsequent course: Anticonvulsant medications were re-adjusted. Valproic acid was added to the carbamazepine. Compliance continued to be a problem. She continued to have at least 1 generalized tonic-clonic and possibly several simple partial seizures per year over the next 4 years.

Comment: The description of the initial clinical phenomena and the subsequent evolution suggest initial discharge in the left frontal eye field (area 8) with subsequent spread to the (left) supplementary motor cortex (an area where there is bilateral representation of the lower extremities) .In contrast to the primary motor cortex where simple clonic movements occur on stimulation, complex postures and bilateral leg movements occur on supplementary motor cortex stimulation .The tonic posture or movement of the right arm would also be consistent with such a pattern of spread. The clonic movements of the upper extremity would be consistent with additional spread to the left motor cortex. The sensation of fear could have reflected spread to the limbic system possible by means of the adjacent cingulate gyrus eventually involving the amygdala. The actual pathology in these areas of frontal lobe consisted of heterotopias of gray matter, (termed double cortex or subcortical band heterotopia) a long-standing migration disorder. With the increasing use of the MRI to investigate patients with

seizure disorders, there has been increasing recognition of such migration disorders. This is an X chromosome linked disorder. In the female with 2 X chromosomes, this is a relatively benign disorder. In contrast in the male with only 1 X chromosome, the effects are much more severe, most neurons never reach their expected destination but instead are arrested in the subcortical white matter. The result is type 1 X linked lissencephaly. The cortex is smooth (lissencephalic) since development never proceeds to the stage of sulci and gyri. Sulci and gyri develop normally in the process of accommodating the large number of neurons that would under normal circumstances reach the cortical layers. Such males have severe psychomotor retardation as well as seizures.

Focal heterotopia and megalencephaly temporal lobe

Case 4-2: This 19-year-old right-handed single white female college student was referred for evaluation of an episodic disorder that had begun one year prior to admission. These episodes were described as beginning with a sensation of feeling “spacey and detached with a tingling sensation throughout the body”. At times there was the sensation of “being encapsulated within a box with voices talking but being unable to respond”. Some observers noted she would sometimes stare for a minute and not respond. After a few seconds, she would be observed to become limp, her fists would clench, the lower limbs would flex and the eyes would roll back. During this time according to witnesses, she would be unresponsive, pale and drooling. After a period of unresponsiveness of 5-7 minutes, she would regain consciousness but would be confused and disoriented for 5-6 minutes. At times she had no recollection that episodes had occurred. These episodes initially occurred once per day but were now occurring 5x per day. As a result, the patient had to temporarily drop out of college.

Past history: growth and development had been normal with no significant trauma. She had been receiving birth control pills for irregular menses for 1-2 years.

Family history’s paternal uncle had seizures beginning at age 30 years. A maternal first cousin had onset of generalized tonic-clonic seizures with fever at age 17 years.

Neurological examination: In detail mental status, cranial nerves, motor system, reflexes, and sensory system were all within normal limits.

Clinical diagnosis: Complex partial seizures, probably of temporal lobe origin.

Laboratory data:

1. Initial EEG, 4 months prior to admission had been normal.
2. *EEG, 24 hours after admission with sleep deprivation* during that period demonstrated a focal abnormality in the right temporal area: focal blunt spike discharges suggesting a predisposition to excessive neuronal discharge originating in the right temporal lobe.
3. *MRI:* There was focal enlargement of the right temporal lobe (focal megalencephaly with considerable heterotopia of grey matter in the white matter between the deformed temporal horn of the lateral ventricle and the overlying lateral temporal gyri (**Fig. 4-2a,b**).

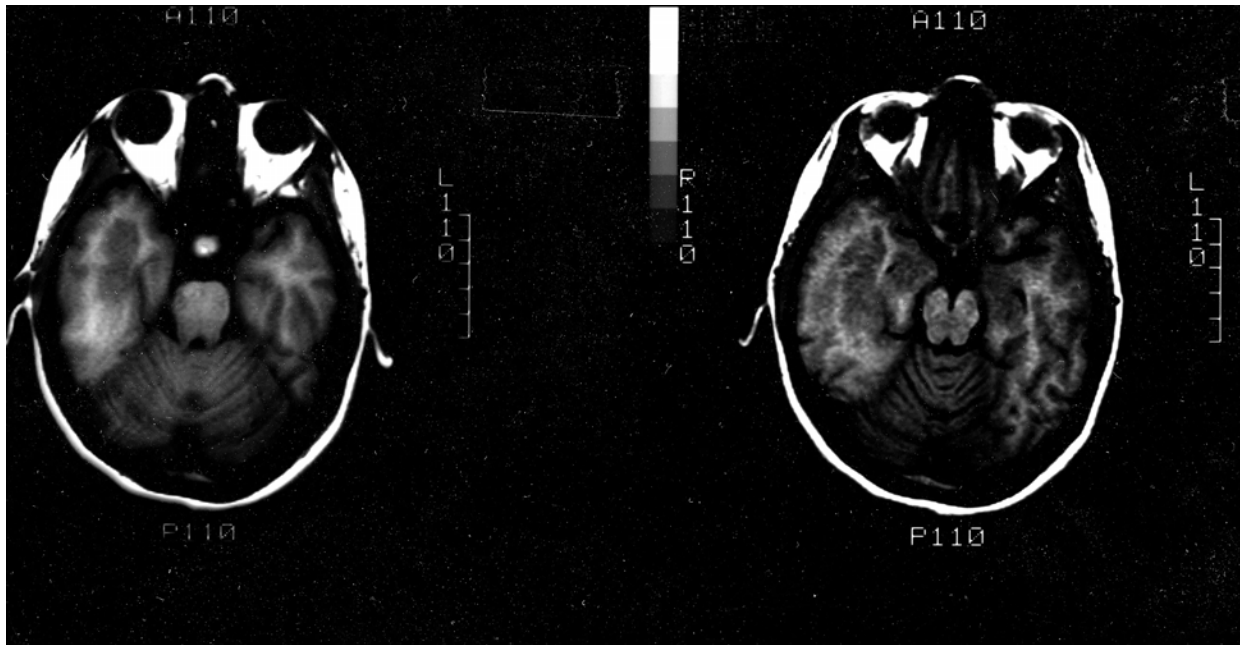


Fig 4-2a;Case 4-2 Focal heterotopia and megalencephaly temporal lobe



Fig4-2b. Focal heterotopia and megalencephaly temporal lobe

Subsequent course: The patient was treated with anticonvulsant medication (carbamazepine) with appropriate therapeutic blood levels and no seizures over the next 4 years of follow up .In addition she received folic acid.

About one year after beginning treatment, she developed an unrelated amenorrhea with elevated prolactin levels and a microadenoma of the pituitary on CT scan. This responded to bromocriptine a DOPA agonist with the lesion disappearing and prolactin levels and menses returning to normal.

Comment: This patient had an unremarkable past history until complex partial seizures developed at the age of 18 years. In general 75% of such seizures are of temporal lobe origin, 25% of extratemporal origin –usually frontal lobe. Initially, the nature of the episodes was unclear because the patient would appear for outpatient visits unaccompanied by witnesses. The patient herself had no memory of the secondary generalization of the seizures and could describe the prodromal events in only a vague and nonspecific manner. It was only when a new neurological consultant was able to interview the actual witnesses that a clear-cut diagnosis of a seizure disorder could be made. The localization to the right temporal area was made on the basis of the EEG. The diagnosis as to the specific pathology was established based on the MRI. Although, this underlying pathology was congenital, the seizures did not appear until age 18. What other factors contributed to the emergence of the seizures at that time will be discussed in later chapters (22, 29).

Agenesis of corpus callosum

Case 4-3: : Patient of Dr. Sandra Horowitz This 20-year-old female warehouse employee was referred for re-evaluation of generalized convulsive seizures that had developed at age 3 years .She had been seizure free for 5 years. She had mild developmental delays. Full scale Wechsler Adult Intelligence score IQ was 82, with a verbal score of 88 and a performance score of 77(all were within low average range). *MRI (Fig.4-3)* demonstrated complete agenesis of the corpus callosum. With associated alterations of gyral and sulcal patterns.



Fig 4-4a. Case 4-3;Agenesis of corpus callosum

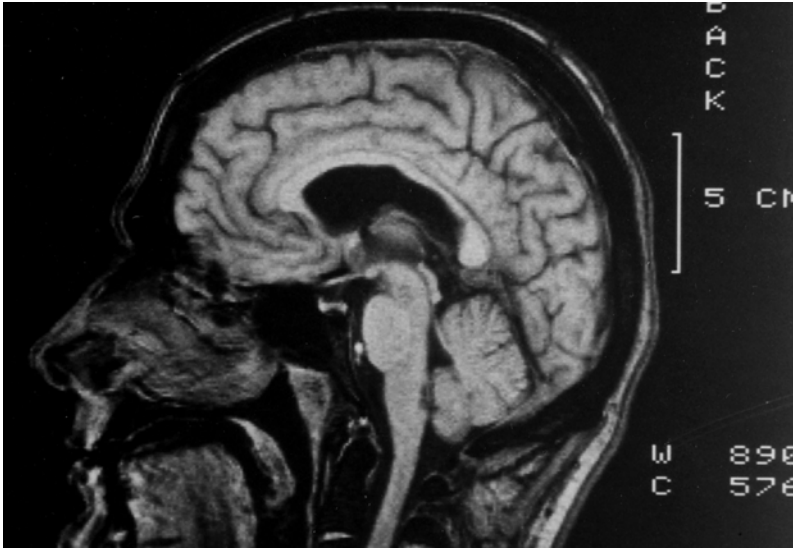


Fig 4-4b . Normal control for 4-3.

Holoprosencephaly

Case 4-4: Patient of Dr. I. Abrams This 10month old white male had severe spastic diplegia (a form of “cerebral palsy”) and severe developmental delays. CT scan (**Fig.4-4**) demonstrated a fusion of the two lateral ventricles and no frontal horns .A large cystic area extended superiorly and posteriorly.

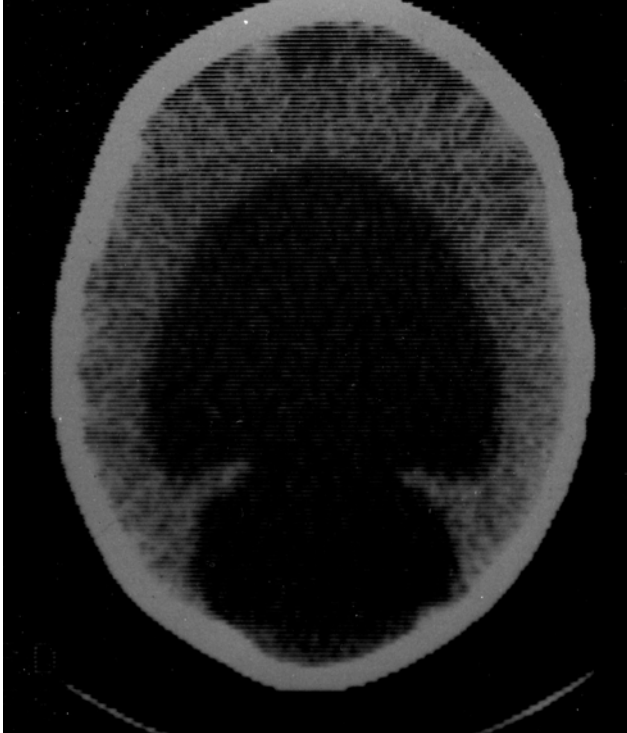


Fig 4-4. Case 4-4. Holoprosencephaly

CHAPTER 6 :DISORDERS OF MUSCLE and NEUROMUSCULAR JUNCTION

Case 6-1 provides an example of a patient with limb girdle muscular dystrophy.

Case 6-1: This 21-year-old white male college graduate was referred for evaluation of bilateral leg weakness. The patient was delayed in walking until age 2. During grammar school, he was the slowest runner in the class and could not keep up with his peers. In high school he first noted minor weakness in climbing stairs. By college he had trouble in climbing one flight. By his senior year, he had difficulty descending stairs. Past history and family history not remarkable.

General physical examination: Unremarkable

Neurological examination: The relevant findings were as follows :

1. Mental status and cranial nerves were normal.
2. *Motor system:* Proximal weakness was present with intact distal strength and normal muscle bulk. At hip¹ strength was 3/5; at shoulders, 4/5. Gower's sign was present in attempting to stand from a recumbent position. Gait was waddling - consistent with proximal weakness at hips.
3. *Reflexes:* Deep tendon stretch reflexes² were absent at triceps and radial periosteal and trace at biceps. Patellar and Achilles reflexes were normal. Plantar responses were flexor.
- 5) *Sensory system:* All modalities were normal.

Clinical diagnosis: Limb girdle muscular dystrophy or a variant of motor neuron disease (chapter 9).

Laboratory data:

- 1) Erythrocyte sedimentation rate (ESR), thyroid studies, and electrolytes were all normal.
- 2) Muscle enzymes, CK, SGOT, LDH and aldolase were all mildly elevated.
- 3) Motor and sensory nerve conduction velocities were all normal.
- 4) *EMG* - demonstrated myopathic features with decreased amplitude and duration of motor units with a full interference pattern on volitional effort.
- 5) *Muscle biopsy* (left deltoid) reported significant dystrophic features: a. Marked variation in muscle fiber size in a random distribution. b. Central position of subsarcolemmal nuclei. c. Significant increase in endomysial connective tissue.

