SRI RAMACHANDRA UNIVERSITY

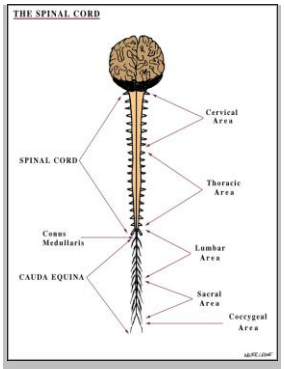
(Declared under section 3 of the UGC Act, 1956)

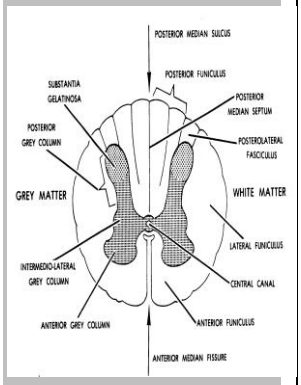
SRI RAMACHANDRA MEDICAL COLLEGE & RESEARCH INSTITUTE

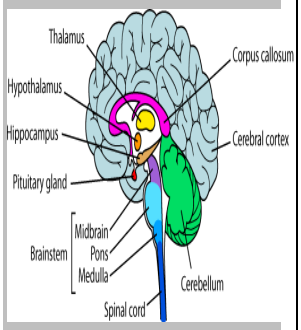
BLOCK III

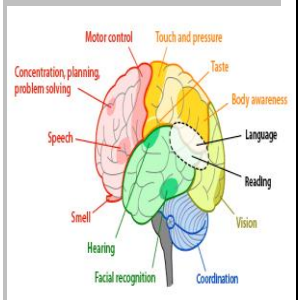
SPINAL CORD
BRAIN
CENTRAL NERVOUS SYSTEM
LIPID METABOLISM

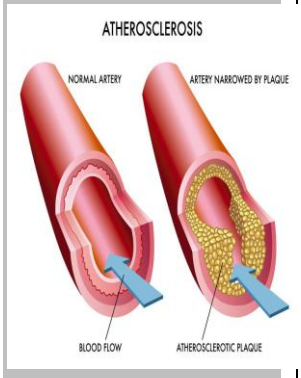
FIRST M.B.B.S. 2016 - 2017











ANATOMY:

Theory	Practicals
• Spinal cord • Medulla • Pons • Mid Brain • Cerebellum • Embryology- Development of skull & vertebra • Fourth ventricle • Cerebrum sulci and gyri • White matter • Lateral Ventricle • Third Ventricle, Epithalamus, meta thalamus • Inter peduncular fossa & Review of brainstem • Thalamus • Basal ganglia • Arterial supply of Brain • Venous Drainage of Brain	• Histology • Osteology • Surface marking **DISSECTION:** • Spinal Cord • Medulla • Pons • Mid Brain • Cerebellum • Fourth ventricle • Radiological Anatomy of skull & vertebra • Lateral ventricle • Third ventricle • Thalamus • Blood Supply of Brain

PHYSIOLOGY:

Theory	Practicals

• Introduction , Receptor, generator potential & properties
• Classification of Nerve, Nerve Injury, Wallerian degeneration and regeneration
• Synapse
• Reflexes
• Spinal cord –
  o Descending tracts
  o Ascending tracts
  o Transection of spinal cord (Complete/ Hemi)
• Cerebellum
• Brain stem - reticular formation, ARAS
• Cerebral cortex
• CSF circulation, functions, BBB, Circum ventricular organ
• Thalamus
• Pain & Analgesic system
• EEG, sleep
• Hypothalamus
• Basal ganglia
• Cerebral circulation and regulation
• Limbic system Learning and memory conditioned reflexes
• Posture, Equilibrium &Vestibular Apparatus
	• General Examination
	• Examination of Sensory System
	• Cerebellar Function Test
	• Examination Motor System
	• Superficial reflexes & Deep reflexes
	• Charts - CNS

BIOCHEMISTRY:

Theory	Practicals
• Digestion of lipids • Fatty acid synthesis, acyl glycerol, lipid storage disorders • Fatty acid oxidation – all types • Metabolism of ketone bodies • Metabolism of cholesterol, bile acids, enterohepatic circulation • Metabolism of chylomicrons and VLDL • Metabolism of HDL, dyslipoproteinemias	• Reactions of Protein - Gelatin, Casein, Peptone • Reactions of unknown protein • Estimation of Total Cholesterol • Charts – Block II & III

BLOCK - III (2016 – 17)