Subsequent Course: Follow Up one year later indicated no progression. Two years later, minor progression was noted with a minor decrease in hand strength. Over the years slow progression occurred. The patient reported at age 38 (17 years after his initial evaluation) that he was still able to walk without assistance. Climbing stairs was a problem. Face and hands were not involved.

Comment: As indicated under neurological diagnosis ,the main differential in these indolent progressive limb girdle disorders is between a myopathic process and spinal muscular atrophy Type III,(Kugelberg Welander disease).The latter disease affects the anterior horn cells ; usually has a somewhat more rapid

¹ The primary grading system for strength is that suggested by the Medical Research Council (MRC) during

World War II: 0=no contractions; 1= flicker or trace of contraction; 2=active movement with gravity eliminated;

3=active movement against gravity; 4=active movement against gravity and resistance; 5=normal power.

The scale is not a linear function- and because of the wide range included in grades 4 and 5 many examiners will grade 4(-), 4, 4(+) and 5(-).

Another less popular approach is to expand the scale into a point scale with grades 0, 1, 2, 3, having the same definition but grade 4-10 representing gradations of the ability against resistance. Such a 10-point scale then readily allows for conversion into %age values. Thus 1=10%, 3=30%, 5=50% etc.

²Deep tendon reflexes are graded as follows: 0=absent; trace=minimally present; 1=hyperactive; 2=normal; 3= hyperactive-brisk; 4=hyperactive-unsustained clonus; 4+ sustained clonus. As above minor gradations maybe superimposed such as 2+, or 3+.

course and will be discussed in chapter 9. In this case the very slow progression, the retention of deep tendon reflexes in the lower extremities and the results of EMG and muscle biopsy were all in favor of a myopathic process. Additional discussion of these less common dystrophies can be found in Padberg 1993.

Case 6-2 provides an example of periodic paralysis.

Case 6-2 (Patient of Dr. Thomas Twitchell): This 30-yr. old white housewife had the onset of episodes of night paralysis at age 9 years. These occurred several times the month but with the administration of potassium supplementation, attacks decreased to 1-2 times per year. At age 29 years, she remarried and was under increased stress. Within 6 months, she began to have frequent episodes of nighttime paralysis again. She could relate her attacks to high carbohydrate meals and cold water exposure as well as to stress. Shortly before the onset of these attacks she had noted a mild persistent weakness in both proximal lower extremities which was non-progressive but did result in difficulty in climbing steps.

Past history and family history: negative.

General physical examination: negative

NEUROLOGICAL EXAMINATION:

1. Mental status: Normal
 2. Cranial nerves: Normal
 3. *Motor system*: There was no atrophy but moderate weakness was found in hip flexors (4/5) and triceps (4/5).
 4. *Deep tendon reflexes*: These were present but relatively quiet at patellar and Achilles. Plantar responses were flexor.
 5. Sensory system: Normal
- Neurologic diagnosis: Periodic paralysis and myopathic process.

LABORATORY DATA

1. *Sedimentation rate, thyroid functions and serum potassium on admission* (3.9 mEq/liter with a normal of 3.9-5.0 mEq/liter). were all-normal. Creatine phosphokinase (CPK) was borderline elevated.
2. EMG and nerve conduction studies were normal

SUBSEQUENT STUDIES AND COURSE: With a baseline potassium of 4.7 mEq/liters, the patient was given 38 grams of glucose solution by mouth plus 5% dextrose in water intravenously plus 15 units of regular insulin. Within 15 minutes after insulin administration, the patient had increased weakness in all four extremities. By 30 minutes, the potassium level had fallen to 2.1 mEq/liter. At 60 minutes, the patient had total paralysis of all four limbs. (quadriplegia) and no deep tendon reflexes could be obtained. She was flaccid unable to lift her head from the bed. However, she was conscious she could speak, and breath and all cranial nerves were intact. EKG did show the typical features of low serum potassium (flat T waves). She was given oral potassium and within 2 hours had returned to her baseline state. She was subsequently treated with potassium supplements plus acetazolamide a drug which affects sodium potassium transport.

Comment: This case of periodic paralysis must be distinguished from the very brief episodes of sleep paralysis which occur in association with the narcolepsy/cataplexy syndrome. In addition cases of primary periodic paralysis must be distinguished from the secondary varieties which occur in relationship to the electrolyte alterations of renal disease, adrenal cortical disease, effects of diuretics, cathartics and in gastrointestinal disorders with severe diarrhea.

The following case demonstrates dermatomyositis complicating ovarian malignancy.

Case 6-3: This 69-yr. old white female two weeks prior to admission developed progressive weakness of all four extremities with proximal more than distal involvement. Because of difficulty swallowing, she had been on a liquid diet for two weeks prior to admission. Past history indicated that three months prior admission she had partial resection of ovarian carcinoma, followed by radiotherapy and chemotherapy.

General physical examination: There was superficial redness, swelling involving the skin of both upper extremities. Liver was enlarged.

Neurological examination

1. Mental status: Intact
2. *Cranial nerves*: Intact except absent gag reflex with difficulty handling secretions.
3. *Motor system*: Weakness of all four extremities proximal greater than distal.

4. *Reflexes*: Deep tendon reflexes were depressed in the upper extremities and absent in the lower extremities. Plantar responses were flexor
 5. *Sensory system*: Intact.
- Clinical diagnosis: Dermatomyositis as a remote effect of ovarian carcinoma.

Laboratory data

1. *Erythrocyte sedimentation rate* was increased to 50 mm per hour; *antinuclear antibody titer* (test for systemic lupus erythematosus) was normal.
2. *Muscle enzymes* (SGOT LDH, CPK) were all significantly increased with creatine phosphokinase elevated to 201/12 units.
3. *EMG*: Abnormal - consistent with polymyositis.

Hospital course:

The patient was treated with high dosage corticosteroids. - (Prednisone). Despite a significant decline in muscle enzymes (CPK from 201 to 9.9, SGOT; 295 to 102 and LDH 320 to 102), the weakness continued to progress. During the last week of life, she had three episodes of aspiration and increasing respiratory distress expiring 7 weeks after onset of neurologic symptoms.

Comment. This patient received a diagnosis of dermatomyositis complicating ovarian malignancy. In such patients deep tendon reflexes may be totally absent. Pharyngeal muscles may be involved. Changes may be present on sensory examination suggesting a peripheral neuropathy, but related to a) paraneoplastic effect of malignancy or b) the effects of chemotherapy. The continued progression of the weakness in this patient is not unusual. The paraneoplastic polymyositis syndrome does not have the favorable response to corticosteroids found in the idiopathic syndrome.

The following case 6-4 provides an example of severe generalized myasthenia gravis.

Case 6-4: This 44-year-old, white, married, machine operator had noted for several years a general sensation of fatigue in his arms and legs at the end of a day. Approximately 6 to 7 weeks prior to admission, the patient began to have more significant difficulty with a marked increase in the degree of intermittent weakness of the arms and legs. At the same time, the patient noted significant slurring of words, difficulty in swallowing, and drooping of the lids. All of these symptoms were transient; they were not present in the morning; they were clearly precipitated by exercise. For example, although the patient would initially have strong chewing movements, as soon as he began to chew repetitively he would develop fatigue of jaw muscles. The degree of ptosis was sufficient to result in difficulty in driving. The patient had been receiving neostigmine 15 mg every 6 hours. He reported that 30 mg every 6 hours produced significant diarrhea and hypersalivation. In addition this dose exacerbated swallowing and chewing problems.

Past history: The patient had a long-standing problem of marked obesity (>300 pounds).

Neurological examination (Four hours after neostigmine 15 mg):

1. Mental status: intact
2. Cranial nerves:
 - a. A significant bilateral ptosis of the eyelids was present. The degree of ptosis was markedly increased by exercise when complete closure of the left eyelid occurred. On repetitive upward gaze, a bilateral weakness of superior rectus developed.
 - b. There was a bilateral facial weakness, worse on exercise, more marked on the right than on the left.
 - c. Jaw movements (opening, closing, and lateral movements) were weak. The degree of weakness was increased by exercise.
 - d. Lateral tongue movements, particularly on sustained pressure, became weak.
3. *Motor system*: There was a significant weakness in shoulder abductors, elbows flexor and extensors, and handgrip. The degree of weakness was markedly increased by repetitive exercise.
4. *Reflexes*: Deep tendon reflexes were symmetrical; plantar responses were flexor.
5. *Sensory system*: All modalities were intact.

Clinical diagnosis: Myasthenia gravis

Laboratory data:

1. Chest x-rays and tomographic studies, thyroid function, and ANA were normal.

2. An *edrophonium (Tensilon) test* was performed. This demonstrated an almost immediate eye-opening effect with the disappearance of the bilateral ptosis. The ptosis, however, had reappeared 3 to 4 minutes after injection of 10 mg of the agent.

Subsequent course: The patient was treated with pyridostigmine and stabilized on a dosage of 90 mg 5 times per day (approximately every four hours). On the dosage his ocular, bulbar and generalized weakness stabilized for three years. Then he developed increasing generalized weakness, bilateral ptosis and respiratory distress and was readmitted in extreme distress with a zero tidal volume. The patient had gradually increased his dosage to 180 mg every three hours. Tensilon test suggested the patient was in a "cholinergic crisis." He was intubated, ventilated and received no medication for 60 hours. Repeat Tensilon test now demonstrated marked improvement in respiratory effort and in skeletal weakness. Pyridostigmine was re-instituted and based on edrophonium tests, the patient was stabilized on 90 mg every 3 hours. A tracheostomy was performed. Thymectomy was considered but the thoracic surgeons considered that the marked obesity constituted too great an operative risk for surgical thymectomy. The patient instead received radiation of the anterior mediastinum, 3000 rads over one month. At the time of discharge tidal volume was now 3000 cc. The patient did well with no additional problems over the next three years. After an exacerbation, he was subsequently treated with long-term prednisone therapy eventually being maintained on alternate day therapy. Thirteen years after his initial evaluation, he had a respiratory arrest followed by cardiac arrest and died after a one-month period of anoxic encephalopathy.

Comment: This patient with generalized myasthenia gravis presented a considerable management problem. At a given dose of pyridostigmine, some symptoms were under-treated, some were well-treated and some were over-treated. Had severe obesity not been present, he would have been a prime candidate for thymectomy. Alternatively, today other means of immunosuppression might be considered (see Keesey, 1998).

CHAPTER 8

Case 8-1 provides an example of a brachial plexopathy and Horner's syndrome in a patient subsequently found to have an apical carcinoma of the lung

Case 8-1: This 57 yr. old right-handed white male retired airport manager was referred for neurological evaluation of progressive pain and weakness left upper extremity plus a left Horner's syndrome. Symptoms began two years previously with mild pain at the left elbow. As symptoms increased, the patient noted one year prior to evaluation a lack of sensation in the ulnar aspect of the left forearm. Eight months prior to admission, the left hand had become swollen and painful. Severe pain on motion at the shoulder also developed. X-rays of hand and shoulder were reported as negative. Chest x-rays reported only minor "old granulomas" at the apex of left lung - (usually taken as evidence of old healed tuberculosis). Six months prior to evaluation drooping of the left eyelid was first noted. Three months prior to admission the patient had the onset of weakness of the left arm. The patient soon noted a decrease in sweating on the left side of face and body.

The rheumatology consultant Dr. Gary Wolf noted additionally a smaller pupil on the left and referred the patient for neurological evaluation.

Past history: The patient had been a heavy cigarette smoker for 30 years (1-2 packs per day) and a "binge" drinker of alcohol.

Physical examination:

1. Distention and firmness of the left supraclavicular area.
 2. Swelling and redness of the left hand and arm with changes in temperature and sweating. (Chronic edema and sympathetic dystrophy)
3. Restriction and pain on motion of left wrist, elbow, fingers with pain.
 4. Blood pressure drop on rapid stand from 170/90 flat to 100/80 standing.

Neurological examination: abnormal findings were present

1. **Cranial Nerves:** A Horner's syndrome was present with mild drooping of the left eye lid (ptosis) a smaller pupil on the left and moderate recession of the left eyeball (the right eye appeared therefore slightly more prominent).

2. **Motor System:** a. Even when the edema of the hand was considered, there was atrophy apparent in the thenar eminence and first interosseous space of the left hand.

b. There was decreased strength in the left upper extremity, which was most marked distally most prominent in the long thumb abductor (radial n.) and short thumb abductor (median n.) and opponens (median n.).

When pain on motion was considered, there was no certainty as to proximal weakness.

c. Minor weakness of the great toe was present bilaterally (Extensor hallucis longus).

3. **Reflexes:** The biceps, triceps and radial deep tendon reflexes were decreased on the left.

4. **Sensation:**

a. Pain sensation was decreased over the left C7 and C8 dermatomes.

b. Pain was decreased in the lower extremities over the feet to the level of the ankles

c. Vibration sensation was decreased at toes and ankles.

Note that the motor and sensory finding in the feet suggested an additional problem of distal peripheral neuropathy.

Clinical diagnosis: Brachial plexopathy and Horner's syndrome due to apical lung tumor (Pancoast tumor)

Laboratory data:

1. Review of previous *chest x-rays* indicated not only the calcifications in the left upper lobe at the apex but also pleural thickness at the apex.

2. Computerized tomography of the lower neck and upper chest after venous injection of the contrast material into the left arm indicated:

a. near occlusion of the left subclavian vein at the level of the first rib.

b. A necrotic mass in the left lower neck posterior to the thymus and carotid sheath and invading the muscular structures of the prevertebral region and arising from or extending to the left apex of the lung.

3) *Nerve conduction and EMG studies* indicated a severe axonal lesion of the lower half of the brachial plexus with a marked involvement of median and ulnar nerves and less of the radial nerve. The cervical 7 and 8 supplied paraspinal muscles were not involved. This localized the problem to the lower plexus and not to roots.

Subsequent course: Biopsy of the left supraclavicular mass revealed adenocarcinoma presumably of pulmonary origin.

The patient received radiotherapy (3000 rads) to the left lung apex and the left supraclavicular area with a decrease of pain and of swelling in the arm. The patient expired 1.5 years after radiotherapy and 3.5 years after onset of symptoms.

Comment: This patient clearly presented as a major problem a neuropathy of the lower half of brachial plexus due to infiltration by an invasive adenocarcinoma of the apex of lung. Malignant tumors of the apex of the lung that involve the brachial plexus and the sympathetic ganglia in this location often carry the name of Pancoast.

The swelling of the arm reflected the occlusion of the venous system draining the arm. The sympathetic changes in the arm and the Horner's syndrome reflected involvement of the chain of sympathetic ganglia.

The distal peripheral neuropathy in the lower extremities may have reflected the previous excessive intake of alcohol -(nutritional) or may have represented a remote effect of malignancy.

Case 8-2 provides an example of a neuropathy of the long thoracic nerve.

Case 8-2: This 29 year old right-handed white housewife was evaluated with a chief complaint of "my right shoulder blade is sticking out". Right shoulder pain began one day after the uncomplicated delivery of her fourth child (without general or local anesthesia). Her arm had not been secured to any arm board. Within 2 weeks she noted transient tingling of the index, middle and ring fingers of the right hand. Within three weeks she first noted prominence of the scapular -winging of the scapula. Any pain had resolved by 6 weeks after onset but the painless winging of the scapula persisted.

Neurological examination: Findings were limited to the following:

Tenderness was present over the right supraclavicular area and in the right axilla (palpation of brachial plexus). In pressing forward against a wall with the outstretched extended right arm there was winging of the medial border of the scapula. The serratus anterior muscle supplied by the lesser thoracic nerve failed to fixate the scapula to the chest wall. The actions of the trapezius muscle were intact (lesions of the accessory nerve supplying the trapezius muscle may also produce winging of the scapula but this occurs on lateral abduction of the arm).

Clinical diagnosis: Long thoracic nerve neuropathy.

Laboratory data: *EMG studies* 10 months after the onset indicated changes of acute and chronic denervation with reinnervation of the involved muscle.

Subsequent course: Follow up several months later indicated no change in her clinical status.

Comment: In many cases involvement of the long thoracic nerve relates to pressure from a knapsack or backpack. However in other cases, the involvement reflects a limited aspect of a brachial neuritis, presumably on an immunological basis. In some cases of brachial neuritis there is a familial predisposition with events such as fever, or pregnancy acting as triggers.

Case 8-3 provides an example of a carpal tunnel syndrome.

Case 8-3. This 83 yr. old right-handed white widow and retired shoe factory worker with a 20-30 year history of rheumatoid arthritis developed an exacerbation of her joint symptoms approximately 1-2 weeks after an influenza immunization. At the same time she had the onset of tingling paresthesia in the palmar area of the left hand and into the median distribution fingers of the left hand: middle, index and ring. The middle finger was most prominent. The thumb was less involved and the fifth finger was not involved. There was pain in the hand particularly on making a fist. She had difficulty-opening bottles with the left hand. The patient had experienced neck pain since 1986. Cervical spine x-rays had indicated considerable degenerative disease.

Physical examination: 1. Blood pressure elevated to 200/90

2. mild inflammatory synovitis in the hands, with mild soft tissue swelling in the wrists, ankles, proximal interphalangeal joints, and metacarpal phalangeal joints.

Neurological Examination: abnormal findings included the following

1. **Motor system:** There was minor weakness in left hand grip and left thumb opponens.
2. **Reflexes:** There was a minor relative decrease in deep tendon reflexes in left upper extremity related to prior cervical disc disease.

3. **Sensory system:** Vibratory sensation was absent at toes but present at ankles reflecting a minor distal peripheral neuropathy or age.

4. **Carpal tunnel:** There was marked tenderness over the left carpal tunnel area with a positive Tinel's sign on palpation or percussion of the median nerve in the carpal tunnel (tingling paresthesias extending from the carpal tunnel into the median nerve supplied fingers).

Clinical diagnosis: Compression of median nerve at carpal tunnel.

Laboratory data: *Nerve conduction studies* indicated severe delays in both sensory and motor conduction for median nerve at carpal tunnel on the left. Mild findings were present on the right.

Subsequent Course: Despite the use of nonsteroidal anti-inflammatory agents, re-evaluation - 2 weeks later indicated additional progression: handgrip was weaker and all the median innervated intrinsic hand muscles were now weak. In addition pain and touch sensation was now decreased in the distribution of the median nerve in both hands. Despite the use of local steroid injections, reevaluation one month later indicated persistence of symptoms, with atrophy present in the thenar eminence on the left. Carpal tunnel surgery on the left hand was performed with improvement of symptoms. When symptoms developed in the right hand, similar surgery was performed with relief.

Comment: The older patient is subject to a multitude of problems that may affect the function of the upper or lower extremities. Thus this patient was subject to cervical disc disease, arthritis, synovitis at the wrist joints and a mild distal peripheral neuropathy. The involvement of the median nerve at the carpal tunnel could however be clearly factored out and treated appropriately. Carpal tunnel syndrome may complicate any process where edema or swelling occurs at wrist or hand: rheumatoid arthritis, trauma, myxedema (Hypothyroid state) or acromegaly (a state associated with excessive production of pituitary growth hormone- see Chapter 16).

The following case 8-4 provides an example of a diabetic mononeuropathy involving the lumbar -sacral plexus. The patient also had a diabetic distal peripheral neuropathy.

Case 8-4: This 75 yr. old right-handed white widow with a one-year history of non-insulin dependent diabetes mellitus had the sudden onset of weakness in the right leg, most prominent at hip and knee, three weeks prior to evaluation.

Shortly thereafter, she had the onset of a severe toothache and like pain in the lateral and anterior surface of the right leg from hip to knee. No symptoms were present in the left leg and no bladder symptoms were present.

Neurological examination: the relevant findings were confined to the peripheral nervous system

1. **Motor system:** Weakness was present in the proximal muscles of the right lower extremity: Hip flexors and extensors 50% of normal (4/5). Quadriceps 40% of normal (4-/5). Hamstring muscles 80% of normal (5-/5).

2. **Reflexes:** Deep tendon stretch reflex was absent at the right patellar compared to left (2+). The right Achilles reflex was 0-trace with reinforcement compared to 1+ on left with reinforcement.

Plantar Responses were weakly flexor

3. **Sensory system:** Pain sensation was decreased in a symmetrical manner over the toes and feet and two thirds of the distance up the calves.

There was in addition a focal deficit in pain sensation over the right third lumbar dermatome.

Vibration was decreased at toes compared to ankles compared to knees in a bilateral manner.

4. **Palpation of nerves:** Significant tenderness was present over both the sciatic nerve at the sciatic notch and the femoral nerve in the femoral canal of the anterior thigh.

Clinical diagnosis: 1. Acute diabetic mononeuropathy: lumbar and to lesser degree sacral plexopathy; 2. Diabetic distal peripheral neuropathy.

Laboratory data: 1. *Nerve conduction studies* indicated slowed conduction over the left sural nerve, absence of conduction right sural nerve and both peroneal nerves - leg to ankle. The *EMG studies* demonstrated acute denervation in sampled muscles supplied by femoral nerve: rectus femoris, vastus medial and iliopsoas. In addition denervation was noted in the right gastrocnemius and the right peroneus longus supplied by major components of the sciatic nerve and to only a mild degree in the L3, L4 supplied paraspinal muscles.

2. *CSF protein* was elevated to 74 mg% consistent with diabetes mellitus and with a polyneuropathy.

Subsequent course: She continued to progress over the next 6 weeks first in proximal muscles then in distal muscles. Evaluation 3 weeks later indicated additional progression in the right leg weakness: greater weakness in previously involved proximal muscles and moderate weakness now in the distal muscles great toe and ankle (70% of normal). Since she had as well a 15-pound weight loss and anorexia, additional studies to rule out pelvic malignancy were obtained with negative results. Re-evaluation 3 months after onset, indicated improvement was now definitely occurring with less weakness. She made good progress until nine months after initial onset of symptoms when increasing weakness developed in the right leg at hip knee and ankle resulting in a fall with a fracture of the right patella and hemarthrosis of the right knee joint. Neurological examination now indicated right hip flexor and extensor and quadriceps at 20% (2/5) with 0 toe and ankle dorsiflexor. There was now a dense sensory loss throughout right leg, affecting all modalities. The patient had minor improvement during a 3-week hospitalization: she was able to ambulate with a walker.

One year after the initial onset of symptoms she had the onset of pain in the left hip area extending into the anterior thigh and then within 2-3 days began to note buckling of the leg at the left knee. Examination now demonstrated on the left, quadriceps was 30% of normal, (3/5) and hip flexors 70% of normal. There was also residual weakness in the right leg: hip flexors and quadriceps 40% of normal (4/5) and right ankle dorsiflexor and everter and toe extensors 10% (1/5) of normal. No deep tendon reflexes were now present in either lower extremity. Tenderness was present over the left femoral nerve in the femoral triangle of anterior thigh.

Because the patient had been receiving anticoagulation for a cerebral embolic event of cardiac origin, a CT scan of the pelvis and abdomen was obtained and this was normal with no hemorrhage into the psoas and iliac muscles. Such a complication of anticoagulant therapy may compress the femoral nerve and lumbar plexus at this point. Slow improvement occurred and the patient was able to return home. Nine months later she was living in her own apartment and was able to ambulate with the use of a cane.

Comment: All of these findings suggested the presence of 1) a mononeuropathy involving the lumbar and to a lesser degree the sacral plexus and the L3, L4 roots contributing to the lumbar plexus (so called “diabetic amyotrophy”), 2) a symmetrical distal peripheral neuropathy predominantly sensory. The mononeuropathy was presumed to be on a vascular basis, the polyneuropathy on a metabolic basis. This case illustrates many of the common peripheral nerve complications of diabetes mellitus. At least 15% of diabetics have symptoms and signs of a peripheral neuropathy, a much larger percentage have asymptomatic findings on examination. In most cases this is a distal symmetrical predominantly sensory polyneuropathy. In this case the initial symptoms related to a mononeuropathy involving the lumbar and to a lesser degree sacral plexus: (diabetic amyotrophy). Despite the vascular etiology for this syndrome, which is often abrupt in onset, it is not unusual for the problem to progress. Eventually the process levels off and slow improvement occurs. However the same syndrome may recur in the same leg or in the opposite leg. In this case, the left lumbar plexus (predominantly femoral nerve) was involved approximately one year after the right leg.

In addition the patient had the findings of a distal symmetrical peripheral neuropathy on a metabolic basis. (See below). Autonomic neuropathies may also occur producing diarrhea, urinary incontinence impotence and orthostatic hypotension.

The following case 8-5 provides an example of an acute post infectious polyneuropathy.

Case 8-5: Approximately two weeks after influenza infection, this 71-year-old right-handed male awoke with tingling of the plantar surfaces of his feet, unsteadiness and weakness at the knees. Over the next 10 days, he experienced a gradual decrease in lower extremity power but no progression of the sensory symptoms. He denied low back pain, bowel or bladder symptoms.

Neurological examination:

1. Mental status and cranial nerves: Intact.
2. *Motor system:* Weakness was present in the lower extremities both proximal and distal slightly greater on right than left. A minimal dysmetria was present in the upper extremities.
3. *Reflexes:* All deep tendon stretch reflexes were absent in upper and lower limbs except for a trace triceps. Plantars demonstrated no response to stimulation.

4. **Sensory system:** There was a mild decrease in pain and temperature sensation over toes. Perianal sensation was normal. To a greater degree, position and vibratory sensation were decreased in the toes.

Clinical diagnosis: Guillain Barré syndrome: acute post infectious polyneuropathy.

Laboratory data:

CBC, glucose, renal functions, liver functions, electrolytes, protein immunoelectrophoresis and ESR (40mm/hr) and MRI of the spine were all normal. *CSF: protein* was increased to 206 mg%, with 0 white blood cells and a glucose of 76mg%. *Serological tests and cultures* were negative. EMG/nerve conduction studies demonstrated slowing of motor nerve conduction velocity. - consistent with a demyelinating neuropathy.

Course: the patient's condition stabilized and he was transferred to a rehabilitation facility.

Case 8-6 provides an example of a patient with autosomal dominant Charcot Marie Tooth disease and slow nerve conduction consistent with type 1A.

Case 8-6: This 50 year old, single, white male was referred for evaluation of progressive weakness of the legs. The patient had a deformity of both feet all of his life which produced difficulty when walking for much of his life. He related this to weakness in feet and difficulty with balance of feet. The patient had developed at some time in the early grade school years difficulty in hands, primarily a weakness in movements of fingers and grip. He felt that he had some atrophy of hand muscles all of his life. Approximately 10-12 years prior to admission, the patient began to note a progression in weakness of his hands. During the last year or two prior to admission, the patient had noted increased difficulty in movements of feet, difficulty in lifting toes and feet. He denied any specific numbness in hands and legs.