SPINAL CORD, BRAIN, CENTRAL NERVOUS SYSTEM, LIPID METABOLISM

Time	Day 1 02.01.2017 MON	Day 2 03.01.2017 TUE	Day 3 04.01.2017 WED	Day 4 05.01.2017 THU	Day 5 06.01.2017 FRI	Day 6 07.01.2017 SAT	Day 7 09.01.2017 MON
8-9 am	S1 Neurology as a specialty **(General Medicine)** **Dr. Srinivasan**	S6 **Case 12 Introduction & Resolution** **(Mal absorption syndrome)**Digestion & absorption of lipids (B) Dr. Vasanthi Pallinti	S10 Fatty acid synthesis, acyl glycerol, lipid storage disorders (B) Dr. Manikandan	S15 Introduction Receptor, generator potential & properties (P) Dr. Dilara	S19 Synapse – II (P) Dr. Roopa	**P** **T** **A**	S27 Spinal cord – II Ascending tracts(P) Dr. Sheela Ravinder
9-11 am	S2A Reactions of Protein - Gelatin (B) Dr. Ben S Ashok & All Faculty	S2B Histology of spinal cord (A) Dr. Padmasini Srinivasan & All faculty	S11A Reaction of casein (B) Dr. A N Vinod & All faculty	S11B Community Medicine/Anatomy Tutorial Dr. Pankaj B Shah & All faculty	S20 A General Examination (P) FULL BATCH Dr. Bagavad Geetha & All faculty		S20 B General Examination (P) Dr. Bagavad Geetha& All Faculty
11-12 noon	S3 **Case 11 Introduction** **(Brown sequard syndrome)** Spinal cord (A) Dr. Pranu Chakravarthi	S7 Medulla - I (A) Dr. Vijaya Kumar	S12 Pons (A) Dr. Kesavi	S16 Classification of Nerve, Nerve Injury, Wallerian degeneration and regeneration (P) Dr. Anbuselvan	S21 Reflexes – I (P) Dr. Bagavad Geetha		**S28** Spinal Cord – III Transection of spinal cord (Complete/ Hemi) (P) Dr. Archana P Kumar
1-2 pm	S4 Introduction, causes of cerebro vascular diseases (CM) Dr. Meriton Stanly	S8 Medulla – II (A) Dr. Vijaya Kumar	S13 Prevention of cerebro vascular diseases (CM) Dr. Meriton Stanly	S17 Synapse – I (P) Dr. Roopa	S22 Reflexes – II (P) Dr. Bagavad Geetha	S24 Spinal cord – I Descending tracts(P) Dr. T. T. Ganesan	S29 **Case 13 Introduction** **(Cerebellar disease)** Cerebellum(A) Dr. Senthil Kumar
2-4 pm	S5 Spinal Cord Dissection / Histology Dr. Vijaya Sagar & All faculty	S9 Spinal cord Dissection / Histology Dr. Ramesh Kumar & All faculty	S14 Medulla Dissection /Histology Dr. Anandarani & All faculty	S18 Pons Dissection / Histology Dr. D. Kesavi & All faculty	S23 Osteology (A) Dr. Ramesh Kumar & All faculty	S25 (2 – 3) Mid Brain (A) Dr. Haripriya S26 (3 – 4) Mid Brain Dissection / Histology Dr. Vijaya Sagar & All faculty	**S30** Cerebellum Dissection/ Histology Dr. Anandarani & All faculty

Venue: Lecture Hall No: IV (II FLOOR - 2B - College Building)