Family history was significant. The patient's brother had a similar deformity of the feet (pes cavus). In addition, the brother had weakness and lack of control of the feet. The patient's mother and grandmother had similar difficulty with foot deformity and weakness in lower extremities. In a collateral line involving many cousins for four generations, multiple family members had developed difficulty in their feet as children, somewhat later in life had developed weakness in feet and occasionally had developed at age 35 or 40 difficulty with weakness and atrophy of hands. In most of these family members, some progression of disability began to occur between the ages of 35 and 50. This was confirmed by the evaluation of a first cousin who developed numbness in foot, foot drop and imbalance in walking at age 30 and weakness and atrophy in the hands at age 35. His examination was similar to the patient in this case.

Neurological examination: mental status and cranial nerves were intact.

1. Motor system:

- a. strength was intact at hip and knee but markedly decreased at ankle dorsiflexors and everter. In upper extremities, shoulders, elbows, and wrists were intact as regards strength; however, all movements in hands were weak without any selectivity as to ulnar, radial, or median. Thus, finger abductors; thumb abductors, opponens and thumb adductor were all weak.
- b. There was atrophy of intrinsic muscles of hands with marked atrophy in the first interosseous space. There was flattening of thenar and hypothenar eminences. Bilateral pes cavus, deformity of the feet was present with slight in turning of both feet at ankles.

2. **Reflexes:** Deep tendon reflexes were everywhere absent and there was no response to plantar stimulation
3. **Sensory system:** pain sensation and touch were decreased in lower extremities to just below the ankles, but intact in the upper extremities. Vibratory sensation was absent at toes and ankles but present at knees and slightly decreased at fingers compared to wrists. Rare errors were made in position sense at toes.

Clinical diagnosis: peroneal muscular atrophy (Charcot Marie Tooth disease)

Laboratory data:

- 1) *Nerve conduction studies* indicated marked slowing of motor nerve conduction velocity in the upper extremities (median and ulnar nerves were studied) consistent with a demyelinating process. *Sensory evoked potentials* were absent. No responses were obtained on stimulation of the peroneal and posterior tibial nerves in the lower extremities.
- 2) *EMG studies* indicated neuropathic changes of denervation: fibrillations.

3) *Muscle biopsy* of calf muscle. (gastrocnemius) was consistent with a neuropathic process: grouped muscle atrophy (similar to **fig 8-16**).

- 4) *Sural nerve biopsy* - indicated that large fiber axons were reduced in number and occasionally fragmented. There was an apparent marked increase in small fiber axons.

Subsequent Course:

Over the next 16 years the patient had a very slow progression. At the time of his death in 1984 at age 66, (apparent cardiac arrest during a minor surgical procedure) he was still able to walk slowly without assistance or the use of a walker or cane. He occasionally did need assistance in rising from a chair. He was able to live by himself and to prepare his own meals.

Comment: This patient presented a slowly progressive peripheral neuropathy that was predominantly motor. The extensive family history suggested an autosomal dominant disorder. The nerve conduction studies were consistent with a demyelinating disorder. This patient would now be classified as CMT 1A.

The following case history(8-7) provides an example of a lumbar root compression secondary to a herniated disk.

Case 8-7: This 37 year old right-handed white female day care worker in relationship to heavy lifting had the acute onset of in the lumbar sacral area shooting as a sharp pain into the left buttock. With therapy she had slight improvement. **One month** later she developed numbness left posterior thigh and left posterior calf to the ankle. Despite light duties at work, she developed 4 months after onset of symptoms, the acute onset of severe pain in the lumbar area now extending to the posterior thigh and subsequently to the posterior calf as a shooting pain. Tingling parathesias now extended into the small toes. The pain in the leg was triggered by coughing triggered by coughing or straining at stool. Despite a prolonged period of bed rest, pain medication and non steroidal anti-inflammatory agents ,no improvement occurred.

Neurological Examination demonstrated the following features(initial neurological evaluation at 6 months after onset of symptoms)

1. *General:* The patient was tearful and in apparent severe pain. She walked with an antalgic gait .She was uncomfortable sitting and was a little more comfortable recumbent on the exam table with the knees in a slightly flexed position.
2. *Motor system:* Calf circumference was 33 cm on the left compared to 35 cm on the right. Significant weakness was present on the left at toe extensors, ankle dorsiflexors, everters and inverters.
3. *Reflexes:* The Achilles deep tendon stretch reflex was absent on the left compared to active (3) right Achilles and both patellar reflexes.
4. *Sensory system:* Pain sensation was markedly decreased on the left side over the L5 and S1 dermatomes and to a considerable degree over S2-5.
5. *Maneuvers:* On straight leg raising ,pain was present in both leg and back at 45-50 degrees on the left .
6. *Lumbar spine and peripheral nerves:* On palpation, there was marked tenderness over the left sacroiliac area and over the left sciatic nerve at the sciatic notch and over the left posterior tibial nerve behind the medial malleolus of the ankle.

Clinical Diagnosis: Massive rupture of disk with involvement of L5,S1 and cauda equina.

Laboratory data : *Plain lumbar spine X-rays* ,1 month after onset of symptoms demonstrated narrowing of the L4-L5 disk interspace. *Immediate MRI,(Fig 8-20)* demonstrated a massive rupture of the disk at the L4-L5 level with inferior extension and marked compression of the cauda equina .

Subsequent course : Because of the severity of findings and the persistence of symptoms ,immediate MRI and neurosurgical consultation were obtained .The patient however , delayed undergoing the recommended surgical procedure. She finally underwent a removal of the ruptured disk ,5 weeks after the initial neurological evaluation. Neurological followup over the next three years indicated that some relief of pain had occurred but she continued to have a foot drop with significant weakness at left ankle and toes, an absent left Achilles reflex, and sensory deficits over the left L 5 distribution. A follow up MRI scan showed only a minimal bulge at L4-L5 interspace with no evidence of nerve root compression.

Comment: The significant factor in this case in establishing the diagnosis of a root compression due to a herniated disk was the historical information regarding the nature and distribution of the pain and tingling paresthesias. The findings of tenderness over the sciatic nerve and its branches and the findings on straight leg

raising were consistent with a radiculopathy. The severe degree of weakness, the depression of the Achilles deep tendon reflex and the wide spread sensory deficit suggested that several roots of the cauda equina had been involve by this massive rupture at the L4-L5 interspace. Most patients with restricted lateral disk herniation at this level will have more limited findings usually involving only the L- 5 nerve root. In patients with long standing severe deficits , surgical therapy is often not successful in reversing all of the neurological deficits

Most patients (75%) with a more limited lumbar radiculopathy respond to a period of strict bed rest for 3 to 5 days on a firm mattress and bed board, nonsteroidal anti inflammatory agents, heat or cold and possibly the temporary use subsequently of a back support. Those who fail this therapy may require local steroid injection or surgical therapy. Only if surgical therapy is a consideration should MRI studies be obtained.

Benign non malignant back pain alone, either acute or chronic is an extremely common complaint Usually it is benign in nature. However a complete history and general physical examination is indicated .to identify immediate precipitating events. In addition ,a survey of ,any past history of malignancy , or change in bowel habits, or urinary pattern or in menses etc must be obtained .If such a survey is negative and no neurological symptoms or signs are present , then neurological consultation and lumbar MRI scan are not indicated .Plain films of the lumbar spine will usually suffice to rule out orthopedic disease. Such benign back pain does not require a course of bed rest .Non steroidal anti-inflammatory agents , modification of posture, heat or cold and weight loss if indicated are appropriate measures,. Activities at work may have to be temporarily modified, use of a support belt or corset may be indicated.

For cervical radiculopathy, at home cervical traction, a cervical collar, cervical ,pillow and, nonsteroidal anti inflammatory agents are usually effective. Most(75%) patients will usually respond to these measures. When these measures fail and radicular symptoms and findings persist, surgical therapy may be considered. At such a time MRI scan is appropriate.

The following case history 8-8 demonstrates the effect of a ruptured cervical disk producing compression of a cervical nerve root.

Case 8-8:This 45 year-old right-handed married white female employed as an educational coordinator was referred for neurological consultation with regard to pain in the neck radiating into left arm with extension into the index and middle finger of the left hand. The symptoms had been present for 2 weeks. The patient estimated that approximately 30% of her pain was in the neck, 30% in the scapular area and 40% in the arm. The pain would shoot into the arm is she coughed or sneezed or strained to move her bowels. The patient had also experienced tingling in the index and middle finger of the left hand but was not aware of any weakness in the hand. 4 months previously the patient had experienced pain in the neck extending to the left shoulder area but that symptom had cleared. Cervical spine x-rays at the time demonstrated narrowing of the C 6-C7 interspace with encroachment on the neural foramen at that level. She had no leg or bladder symptoms. In the last several days prior to consultation the patient had developed twitching of biceps and triceps muscles.

Neurological examination:

1. *Mental status, cranial nerves, and motor system:* All were intact.
2. *Reflexes:* The left triceps deep tendon stretch reflex was absent or reversed. All other deep tendon reflexes and plantar responses were intact.
3. *Sensory system:* Pain sensation was decreased over the left index and middle fingers.
4. *Neck:* Rotations were limited to 45 degrees and pain was present on hyperextension. There was tenderness over the spinous processes of C 7 and T1 and over the left supraclavicular area.

Clinical diagnosis: Cervical 7 radiculopathy secondary to lateral rupture of disk.

Subsequent course: The use of cervical traction, cervical collar, nonsteroidal anti-inflammatory agents, and various pains and anti muscle spasm agents and various measures in physical at therapy fail to produce any relief. Epidural injection produced no relief. Finally, 4 weeks after her initial evaluation, the patient now indicated she was willing to consider surgical therapy. This had been strongly recommended since per pain was now predominantly in the arm and her examination now demonstrated significant weakness at the left triceps muscle in addition to a persistence of her earlier findings. **MRI (Fig. 8- 21)** demonstrated a lateral disk rupture at the C 6 -7 interspace. The patient underwent a left sided laminectomy at that

level with removal of ruptured disk material. When seen in follow up 3 months after surgery she no longer had pain in the neck and arm. Strength had returned to normal she continued to have a minor residual tingling and decrease in pain sensation over the index finger. There had been a minor return of the left triceps deep tendon stretch reflex.

Comment: Radiation of pain and numbness in his case suggested involvement on the C 7 nerve root. The triceps muscle is innervated by the cervical nerve roots 6, 7, and 8. The C 7 nerve root provides the major supply. The sensory examination confirmed the involvement of the C 7 root. The laboratory data : particularly the MRI confirmed the level of root involvement and indicated the specific pathology. At the time of surgery, 80% of pain was present in the arm, and the patient had significant benefit from the surgical procedure .

CHAPTER 9:SPINAL CORD

The following case history presented illustrates the syndrome of spinal cord compression secondary to cervical disk disease.

Case 9 - 1: (patient of Dr. Thomas Mullins): This 34 year-old white female bookkeeper 2 days prior to admission noted a transient 6 hour period of weakness in both her legs. One day prior to admission, she developed pain in the right side of her neck, her right shoulder and right upper arm, in addition to spasm of the neck muscles and stiffness of the neck. On the morning of admission, she noted a weakness in the right leg and was unable to walk without assistance. At the same time, she noted intermittent prickly sensations (paresthesias) in both lower extremities. For 2 weeks prior to admission, she had performed a considerable amount of carpentry and painting with her head and neck in a hyper extended position. There was a significant past history of anxiety and depression.

Neurological examination: Relevant neurological findings were limited to the following:

1. *Motor system:* a. Strength: Weakness was present in the right upper extremity most prominent at the triceps and wrist extensors (4/5) with a lesser degree of weakness at deltoid, pectorals, wrist flexors and finger abductors. Alternate hand movements in the right upper extremity were impaired due to weakness. A minor degree of weakness was present at right ankle dorsiflexion (4.5/5).
b. Gait. A variable impairment of function of right lower extremity was present in walking. There was circumduction at the right hip. At times the gait was ataxic. The heel-to-shin test and repetitive toe tapping in the right lower extremity were impaired.
2. *Reflexes:* a. Deep tendon stretch reflexes were active at 3 throughout; however sustained ankle clonus was present on the right with 2 beats of ankle clonus on the left.
b. Plantar responses were extensor bilaterally (bilateral sign of Babinski)
3. *Sensory system:* a. Vibratory sensation was decreased in the right lower extremity at toes ankle and knee with associated proprioceptive deficits
b. Pain sensation was decreased in the left lower extremity from the toes to the groin. The entire buttock and the perianal area were also involved in this deficit.

Clinical diagnosis: Partial Brown-Sequard syndrome due to acute ruptured cervical disk involving the right side of cervical cord.

Laboratory data:

1. *Cervical spine x-rays* demonstrated minimal narrowing of the C 5-C6 interspace
2. The patient was unwilling to undergo an MRI study of the spine. She did agree to a CT myelogram. The *myelogram* demonstrated a large extradural abnormality at the C 5-C6 disk level. The *CT scan* at the time of this myelogram demonstrated a probable extruded disk at the C5-C6 level to the right of the midline displacing the spinal cord posteriorly and to the left. This extradural mass extended as high as C4-C5 and as low as C 6 -C 7 (**Fig.9-3**)
3. *Cerebral spinal fluid protein* was significantly elevated to 141 mg per 100 ml (normal is less than 45mg %), consistent with a spinal cord block.

Subsequent course: The patient was placed in a cervical collar. Within 1 day of admission, she had less pain in the neck and shoulder and strength of the right upper extremity had returned to normal. Within 3 days of admission, strength and sensation in both lower extremities had returned to normal although the reflexes in the lower extremities remained hyperactive. With continued use of the cervical collar and a restriction in her activities, she continued to do well. She was unwilling to have any neurosurgical procedure undertaken to remove the ruptured disk. Periodic follow-up over the next 8 years indicated no recurrence of neurological symptoms.