Case Resolution venue: Seminar Hall

BLOCK - III (2016 – 17)
SPINAL CORD, BRAIN, CENTRAL NERVOUS SYSTEM, LIPID METABOLISM

Case

Time	Day 8 10.01.2017 TUE	Day 9 11.01.2017 WED	Day 10 12.01.2017 THU	Day 11 13.01.2017 FRI	Day 12 17.01.2017 TUE	Day 13 18.01.2017 WED	Day 14 19.01.2017 THU
8-9 am	S31 Cerebellum – I (P) Mr. A.J. Bugari	S36 Fourth ventricle (A) Dr. T. Vijaya Sagar	S40 **Case-14 Introduction-Hemiplegia** Cerebral cortex – I (P) Dr. Teena Lal	S45 Cerebral cortex II (P) Dr. Teena Lal	S49 Biochemistry Block II Charts (B) Dr. Leena Chand	S54 CSF circulation functions BBB, Circum ventricular organ (P) Dr. Padmavathi	S 58 Lateral Ventricle (A) Dr. Kesavi
9-11 am	S 32 A Physiology Tutorial – I (P) Dr. Padmavathi & All Faculty	S 32B Examination of Sensory System (P) Dr. Roopa & All Faculty	S 41A Reactions of Peptone (B) Dr. Vijaya Srinivasan & All faculty	S 41B Examination of Sensory System Revision (P) Dr. Roopa & All Faculty	S 50 A Physiology Tutorial – III (P) Dr. Priscilla Johnson & All faculty	S 50 B Examination Motor System –(P) Dr. Teena Lal & All faculty	S 59 A Reactions of unknown protein (B) Dr. Nithin Kumar & All faculty
11-12 noon	S33 Embryology-Development of Brain (A) Dr. Vijaya Sagar	S 37 Cerebrum I- sulci and gyri (A) Dr. Anandarani	S42 Cerebrum II (A) Dr. Anandarani	S46 Embryology-Development of Brain (A) Dr. Vijaya Sagar	S51 White matter - I (A) Dr. Senthil Kumar	S55 Surface Marking (A) Dr. Anandarani	S 60 Inter peduncular fossa / Review of brainstem histology (A) Dr. Ramesh Kumar
1-2 pm	S34 Cerebellum - II (P) Mr. A.J. Bugari	S 38 Brain stem - reticular formation, ARAS (P) Dr. Abirami	S43 Fatty acid oxidation – all types (B) Dr. Ganesh	S47 Osteology revision (A) Dr. Anandarani & All faculty	S52 White matter - II (A) Dr. Srimathi	S 56 Physiology theory Revision CNS – I (P) Dr. Priscilla Johnson	S 61 Thalamus (A) Dr. T. Vijaya Sagar
2-4 pm	S35 Cerebellum Dissection Dr. D. Kesavi & All faculty	S39 Fourth ventricle Dissection Dr. T. Vijaya Sagar & All faculty	S44 Cerebrum Dissection Dr. Ramesh Kumar & all faculty	S48 Physiology tutorials – II (P) Dr. Padmavathi & All faculty	S 53 Lateral ventricle & White matter Dissection Dr. T. Vijaya Sagar & All faculty	S 57 Third ventricle Dissection Dr. Ramesh Kumar & All faculty	S62 Lateral ventricle & Thalamus Dissection Dr. Kesavi & All faculty

Venue: Lecture Hall No: IV (II FLOOR - 2B - College Building) **Case Resolution venue: Seminar Hall**

BLOCK - III (2016 – 17)
SPINAL CORD, BRAIN, CENTRAL NERVOUS SYSTEM, LIPID METABOLISM

Time	Day 15 20.01.2017 FRI	Day 16 21.01.2017 SAT	Day 17 23.01.2017 MON	Day 18 24.01.2017 TUE	Day 19 25.01.2017 WED	Day 20 27.01.2017 FRI	Day 21 30.1.2017 MON
8-9 am	S63 Thalamus (P) Dr. T. T. Ganesan	S67 Hypothalamus II (P) Dr. Sheela Ravinder	S72 Basal ganglia I (P) Dr. Dilara	S 76 Cerebral circulation and regulation (P) Dr. Roopa	S 81 Limbic system Learning and memory conditioned reflexes (P) Dr. Archana P Kumar	S 85 Metabolism of HDL, dyslipoproteinemias (B) Dr. Jothimalar	S 90 Physiology Revision (P) Mr. A.J. Bugari
9-11 am	S 59 B Examination Motor System – Revision (P) Dr. Teena Lal & All Faculty	S 68A Histology revision Dr. Pranu Chakravarthi & All faculty	S 68 B Cerebellar Function Test (P) Dr. Archana P Kumar & All faculty	S 77 A Physiology Tutorial - V(P) Dr. Padmavathi & All Faculty	S 77B Superficial & Deep reflexes (P) Dr. Sheela Ravinder & All faculty	S 86A Discussion- Block III charts & Estimation of Total Cholesterol (B) Dr. Malini & All Faculty	S 86 B Superficial, Deep reflexes Revision (P) Dr. Sheela Ravinder & All faculty
11-12 noon	S64 Pain & Analgesic system (P) Dr. Anbuselvan	S69 EEG, sleep (P) Dr. Bagavad Geetha	S73 Basal ganglia II (P) **Case 15- Parkinson's disease resolution (Large group)** Dr. Dilara	S 78 Metabolism of ketone bodies (B) Dr. Nalini Ganesan	S 82 Metabolism of cholesterol, bile acids, enterohepatic circulation (B) Dr. M. Santhi Silambanan	S 87 Anatomy Theory Revision (A) Dr. Vijaya Sagar	S 91 Physiology Theory Revision (P) Dr. Abirami
1-2 pm	S 65 Hypothalamus I (P) Dr. Sheela Ravinder	S70 **Case 15 Introduction (Parkinson's disease)** Basal ganglia(A) Dr. Anupriya	S74 Arterial supply to Brain (A) Dr. Muthu Kumar	S 79 Venous Drainage of Brain (A) Dr. Padmasini Srinivasan	S 83 Metabolism of chylomicrons and VLDL (B) Dr. Satish Murthi	S 88 Posture, Equilibrium & Vestibular Apparatus (P) Dr. Teena Lal	S 92 Biochemistry Revision (B) Dr. Manikandan
2-4 pm	S66 Cases 11,13,14 Resolution (Small groups) Dr. Vijaya Srinivasan & All faculty	S71 Physiology Ttutorial – IV Dr. Dilara & All Faculty	S75 Blood Supply of Brain - I Dissection - (A) Dr. T. Vijaya Sagar & All faculty	S 80 Blood Supply of Brain – II Dissection - (A) Dr. Ramesh Kumar & All faculty	S 84 Osteology Revision (A) Dr. Anandarani & All faculty	S 89 Physiology Charts (P) Dr. Archana P Kumar	S93 Biochemistry Tutorial (B) Dr. M. Ganesh & All Faculty