Comment: The analysis that resulted in the localization of the pathology in this case involves the following steps. The initial symptom of transient weakness in both lower extremities does not allow clear-cut localization but might suggest spinal cord or brain stem or bilateral parasagittal motor cortical locations. The subsequent

development of neck pain followed by weakness in the right lower extremity with paresthesias in both lower extremities clearly pointed to a cervical spinal cord location. The findings on neurological examination clearly indicated many of the components of a Brown Sequard syndrome. Weakness in the right arm and leg (right lateral column-cortical spinal tract) was combined with right-sided posterior column findings (decreased vibration and proprioception in the right lower extremity) and right-sided lateral spinal thalamic findings (decreased pain sensation in the left lower extremity). The ataxic gait and the impairment on the heel-to-shin tests in the right lower extremity most likely reflected the proprioceptive deficits in this extremity due to posterior column involvement. However involvement of the spinal cerebellar pathway might also have contributed to these findings. The impairment of alternating hand movement in the right upper extremity most likely reflected the significant weakness in the right upper extremity.

As regards the nature of the pathology, the relatively acute onset of neck pain and spasm associated with these findings after a period of prolonged hyperextension would raise the possibility of a ruptured cervical disk compressing spinal cord and nerve root. When a ruptured disc is present, hyperextension will increase the degree of spinal cord compression. Improvement in this case appeared to follow the use of a cervical collar to limit hyperextension. Almost all cases of this type would undergo surgical resection of the disk to prevent future spinal cord compression. Certainly, this patient was very fortunate not to have a recurrence of symptoms over the next 8 years. With time, a ruptured disk in the epidural space desiccates with a reduction in size and presumably a decrease in the degree of spinal cord and nerve root compression. It would have been a value to obtain a follow-up MRI scans to confirm such a decrease in degree of spinal cord compression. Patients with a severe degree of anxiety or with panic attacks often become claustrophobic in the MRI scan machine or refuse to even consider this study. Newer scanners utilize an open design as opposed to the closed design of earlier units. The MRI scan remains the study of choice in patients with cervical spine pathology. (Fig.9-4)

The following case history provides an example of epidural metastatic tumor compressing the spinal cord:

Case 9-2: This 55 year-old white housewife first noted pain in the thoracic - right scapular area, 5 months prior to admission. Three months prior to admission, a progressive weakness in both lower extremities developed. One month prior to admission, the patient had been able to walk slowly into her local hospital. Over the next 2 weeks she became completely bed ridden unable to move her legs or even to wiggle her toes. During the last 2 weeks prior to her neurological admission, the patient had noted a progressive pins and needles sensation involving both lower extremities. At the same time she developed difficulty with the control of bowel movements and urination.

Past history: At age 40, 15 years prior to this admission, a left radical mastectomy had been performed for an infiltrating carcinoma of the breast with regional lymph node involvement. A hysterectomy had also been performed at that time.

Neurological examination: The following abnormal findings were present:

1. *Motor system:* a marked relatively flaccid weakness was present in both lower extremities with retention of only a flicker of flexion at the left hip.

2. *Reflexes:* patellar deep tendon stretch reflexes were increased bilaterally with a 3 + response. Achilles reflexes were 1 + bilaterally. Plantar responses were extensor bilaterally (bilateral sign of Babinski). Abdominal reflexes were absent bilaterally.

3. *Sensory system:*

a. Position sense was absent at toes, ankles, and knees and impaired at the hip bilaterally.

Vibratory sensation was absent below the iliac crests bilaterally.

b. pain sensation was absent from the toes through the T 6-T 7-dermatome level bilaterally with no evidence of sacral sparing.

4. *Spine:* Tenderness to percussion was present over the midthoracic vertebrae (T4 and T5 spinous processes)

Clinical diagnoses: Spinal cord compression at T4-T5 vertebral level most likely secondary to metastatic epidural tumor.

Laboratory data:

1. *X-rays of the chest* demonstrated multiple nodular densities in both hilar regions of the lung, presumably metastatic in nature. In addition, the T4 and T5 vertebrae were involved by destructive (lytic) metastatic lesions. Lytic metastatic lesions were also present in the head and neck of the left femur.

2. An *emergency myelogram* demonstrated a complete block to the flow of contrast agent at the T5 level. An extradural lesion was displacing the spinal cord to the left.

Subsequent course: The neurosurgeon, Dr. Peter Carney, performed an emergency thoracic T3 -T4 laminectomy for the purpose of decompression. A gelatinous and vascular tumor was present in the epidural space displacing the spinal cord. Adenocarcinoma presumably metastatic from breast was removed from the vertebral processes, laminae and epidural space. A slow moderate improvement occurred in the postoperative period. Examination 3 weeks following surgery indicated that movement in the lower extremities had returned to 30% of normal and pain sensation had returned to the lower extremities to a moderate degree. Radiation therapy was subsequently begun.

Comment: This patient presents a typical pattern of the evolution of an epidural metastatic tumor compressing spinal cord. Midthoracic-scapular pain had been present for 2 months when a slowly progressive weakness of both lower extremities evolved over the subsequent 2 ½ months. At that point the patient had a marked flaccid weakness of both lower extremities with only minimal preservation of the hip flexors. The flaccid nature of the paraparesis may well have reflected the continued effects of spinal shock related to the final progressive events. In many cases, the evolution of motor and sensory deficit is much more rapid. When finally transferred to a neurological service, a dense sensory deficit for pain and touch was present almost up to the actual level of compression. Such findings plus the flaccid paralysis carry a very poor prognosis for any recovery of function following surgery. At the present time, in most neurological centers, radiation therapy combined with high dosage corticosteroids is considered to be the treatment of choice where the nature of the epidural compressive lesion is clear-cut. Lymphomas are often particularly radiosensitive. When the nature of the compressive lesion is unknown or the compression is the result of collapsed bony components or the neurological findings are evolving rapidly despite radiotherapy, then surgery is indicated. In other instances, surgery is also indicated, when the primary tumor is already known to be non radiosensitive, or when maximum radiotherapy has already been delivered to the region of the spinal cord for example in the treatment of vertebral metastases. In this case, the history of carcinoma of the breast was remote (15 years). Therefore the question was raised as to whether another primary lesion was the source of the metastatic tumor for example lung etc. It should be noted however, that even when lymph node involvement has not been present in carcinoma of the breast, metastatic lesions might appear in bone, brain, lung or epidural space etc 5 or 10 years after the apparent complete resection of the primary breast lesion. In this case, a myelogram was performed, at the present time; the most appropriate diagnostic procedure would be an MRI scan. However in circumstances where that study cannot be performed, on an emergency basis then an emergency myelogram (or myelogram-CT) is appropriate. In this case, the presence of persistent mid thoracic - scapular back pain in a patient with a past history of breast malignancy should have prompted a search for metastatic lesions in vertebrae. In any case, the earliest development of motor or sensory symptoms in a patient with a past history of malignancy and back pain should lead to prompt neurological evaluation and investigation. (The present standard of investigation would include appropriate MRI study of the spine, which has the advantage of allowing studies not only of the specific area of compression but also of the spinal cord above and below the area of compression. Thus other epidural lesions may be identified). The best treatment of metastatic spinal cord compression is a high index of suspicion and early recognition to prevent the poor prognosis associated with a dense paraparesis and associated dense sensory level.

The following case history 9-3 demonstrates the effect of a Schwannoma compressing the spinal cord.

Case 9 - 3: This 65 year old right-handed female first noted weakness in her legs and pain in the lower thoracic spine 18 months prior to admission. Coughing would cause the pain to radiate around into the left flank and left lower quadrant. Two months prior to admission, she developed numbness “diminished feeling to the skin “which began in the toes and now extended to the waist. Weakness had also progressed. For the last week the patient had difficulty in urination, unable to completely empty her bladder.

Neurological examination: The following abnormal features were present:

1. *Motor system:* Mild weakness was present in both legs distal more prominent than proximal
2. *Reflexes:* a. The patellar and Achilles deep tendon stretch reflexes were increased bilaterally
 - b. The plantar responses were equivocal bilaterally
3. *Sensory system:* a. Pain and touch sensation was decreased bilaterally from the L1 dermatome down to the toes with out sacral sparing with more marked involvement on the left.
 - b. Position sense was decreased bilaterally at toes but somewhat more marked on the right. Vibratory sensation was decreased bilaterally below L1-D12.

4. *Spine*: Percussion over the D10 spinous process produced pain radiating around in to the left lower quadrant and inguinal area. Coughing produced a similar phenomena.

Clinical diagnosis: Extrinsic probable intradural tumor compressing spinal cord at the D(T)-10 vertebral level, possibly a schwannoma

Laboratory data: *Neuroimaging studies* demonstrated an intradural extramedullary tumor arising from the left D 11 nerve root and compressing the spinal cord..

Subsequent course: Resection of the tumor, a Schwannoma by the neurosurgeon, Dr. Michael Scott produced a significant resolution of symptoms.

Comment: The progressive 18 month course of motor and sensory findings in the lower extremities extending to the waist all suggested a benign intradural extra medullary tumor. The possibility of a tumor arising from the D (T) 10, 11 nerve root was suggested by the history and findings of coughing reducing pain radiating in to the left lower quadrant In addition , the examination demonstrated clear-cut tenderness and reproduction of symptoms by percussion over the T 10 vertebral spinous process.

The following case history 9-4 presents the diagnostic dilemma seen in cases of transverse myelitis.

Case 9-4: (patient of Dr. Thomas Mullins and Dr. Bernard Stone): This previously healthy 42 year-old white female awoke 3 days prior to admission with sudden onset of a dull aching mid thoracic back pain and tingling of her lower extremities. Over the next 12 hours her T6- T 8 back pain became severe and she developed mild weakness of the lower extremities and urinary retention. A an emergency myelogram revealed a widened spinal cord at T8. over the next 24 hours per back pain and decreased in intensity, sensation and strength improved that she continued to have urinary retention. At that time bilateral Babinski signs were found. She was treated with high dosage corticosteroids (dexamethasone). The patient had experienced 2 previous episodes of back pain in the T6-T8 distribution but without any neurological symptoms.

Neurological examination: The following abnormal findings were present

1. *Motor system:* a. Strength at hip flexion and extension with moderately weak bilaterally (4/5).
b. Gait was ataxic with occasional side steps; she was unable to perform tandem gait
2. *Reflexes:* Patellar deep tendon stretch reflexes were hyperactive bilaterally, but plantar responses were flexor
4. *Sensory system:* There was decreased sensation for pinprick in the S- 3 distribution and asymmetric loss of vibration sense in both lower extremities more so on the right than left.

Clinical diagnosis: Transverse myelitis, etiology uncertain

Laboratory data:

1. *Myelogram-CT scan of the dorsal spine* indicated a widened spinal cord at the T 7 level.
2. *MRI scan* confirmed the enlargement of the spinal cord at T7-T8 (**fig.9-9 A**).
3. *CSF protein* was elevated to 55 mg%; no significant cells were present
4. *Spinal angiography* with catheterization of T6 through T 11 radicular arteries on left and right revealed no vascular malformation.

Subsequent course: Significant improvement occurred. Neurological examination, 2 months after onset of symptoms indicated only bilateral Babinski signs and decreased pinprick over the right perineum. CT/myelography at that time indicated widening of spinal cord at T7-8 with a possible small cavity at the T6 level. Repeat MRI scan 7 months after onset of symptoms, demonstrated considerable resolution of the thoracic lesion. Neurological follow-up after 7 years detected no additional symptoms or signs.

Comment: In the era before MRI and spinal CT/myelography, this patient would have been placed in the general category of transverse myelitis . How many cases of transverse myelitis reported in that era would have that general diagnosis today is unclear. In this case, a possible hemorrhage or hemorrhagic component was suspected was never confirmed, in terms of CSF studies and no malformation was identified. Nevertheless, the previous episodes of back pain in the same thoracic area might raise the question of a very minor vascular malformation which had been destroyed in the process of a small intrinsic hemorrhage. The absence of additional symptoms over the next 7 years would make multiple sclerosis unlikely. Cranial MRI scan could have answered the question of additional lesions in nervous system but was not performed in this case. A

number of viral diseases are associated with a myelitis ,but these generally produce an increased cellular response in the CSF.

The following case 9-5 provides an example of syringomyelia.

Case 9 - 5: This 33 year-old female credit union manager had a 3-year history of intermittent pain and paresthesias extending from the left cervical area to the left arm and hand predominantly involving the middle finger. In the last 3 months, weakness of the left arm and hand developed and paresthesias of the left arm had become more continuous.

Neurological examination: The following abnormal findings were present:

1. *Motor system:* Mild weakness of the left triceps muscle
2. *Reflexes:* There was depression of all deep tendon stretch reflexes in the left upper extremity
3. *Sensory system:* There was a selective cape like decrease of pain and temperature sensation in the left upper extremity (shoulder and arm). In addition, there was a selective decrease in pain sensation over the T 3-T5 dermatomes on the right.

Clinical Diagnosis: syringomyelia

Laboratory data:

1. *MRI scan of the spinal cord* demonstrated an extensive cavity extending from C2 to T 9 (**Fig.9-12**). The cavity was irregular, with a major enlargement of the spinal cord at the T 4 vertebral level.

2. *MRI scan of the head* demonstrated a type 1 Arnold Chiari malformation with displacement of the cerebellum below the foramen magnum (**Fig.9-13**).

Subsequent course: Dr. Alex Danylevich performed a laminectomy at T4 and shunted the large cavity into the subarachnoid space.

Comment: The findings in syringomyelia may be asymmetrical. In this case, the dissociated sensory deficit for pain involved segments C4-C8 on the right and T3-T5 on the left. Although weakness was present in the left upper extremity with depression of deep tendon stretch reflexes, atrophy of muscle had not yet developed and no long tract findings were present.

The following case history 9 -6 presents an example of a more complex advanced case of syringomyelia and syringobulbia

Case 9-6 (patient of Dr. Sandra Horowitz): This 60 year-old white male maintenance worker 5 years prior to admission had the relatively sudden onset of a novocaine like sensation behind the right ear and transient numbness of the right arm and leg. 3 years prior to admission he began to drop objects from the right hand, and developed decreased sensation in the right arm. On several occasions he was unaware that he burned his right arm and hand. The patient had sustained lumbar trauma at age 20 requiring lumbar spine fusion. A sister had died of a brain tumor.

Neurological examination: The following abnormal findings were present:

1. *General observations:* There were numerous scars over the right hand and arm and to a lesser degree of the left hand.
2. *Cranial nerves:* The following abnormalities were present: (a) a dysconjugate rotary nystagmus most marked on gaze to the right and greatest in the abducting eye (b) Decreased pain and temperature over all 3 divisions of the right trigeminal nerve with decreased corneal sensation. Touch sensation was intact. (c) Head was tilted to the left.
3. *Motor system:* The following findings were present: (a) Strength was intact. (b) Gait was broad based and ataxic the patient was unable to do tandem walking. Eye closure did not change these findings suggesting a cerebellar basis for these abnormalities. (c) Minimal incoordination was present on finger-to-nose testing and heel-to-shin testing of the right arm and leg.
4. *Reflexes:* All upper extremity deep tendon stretch reflexes were 0 to 1. The lower extremities were 2 + and plantar responses were flexor
5. *Sensory system:* There was a marked decrease in pain and temperature sensation over the C 2 - T4 dermatomes on the right and to a lesser degree in the same distribution on the left. In contrast ,position ,vibration and light touch sensation were intact.

Clinical Diagnosis: Syringomyelia and syringobulbia

Laboratory data:

1. A *myelogram* showed a diffuse expansion of the cervical spinal cord from T2 to C1. *CT scan at 4-5 hours*, after this study confirmed the diffuse expansion of the spinal cord and also showed a small syrinx at the C2 level.

2. *MRI scan (Fig.9-14)* indicated a clearly defined central defect beginning at the cervical 2 segment and continuing at least to the cervical thoracic junction.

Subsequent course: The neurosurgeon Dr. Bernard Stone performed an extensive laminectomy in the upper dorsal-cervical spine area. The posterior spinal cord was thinned out “almost paper thin” particularly on the right side corresponding to the transverse images of the MRI scan. A cystic cavity was found at a depth of less than 1 mm. Using microsurgical technique, a small 1 mm incision was made with the laser into the spinal cord on the right just posterior to the root entry zone. A thin silastic tube was inserted into the cavity following continuous drainage into the subarachnoid space. Following surgery, the patient demonstrated a moderate improvement in his gait and minor subjective sensory improvement. He no longer sustained burns of the arm. However, 1 year after surgery, progression resumed. At 2 years following surgery he had weakness of the right arm and a severe ataxia. Pain and temperature sensation were now deficient over the entire right side of the body as well as the right arm and right foot. In addition position and vibratory sensation were now impaired in both lower extremities at the foot. Repeat MRI scan demonstrated a slightly larger syrinx. His condition stabilized over the next 3 months and then began to progress with increased rotatory and down beat nystagmus suggesting increased brain stem involvement.

Comment: The initial symptom of the tingling behind the right ear, suggested that the cervical spinal cord was involved as high as the C2-C3 segments. The painless burns and trauma to the hands right greater than left as well as the dissociated sensory loss on the neurological examination all suggested involvement of the decussating pain and temperature fibers in the anterior white commissure. The late involvement of position and vibratory sensation in the lower extremities was predicted from the findings of the MRI scan and of surgery.

The selective decrease in pain and temperature sensation over all 3 divisions of the trigeminal nerve on the right indicated involvement of the descending spinal tract of the 5th cranial nerve either at a medullary level or at the level of the upper cervical spinal cord. This will be further discussed in the brain stem chapters. The occurrence of nystagmus which was greater in the abducting eye might suggest involvement of the medial longitudinal fasciculus at a low pontine level and this will be discussed in the brain stem chapters. Nystagmus may also occur in syringomyelia, because an associated syringobulbia is also present, with involvement of the vestibular nuclei or because of the effects of an associated Arnold-Chiari malformation. Down beat nystagmus is frequently seen in the Arnold-Chiari malformation. It is important to realize that syringomyelia and syringobulbia are progressive diseases as demonstrated in this case. This case suggests that it is not always possible to demonstrate a continuous appearance of the syrinx. The cavity particularly at a brain stem level may be a narrow slit which may not be imaged by the MRI particularly by the earlier generation of MRI scanners (the study was performed in 1987).

Case history 9-7 presents an example of poliomyelitis occurring in a non-immunized adult patient who was evaluated on June 14, 1968.

Case 9-7: This 54 year old white housewife developed on June 4th 1968, a poorly defined illness characterized by fever malaise, headache, nausea and loss of appetite. Approximately 5 days later she noted an aching sensation in her right leg and then rapidly developed a weakness and then a paralysis of the right lower extremity. The following day, the left leg also became weak. She was unable to get out of bed to stand or to walk. No sensory symptoms or radicular pains were present. She had to compress her abdomen in order to void. Temperature rose to 101 degrees.

Past history: The patient had never received any type of poliomyelitis immunization.

Neurological examination (10 days after onset): *Mental status and cranial nerves :intact*

1. Motor system:

- a. Fasciculations were present in the thigh muscles bilaterally.
 - b. Strength was decreased as follows: right biceps: 4+/5 (80%), right triceps: 2/5 (20%), right lower extremity 0/5 except minimal wiggle of toes, unable to lift left leg off of bed, (1/5) with marked weakness of proximal thigh muscles :1/5 (10%) but with intact distal strength.
2. *Reflexes:* a. Deep tendon stretch reflexes were 2/4 except for the right triceps, patellar and Achilles which were absent bilaterally. b. Plantar responses: The left was flexor. There was no response on the right.

3.Sensory system: Intact

Clinical diagnosis: Acute anterior poliomyelitis

Laboratory data:

1.CSF: Initial studies on 6/9/68: 15cells /cu mm.(9 lymphocytes ,6 polymorphonuclears, protein 85mg% ,Glucose normal at 60mg%. Repeat studies on 6/10/68 now indicated 26 lymphocytes per cu mm.

2.*Viral studies* following transfer to the infectious disease service of the New England Medical Center indicated isolation of poliomyelitis virus type I from the stool. When acute and convalescent serum were compared a rise in antibody titers to poliomyelitis virus was apparent.

Subsequent course: The severe leg cramps were relieved by warm wet packs. Over a period of several days following the above evaluation, the right triceps deep tendon reflex returned and within an additional period of several days ,strength in the right upper extremity had returned to normal. After several additional weeks, strength in the left lower extremity improved ,but the right lower extremity remained unchanged despite intensive physiotherapy. At the time of rehabilitation hospital discharge on 9/27/1968, the patient had been fitted with long leg braces and trained in the use of crutches, with which at the time of discharge she was able to ambulate and to accomplish the activities of daily living.

Comment: Acute anterior poliomyelitis was formerly primarily a disease of children and young adults ,since this was the population with the lowest previous exposure and therefore the lowest level of immunity. Occasional cases did occur in middle aged or older adults (one of the most notable being that of Franklin D. Roosevelt). As discussed above ,with the development of immunization to the common strains of the virus, there has been an almost total elimination of the disease in modern industrial societies where the rare cases that occur are primarily in non immunized individuals .

From the neurological standpoint, the neurological findings were restricted to a lower motor neuron syndrome manifested by flaccid weakness, a loss of deep tendon reflexes and fasciculations. Fasciculations represent apparent spontaneous contractions of motor units: the group of muscle fibers supplied by a single anterior horn cell. Although occasional fasciculations may occur in the majority of normal individuals as a benign phenomenon, the occurrence of frequent fasciculations usually represents ,the dysfunction of a diseased anterior horn cell. At times the basic pathological process is actually present in the anterior root or the proximal peripheral nerve. Although actual atrophy was not found in this patient during the acute phase of her illness, an examination in later years would demonstrate a significant degree of atrophy in those muscles still affected by a flaccid weakness.

The spinal fluid findings in this case were typical of a mild aseptic meningitis i. e. a nonbacterial meningitis. This type of CSF formula is often found in viral infections of the central nervous system.

The occurrence of cramps as a prominent feature may reflect involvement of the posterior horn interneurons(found in acute cases which come to autopsy) or perhaps may be due to involvement of the gamma motor neurons. The major impact of the disease however is on motor neurons.

The following case history 9-8 demonstrates the full clinical extent of a classical case of ALS.

Case 9-8: This 66 year-old white married male merchant, 9 months prior to evaluation had the insidious onset of a progressive weakness and atrophy involving his lower extremities. Subsequently the upper extremities were involved to a lesser degree by weakness and atrophy. Three-month prior to evaluation, the patient had the onset of thickness of speech, a difficulty in swallowing solids and to a lesser degree liquids. At the same time stiffness in both lower extremities developed. There had been no sensory symptoms, no urinary symptoms, and no change in mental status. There had been a weight loss of 30 pounds.

Neurological examination : Mental status and sensory system were intact. The following abnormal findings were present.

1.Upper motor neuron findings involving the cranial nerves:

V. The jaw jerk was hyperactive (increased deep tendon stretch reflex).

2. Lower motor neuron findings involving the cranial nerves:

VII. A bilateral peripheral paralysis was present involving the upper and lower face with a paucity of facial expression. (see comment below)

IX, X. Although a gag reflex was present, elevation of the uvula was poor. The voice was hoarse and speech was of low volume.

XII. Ridges of atrophy and fasciculations were present along the lateral borders of the tongue

3. Lower motor neuron (anterior horn cells of spinal cord) findings were widely present:
 - a. Widespread muscular atrophy was present in the shoulders, intrinsic hand muscles and proximal leg muscles
 - b. Widespread fasciculations were present at rest in all 4 extremities
 - c. A significant degree of proximal and distal weakness was present in all 4 extremities. Lower extremities were affected to a greater degree than upper particularly in the distal muscle groups. Hip flexors and extensors were 50% of normal. Ankle dorsiflexors and toe extensors were 30% on the right and 10- 20% on the left.
 - d. The patient was able to arise from a chair but could only walk a short distance without assistance
4. Upper motor neuron findings were present in the extremities :
 - a. The deep tendon stretch reflexes at the biceps, triceps, and patellar were hyperactive at 3 +. However the right Achilles reflex was 2 + and left was decreased at 0 to 1.
 - b. The plantar responses were both extensor (bilateral sign of Babinski).

Clinical diagnosis: amyotrophic lateral sclerosis (fully developed-classic type)

Laboratory data:

1. *Biopsy of the right quadriceps muscle* revealed the changes seen in various stages of denervation atrophy .The distribution of atrophy and fatty replacement was clearly in a grouped motor unit pattern.
2. A complete blood count, sedimentation rate, and cerebrospinal fluid examination were all normal.

Subsequent course: The patient experienced additional difficulty in swallowing .He expired 3 months after the above evaluation, approximately 1 year after the onset of his disease.

Comment: The history and findings in this case indicated the initial involvement of the lower motor neurons involving all 4 extremities with the production of weakness and atrophy. Six months later, the patient had clearly developed brain stem symptoms and upper motor neuron findings affecting the lower extremities. On examination, there was clear-cut evidence that the brain stem symptoms reflected both upper motor neuron cortical bulbar involvement as well as lower motor neuron bulbar paralysis. Thus the jaw jerk was hyperactive (an upper motor neuron finding). In contrast, the poor elevation of the uvula, hoarseness and low voice volume as well as the atrophy and fasciculations involving the tongue all suggested lower motor neuron involvement of the bulbar motor neurons. The bilateral peripheral facial involvement without atrophy or fasciculations may well have indicated bilateral corticobulbar involvement. The examination also confirmed the presence of both upper and lower motor neuron findings involving the extremities. The deep tendon stretch reflexes were hyperactive except for the left Achilles reflex that was depressed corresponding to the most marked weakness in the left foot. Bilateral Babinski signs were also present consistent with bilateral corticospinal tract involvement. The widespread atrophy, fasciculations and weakness were all consistent with a widespread involvement of lower motor neuron of the anterior horn.

Amyotrophic lateral sclerosis is a progressive disease without a clear-cut treatment. The use of agents which have some action as glutamate antagonists (such as riluzole) may slow the rate of progression to a minor degree .The use of nerve growth and factors has not produced clear-cut improvement.

Death occurs due to the involvement of pharyngeal muscles resulting in aspiration (and aspiration pneumonia) and poor nutrition. Respiration is compromised by aspiration pneumonia and by involvement of the muscles of respiration (intercostal, diaphragm, and accessory muscles). In most patients, cognitive function is well preserved. Many patients wish to provide advanced directives as to whether such measures as tracheostomy, artificial respiration, or long-term nutritional supplementation by percutaneous gastrostomy or the use of antibiotics are to be performed. With these measures, life may be prolonged but without any reversal of the course of disease.

The following case 9-9 provides an example of tabes dorsalis.

Case 9-9: (patient of Dr. John Sullivan): For 4 years prior to admission this 40 year-old white male had leg pains and staggering gait. His leg pain occurred spontaneously but was worsened with exposure to cold and wet weather. The pain seemed to shoot from his feet and occasionally from his knees up the leg into the region of the hip lasting but a few seconds. The patient likened the pain to the raking of a sharp instrument up his legs. The pains would recur repeatedly for varying periods of time from 30 minutes - 3 hours. They could shift from one leg to the other. When the pain was severe, the patient was unable to bathe because the temperature of the water would increase the pain. During this period of time, his walking had deteriorated. He had to look constantly to see where his feet were placed and if it were the least bit dark he had much difficulty staggering about because he was unable to control his feet. The patient did not recognize any difficulty with urinary bladder function but additional questioning revealed that frequently he would go 18 to 20 hours without voiding. For 3 years, this patient had taken large amounts of an opiate (paregoric) in an effort to relieve his discomfort. More recently, he had added an additional addictive habit, the use of sodium Amytal 6 times a day to decrease the severity of his symptoms.

Neurological examination: the following abnormal features were present:

1. *Cranial nerves:* the pupils were small and slightly irregular. Neither pupil reacted to light but did react to accommodation.
2. *Motor system:* although strength was intact, a gross ataxia of stance and gait was present. This was most marked when eyes were closed, less marked when the eyes were open and the patient was watching his legs. There was a significant heel-to-shin dysmetria with a similar pattern as regards worse with eyes closed; better when the eyes were open and the patient observed the movements. Romberg test was positive.
3. *Reflexes:* Deep tendon stretch reflexes were absent in the lower extremities at patella and Achilles, but well preserved in the upper extremities at 2 +. There were no responses to plantar stimulation.
4. *Sensory system:* There was an area of decreased pain sensation over the tip of the nose and in relationship to both nipples in a roughly circular area. Position sense was grossly defective even for large amplitude movements at toes and ankles. Vibratory sensation was absent at toes and present but diminished at the ankles.

Clinical diagnosis: Neurosyphilis: tabes dorsalis

Laboratory data: clinical diagnosis was confirmed by positive *serological findings* in both serum and cerebrospinal fluid.

Comment: This classic type of case of tabes dorsalis, which was still seen frequently in the 1950's and 1960's, would be very rare today. Whether we will see this type of neurological problem, as a late effect of the increased number of syphilis cases of the 1970 and 1980's remains uncertain. Complete or partial treatment of the primary or secondary manifestations may well modify the late effects. In addition; the frequent use of antibiotics for other conditions many also have provided partial treatment of otherwise unrecognized cases.

The epidemiologic data may be reviewed as follows. As regards the total impact of syphilis the following statistics should be considered. In the United States during the 1940's prior to the full impact of the antibiotics, the total number of new cases of primary and secondary syphilis reported annually was close to 100,000. By 1956, this number had fallen to 6,000 new cases. Subsequently related to changes in sexual behavior and the emergence of the AIDS epidemic such new cases had increased by 1990 to approximately 60,000 per year. A steady decline has occurred since that time. The total number of all cases reported annually was approximately 500,000- 600,000 in the early 1940's. These figures then had declined to approximately 64,000 by 1987. However total cases had increased again to approximately 134,000 by the early 1990's.

In studies during the pre antibiotic era, of patients with untreated primary and secondary syphilis, approximately 28% developed manifestations of tertiary syphilis with a greater impact on males than females. Cardiovascular syphilis involving the aortic valve and the aorta was found in 10% patients during life and in 22% (females) - 35% (males) of patients who eventually came to autopsy. In some autopsy series this percentage was even higher at 40 - 60%. The disease of the ascending and transverse segments of the thoracic aorta, often resulted in the formation of aneurysms and dissection. Many of these cardiovascular cases could have secondary neurological vascular complications involving brain and spinal cord.

Symptomatic neurosyphilis, developed in 7 - 9% of the untreated patients: meningovascular in 2 to 3%, general paresis in 2-5 % and tabes dorsalis in 1 -5%. While these figures indicate that the majority of patients with untreated syphilis did not develop neurosyphilis, the large number of patients infected each year produced an eventual significant number of patients with neurological disability.

If all tertiary asymptomatic and symptomatic cases of neurosyphilis are considered in terms of the predominant category, 16% are included in the meningeal-vascular group, 12% in the general paresis group, 30% in the tabes dorsalis group and 31 % in the asymptomatic group. Asymptomatic patients had evidence of infection in the CSF but no clinical symptoms or signs.

The diagnosis of tabes dorsalis is dependent on the recognition of the clinical pattern of disease. It may not be possible to obtain a reliable history of the primary or secondary lesions. The clinical diagnosis is confirmed by serological tests of the serum and by cerebrospinal fluid examination demonstrating a positive serological test, some mild increase in mononuclear cells, a mild elevation of protein and an increase in gamma globulin. The serological test are of 2 types: 1) the nonspecific reagin antibody tests such as the RPR and the VDRL. 2) The specific treponemal antibody test such as the fluorescent treponemal antibody absorption test (FTA ABS). As regards the nonspecific antibody tests, a positive serum test alone indicates only previous infection without necessarily indicating neurosyphilis. Moreover a false positive test may occur in other febrile illnesses and other immunological disorders. A false negative nonspecific test in the serum may occur in up to 30% of patients with chronic neurosyphilis. The specific antibody tests on serum are positive in almost all cases of neurosyphilis. The positive nonspecific test of the spinal fluid, when contamination of the spinal fluid by blood has been ruled out is diagnostic of neurosyphilis.

Penicillin is the treatment of choice of neurosyphilis. The current recommendations of the U.S. public health service are that the patient receives 24,000,000 units a day intravenously for at least 14 days. This should eliminate the activity of the organism. However many of these symptoms and signs will persist since the chronic damage to nerve roots and nervous system from the meningeal or the meningoencephalitic inflammation or vascular components has already occurred. A reexamination of the spinal fluid at 6 months may continue to show a weakly positive serological test for syphilis but all other abnormalities should clear. The serum nonspecific serological tests may continue to remain weakly positive.

Case 9-10 provides an example of combined system disease.

Case 9-10: This 48 year-old house painter had a 16-week history of progressive impairment of gait mainly unsteadiness and imbalance worse in the dark than in the light and tingling paresthesias of all his toes. Twelve weeks prior to admission, tingling began in his fingers. Weakness had not been a major complaint although he had noted shortly before admission some sense of heaviness in his legs on climbing steps.

Neurological examination: the following abnormal features were present.

1. *Motor system:* The patient had minor difficulty walking a tandem gait with eyes open. His gait was worse with eye closure. The Romberg test was positive.
2. *Reflexes:*
 - a. Deep tendon stretch reflexes were 2 + excepting Achilles which were 0.
 - b. Plantar responses were extensor (bilateral sign of Babinski).
3. *Sensory system:* Vibratory sensation was absent at toes, ankles and knees. Position sense was decreased at toes. There was a minimal decrease in pain and touch sensation over the toes.

Clinical diagnoses: Combined system disease

Laboratory data:

1. *Hematocrit* was slightly low at 34%. *Blood smear* indicated macrocytosis of red blood cells and hypersegmentation of the polymorphonuclear leukocytes.

2. No *vitamin B12* was detected in the serum (normal values are 200-900 pg/ml). The *Schilling test* without intrinsic factor indicated 1% urinary excretion of the orally administered radioactive vitamin B12. When the Schilling test was repeated with the addition of orally administered intrinsic factor, the urinary excretion of radioactive vitamin B12 increased to 12% (normal values are 8 to 22% excretion). There was a good reticulocyte response to the administration of the vitamin B12.

3. *Bone marrow aspiration* indicated megaloblastic changes in the erythroid series.

4. There was no gastric acid on *gastric analysis* even with histamine stimulation. *Gastric cytology* was negative for cancer cells. *Upper GI series* was normal.

Subsequent course: The patient was treated with intramuscular injections of 100 mcg of vitamin B12 daily for 14 days and then was switched to 1,000 mcg once a month. [The current recommendations are 1,000 mcg of vitamin B12 (cyanocobalamin) daily for 5 days then weekly for an additional 3 weeks and then monthly for the lifetime of the patient]. When seen in follow-up at 5 months following his hospitalization, the patient reported exhibited improvement in gait. He was now able to walk a tandem gait with eyes open. His Romberg test however remained positive. Deep tendon stretch reflexes and plantar responses were unchanged. Sensory examination now indicated that position sense was intact although vibration was still absent at the toes and ankles and the minimal deficit in pain and touch over the toes was unchanged.

Comment: The findings in this case, suggested predominant involvement of the posterior columns of the spinal cord with a sensory ataxia, with distal paresthesias of the extremities and an absence of position and vibration at toes and ankles. The deficit in position and vibration was far out of proportion to the minimal involvement of pain and touch sensation. These symptoms could not then have been related simply to a peripheral neuropathy. Nevertheless some peripheral nerve involvement was undoubtedly present since the Achilles deep tendon reflexes were absent and there was a minimal distal decrease in pain sensation. There was also clear-cut involvement of the corticospinal system since bilateral Babinski's signs were present. The administration of vitamin B12 would be expected to readily reverse the hematological changes and this was already evident in the reticulocyte response to the early vitamin B12 administration.

As regards the neurological disease, at an early stage, some of these symptoms may represent a dysfunction of myelin and axons without actual structural damage. When patients are treated early, at a stage when axonal damage has not yet occurred and damage to myelin is minor, a significant improvement may occur although some neurological signs may still be present on examination. The objective is always to prevent progression and disability in this treatable disease. When treatment is delayed so that severe damage to myelin and subsequently to axons has occurred significant disability may remain, although progression should be prevented. Patients with gastric carcinoma may also have a deficiency of intrinsic factor and for that reason gastroenterology studies were performed.

The following case history 9-11 provides an example of the total life history of a patient with Friedreich's Ataxia

Case 9-11: This part-time college student was initially seen for evaluation of a progressive ataxia at age 22 years. At age 9 years, the patient had noted the onset of a progressive change in handwriting and then an impairment of hand coordination. Difficulty in walking and balance had been initially noted at age 12. An evaluation at the Children's Hospital Medical Center in Boston at age 15 indicated a positive Romberg test, and an absence of deep tendon stretch reflexes. Up until age 18 years, the patient been able to walk holding on to the walls. Subsequently he required the assistance of 1 person. By age 21 he required the assistance of 2 people. At age 18 years, a progressive change in voice began. At the same time, the patient noted a weakness in both lower extremity with "a collapsing at the knees". In recent years, a change in vision had occurred requiring frequent changes of glasses. Despite these symptoms, the patient continued to do relatively well as a part-time college student. The patient had been adopted at an early age and no information concerning parents or siblings was available.

General physical examination: The heart rate was irregular

Neurological examination: The following abnormal features were present:

1. *Cranial nerves:* The following abnormal findings were present:

- a. Extraocular pursuit movements were jerk like rather than smooth
- b. There was frequent facial grimacing.
- c. Dysarthria was present with slurring of speech.

2. *Motor system:* multiple abnormalities were present:

- a. There was minor atrophy of the hand muscles and a more marked atrophy in the muscles of the lower legs and feet.
- b. There was mild weakness in the distal portions of the upper extremities and in the hands with a more significant weakness in the lower extremities most marked distally.
- c. Hypotonia was present in all 4 extremities with excessive rebound on passive motion and release .
- d. There was a marked bilateral intention tremor on finger-to-nose testing and a marked impairment of alternating movements of the hands and fingers. (An intention tremor is a

movement perpendicular to the line of movement and usually implies disease of the cerebellar hemisphere or of pathways related to the lateral cerebellum). A significant tremor of the head was also present.

- e. The patient was unable to stand or walk except with the support of 2 individuals. Attempts to have him stand on a broad based indicated a marked truncal ataxia which usually implies disease of the midline cerebellum or of fiber systems related to the midline cerebellum.
- 3. *Reflexes*: a. Deep tendon stretch reflexes were everywhere absent.
 - b. Plantar responses were equivocally extensor bilaterally.
- 4. *Sensory system*: The following abnormalities were present:
 - a. There was a distal decrease in pain sensation in the lower extremities up to the ankles
 - b. Vibratory sensation was totally absent at toes and ankles and decreased at knees. This modality was also absent at the fingertips and markedly decreased at wrists.
 - c. Joint position sense was markedly defective at the toes and defective to a lesser degree at the fingertips.

Clinical diagnosis: Friedreich's ataxia

Laboratory data: The *electrocardiogram* demonstrated the following features: A marked sinus arrhythmia, occasional nodal beats and premature atrial contractions. In addition abnormal T-wave inversions occurred.

Subsequent course: The patient was able to complete college. Using a motorized wheelchair and other aids, he was able to function as an accountant and as the town auditor. Follow up visits over the next 20 years indicated continued progression with the development of bilateral optic atrophy, bilateral sensory-neural hearing loss, bilateral cortical bulbar findings, increasing dysarthria and increasing motor and sensory deficits in all 4 extremities. After increasing cardiac difficulties he expired at age 41. Throughout the course of his disease, mental status and motivation were extremely well preserved.

Comment: The early symptoms and findings based upon the neurological examination when the patient was 15 years of age clearly indicated predominant involvement of posterior columns and an absence of the deep tendon stretch reflexes. The history at that time also suggested a problem in coordination of hand movements suggesting the possibility of some cerebellar involvement at that time. His subsequent evaluation at age 22, indicated that progression of the posterior column disorder had occurred. In addition there was now evidence of severe disease of the cerebellum or cerebellar pathways: Intention tremor, impairment of alternating hand movements, ataxia of the trunk and a dysmetria of eye movements. Moreover there was also evidence of a distal sensory motor peripheral neuropathy. Equivocal plantar responses were also now present. Dysarthria was also very apparent. With time the involvement of all these systems progressed. In addition involvement of the optic nerves and the 8th cranial nerve for hearing added to the severe disabilities. At the time that this patient was initially seen and followed, a genetic testing for this disorder was not available. Today, a specific diagnosis could be established through the use of the specific genetic tests for the expansion of the GAA trinucleotide repeats on chromosome 9.

The following case provides an example of multiple sclerosis involving primarily the cervical spinal cord from a clinical standpoint but with more extensive involvement demonstrated on MRI studies.

Case 9-12: This 32 year old right handed single white female registered nurse and mother of a 12 year old child was referred in Sept. 1997 for evaluation of tingling paresthesias in the lower extremities of 6 months duration. This began in the toes of the right foot, then shortly thereafter the toes of the left foot. These symptoms gradually spread up the legs reaching the level of the buttocks posteriorly, and anteriorly to the rib margin on the right and to the area between the rib margin and the umbilicus on the left. Three to 4 months prior to evaluation, she developed tingling of the ring and 5th fingers bilaterally (both median and ulnar surfaces). Six weeks prior to evaluation, a positive Lhermitte's sign developed: flexion of the neck produced electric shock sensations that extended down from the buttocks into lower extremities. EMG/nerve conduction studies 5 months and 1 week prior to the evaluation were reported as normal. An MRI of the lumbar spine 10 months previously had been reported as normal.

Past history: 1. Arthroscopic surgery for left knee problems 9 and 1 month prior to the evaluation.

2. Previous carpal tunnel injury left hand, without neurological residuals.

3.Previous gall bladder surgery.

Neurological examination:

The patient was excessively weighted (205 #) for her height (5'3"). She had a short neck with a positive Lhermitte's sign. Flexion at neck produced electric shocks extending from the buttock areas into the lower extremities. There was no local cervical tenderness

1. Mental status: intact
2. *Cranial nerves*: intact with excellent visual acuity and no scotomas.
3. *Motor system*: intact. The gait was antalgic reflecting the left knee problems.
4. *Reflexes*: Deep tendon reflexes were 2+ throughout. The left plantar response was extensor; the right equivocal.
5. *Sensory system*: Pain and cold were decreased from the toes to L1-L2 vertebrae posteriorly (but possibly at times to the rib margin on the right), and anteriorly to D7 dermatome on the right and to D9 dermatome on the left.
Vibratory sensation was bilaterally decreased at toes, ankles, and knees with a greater defect on left than right Position sense was intact.

Clinical diagnosis: Cervical myelopathy. While the Lhermitte's sign could be seen in multiple sclerosis, this sign also could be produced by compression of posterior columns.

Laboratory data:

1. *MRI cervical spine (Fig.9-22)* large demyelinating focus was present at C1-C2 involving primarily the right half of the spinal cord (the findings would have predicted bilateral involvement greater on the left half.
2. *MRI brain (Fig 9-23)*: multiple demyelinating lesions were present in both cerebral hemispheres.
3. *CSF*: abnormal:
Cell counts: 39 WBC in tube #1 and 19 WBC in tube #4 with differential of 95% lymphocytes and 5% monocytes

Immunoglobulin G index (comparison of the ratio of csf IgG /csf albumin to the ratio of serum IgG /serum albumin) was markedly elevated to 3.2 (normal +3 standard deviations =0.85).

Two *oligoclonal bands* were present (normal= 0-1).

Calculated Immunoglobulin synthesis in central nervous system markedly increased to 54mg/24hours(normal <12)

4. Visual evoked response: normal
5. ESR and WBC normal

Subsequent course:

The patient received a 5-day course of high dose (1000mg/day) intravenous methylprednisolone with some improvement in the sensory symptoms in the legs. Deficits in pain sensation persisted, although vibratory sensation returned to normal and plantar responses were no longer extensor. When dysesthesias developed in the left leg 8 months later in May 1998, with impairment of position and vibratory sensation in both lower extremities, she was retreated with intravenous methylprednisolone and then was begun on immuno-modulatory therapy with beta-interferon (Betaseron). An additional exacerbation attributed to spinal cord occurred in Oct. 1998. In Feb 1999 because of a mild elevation in liver enzymes, the beta-interferon was discontinued. A new episode localized to brain stem (vomiting, ataxia, and horizontal nystagmus) then occurred and the patient was begun on treatment with glatiramer acetate (Copaxone or copolymer I). This is another form of immunomodulatory therapy composed of a mixture of polymers of 4 amino acids one of which is a peptide fragment of myelin basic protein. Over the next 10 months, she had one exacerbation related to spinal cord. The following case history 9-13 includes several episodes indicating clear-cut clinical involvement of the spinal cord in a patient with multiple sclerosis followed over a number of years. In addition several episodes relevant to brainstem also occurred.

Case 9-13: At age 29 years, this white married male real estate broker and flyer awoke one morning with tingling paresthesias involving the left hand which slowly spread to involve the left half of the trunk and left leg. Symptoms improved that morning, then recurred and also involved the right arm. Shortly thereafter, incoordination and weakness of the left arm developed.

Neurological examination at that time demonstrated decreased touch pain and temperature sensation over the entire left arm, trunk, thigh and plantar surface of the foot. A cervical spinal cord lesion was suspected, but the cervical myelogram, CSF fluid and immunological studies were all normal. Over the next several weeks the patient made a complete recovery.

At age 31, the patient developed over a period of 7- 10 days, a progressive flaccid weakness and tingling of the left hand accompanied by a weakness of the distal left leg. Deep tendon reflexes were increased on the left and a left Babinski sign was present. When numbness and weakness of the left side of the face then developed, a right cerebral hemisphere lesion was suspected. However all diagnostic studies available at that time including a right carotid arteriogram, an electroencephalogram and brain scan were normal. Within 4 days, a significant improvement had occurred with only the reflex findings remaining.

At age 32, in association with a minor viral infection and fever, the patient developed progressive weakness of the right arm and leg followed by a disturbance of speech, a dysarthria. A lesion of the left internal capsule was suspected.

One month later, as these symptoms were beginning clear the patient developed a bilateral impairment of central vision, urinary retention and left-sided weakness.

Neurological examination now revealed a central and para- central scotoma (a defect in vision suggesting a lesion of the optic nerve). An independent scotoma, was also present in the nasal field of the left eye. A mild distal right hemiparesis was present with increased deep tendon reflexes and a Babinski sign on the right. Within 2 days a significant degree of improvement had occurred in all symptoms and signs. Based on the urinary retention, a possible lumbosacral spinal cord lesion was suspected. In addition a cervical spinal cord and bilateral optic nerve lesions were also presumed to be present.

Two weeks later, the patient developed burning pains over the right side of the face involving the eye, tongue, and upper teeth. These symptoms suggested involvement of the trigeminal system at a pontine or medullary level. These symptoms resolved over several days and the patient was then asymptomatic for the next 10 months.

At age 33, the patient awakened with a numbness and tingling paresthesias below the knees which gradually ascended that day to involve primarily the buttocks and perianal areas. Later that evening, the patient began to have difficulty in voiding and required catheterization by his local physician. In addition a general sensation of weakness of the lower extremities was noted.

Neurological examination: The following abnormal findings were present:

1. *Motor system:* a. A minor decrease in strength was present bilaterally at hip flexors and ankle dorsiflexors.
b. Gait was broad based with ataxia present on attempts to walk heel to toe. A positive Romberg test was present.
2. *Sensory system:* a. A dense bilateral deficit in pain sensation was present over the lower sacral segments (S 3, S 4, and S 5) with a circular distribution about the anus. Temperature sensation was relatively well preserved.
b. A marked bilateral decrease in vibratory sensation was present at the toes and ankles with a lesser decrease at the knees. Position sense was relatively well preserved.

Clinical diagnosis: Relapsing/remitting type of multiple sclerosis. "Benign type of multiple sclerosis". This episode represented an acute lesion at the level of sacral spinal cord.

Laboratory data: *Cystometrogram* indicated a defect in reflex voiding in response to distension of the bladder. The patient had no sensation of distension up to 450 cc of saline but as distension of the bladder was increased he had a progressive increase in discomfort. No spontaneous voiding occurred even after a total of 750 cc had been instilled. Normally the sensation of distension and desire to void begins to occur at 200 cc and spontaneous voiding occurs at 450 cc.

Subsequent course: Significant improvement again occurred without specific therapy. On the 2nd day in the hospital the ability to void had returned. By the 5th day the neurological examination was normal except for the broad based gait.

Ten days later, an exacerbation occurred with difficulty in voiding and weakness and numbness in the right lower extremity requiring re admission to the hospital.

Neurological examination now revealed that deep tendon stretch reflexes in the lower extremities were now hyperactive with bilateral Babinski signs and absent abdominal reflexes. Pain sensation was now decreased below the level of the umbilicus bilaterally but more marked on the left. Vibratory sensation was markedly decreased below the level of the T12 spinous process bilaterally but more marked on the right. Position sense was markedly defective at the toes on the right, with a minor defect on the left. After a week a bed rest in the hospital, almost all of the symptoms resolved. This episode was attributed to a lesion at the level of a thoracic spinal cord essentially a transverse myelitis. While a bilateral involvement had occurred, it was evident that many components of a right-sided Brown-Sequard spinal cord syndrome were present.

Three months later the patient developed tingling paresthesias of the left side of the face, accompanied by a paralysis of all facial muscles on left side and a decrease in hearing in the left ear. These brain stem symptoms suggested a lesion at the left pontomedullary junction.(Refer to brain stem chapter) and soon cleared.

Periodic examinations over the next 8 years, indicated no significant exacerbations of the disease process and no significant disability. He did have a minor tremor. In the interim the patient continued to pursue his usual business activities and continued to pilot his own airplane. He gave up flying at age 46 and purchased a 37 foot sailboat which he often sailed solo to Florida and the Bahamas. He experienced occasional bladder and balance problems and a minor tremor but these did not interfere with his activities. He expired at age 50 of a massive myocardial infarct.

Comment: This patient expired in 1984, just before the availability of the MRI scan. From a clinical standpoint, there would be little doubt concerning the diagnosis of multiple sclerosis of a relatively benign relapsing/remitting type. This patient clearly had dissemination of lesions in time and space which involved the spinal cord at multiple levels, the brain stem, the cerebral hemispheres and the optic nerves. From the standpoint of the spinal cord as delineated above this patient had various types of syndrome. He did not manifest a phenomenon frequently encountered in patients with involvement of the posterior columns in the cervical area: Lhermitte's sign. Sudden flexion of the neck induces a tingling electric shock sensation down the spine into the buttocks and at times into the legs. From a diagnostic standpoint other causes of lesions disseminated in time and space such as vasculitis, lupus erythematosus and neurosyphilis were essentially eliminated by the negative findings of arteriography, sedimentation rate, immunological studies and CSF serology.

This patient was extremely fortunate in the sense that over the 21 years of his symptomatic disease, he did not develop secondary progression. The majority of patients with this history would sooner or later experience symptoms or demonstrate signs which did not resolve and which might provide a disability of minor or major degree. The studies of Percy published in 1971 covering all cases seen in Rochester Minnesota 25 years after onset of multiple sclerosis indicated that one-third of the patient's were still working and 2/3 were still ambulatory. The earlier studies of McAlpine published in 1961, indicated that among patients followed for a minimum of 10 years, approximately one-third were dead, one-third were disabled, and one-third had no physical restrictions were disabilities that affected work or home life. It is evident that this earlier study underestimated benign or mild cases of the type that were probably lost to follow-up.

Why did this patient have such a benign course? Did he have a genetic background which might have predisposed him to a benign type of multiple sclerosis? In this case, there is additional information that suggests such a predisposition. The patient's older brother, a naval flyer had been hospitalized at age 33 with a diagnosis of parainfectious myelitis. Over 3 days, the brother developed a Brown Sequard syndrome with weakness of left arm and leg accompanied by increased left-sided deep tendon stretch reflexes and left Babinski sign in addition to a deficit in pain and temperature sensation below the C 4 segment. CSF examination indicated an increased number of cells (50 lymphocytes) with a minor increase in protein (53 mg/100 ml) and a probable increase in the percentage of gamma globulin. The patient recovered completely over a period of 3 weeks. He returned to his duties as a naval flier and experienced no additional

episodes during the succeeding 27 years. The brother's case would be labeled as an acute post infectious myelitis and would be included as a type of transverse myelitis discussed earlier in this chapter.

Present clinical and MRI studies indicate that most patients with relapsing/remitting multiple sclerosis do have an increasing lesion load resulting eventually in symptoms or signs that do not resolve. The present approach then is to utilize early in the disease course agents that modify the immune system. Agents such as the beta interferons decrease relapses and secondary progression. The effects are evident from both a clinical and MRI standpoint.

Acute exacerbations are usually treated with high-dose intravenous corticosteroids with the patient receiving 1,000 mg a day of methylprednisolone for 5-7 days. This shortens the course of the exacerbation with the possibility of less residual disability. There is no clear-cut therapy for primary progressive multiple sclerosis although various major immunological therapies have been investigated.