Venue: Lecture Hall No: IV (II FLOOR - 2B - College Building) **Case Resolution venue: Seminar Hall**

Case 11

Brown-Sequard Syndrome Caused by Cervical Disc Herniation

Chih-Hsiu Wang, Chun-Chung Chen, Der-Yang Cho

Department of Neurosurgery, China Medical University Hospital, Taichung, Taiwan, R.O.C.

Brown-Sequard syndrome caused by a herniated cervical disc is rare. We report a 44-year-old male patient who presented with left limb weakness and diminished sensation to pain and temperature on his right side below the C4 dermatome. A large protruding disc on the left side of the C3-4 disc space with cord compression was present on MRI. Brown-Sequard syndrome caused by herniated cervical disc was diagnosed. The patient underwent microdiscectomy and anterior cervical fusion by polyetheretherketone (PEEK) cage containing a core of biphasic calcium phosphate ceramic (triosite). Postoperatively, motor and sensory function returned to normal. Characteristic findings of discogenic Brown-Sequard syndrome are 1) contralateral deficit in sensation of pain and temperature of more than a few levels below the level of cord compression and 2) paracentral protrusion of the disc with cervical spinal stenosis. Early surgical intervention is always recommended. **(Mid Taiwan J Med 2006;11:62-6)**

Key words

Brown-Sequard syndrome, cervical disc herniation, surgical decompression

INTRODUCTION

Brown-Sequard syndrome involves ipsilateral loss of motor function due to corticospinal tract compression, combined with contralateral loss of sensation of pain and temperature caused by spinothalamic tract dysfunction. The most frequent causes of this syndrome are traumatic injuries to the spinal cord and spinal cord tumors (metastatic or intrinsic). Herniation of a cervical disc has rarely been considered to be a cause of Brown-Sequard syndrome. We report a case of C3-C4 herniated cervical disc causing a severe left hemicompression of the spinal cord, resulting in Brown-Sequard syndrome.

CASE REPORT

A previously healthy 44-year-old man developed left upper limb weakness one month prior to presentation. During the one-month period, the weakness extended to include the left lower limb. Motor examination revealed weakness of the left arm and a weakness and spasticity in the left leg, with stiff gait. On neurological examination, the man presented with diminished sensitivity to pain and temperature in the right arm and leg, with a sensory level beginning at C4. On deep tendon reflex examination, a reduction of the left biceps reflex and a hyper-reflexia of the left lower extremity were noted. The plantar response was extensor on the left side.

Magnetic resonance imaging of the cervical spine showed a large left extradural paramedian C3-C4 disc herniation, with cord compression (Fig. 1). A standard microsurgical anterior approach to the C3-C4 interspace was used, and a discectomy was performed. A large amount of disc material was herniated posteriorly, compressing the left spinal hemicord and the left C3 nerve root. After a complete decompression of neural structures, an interbody fusion was

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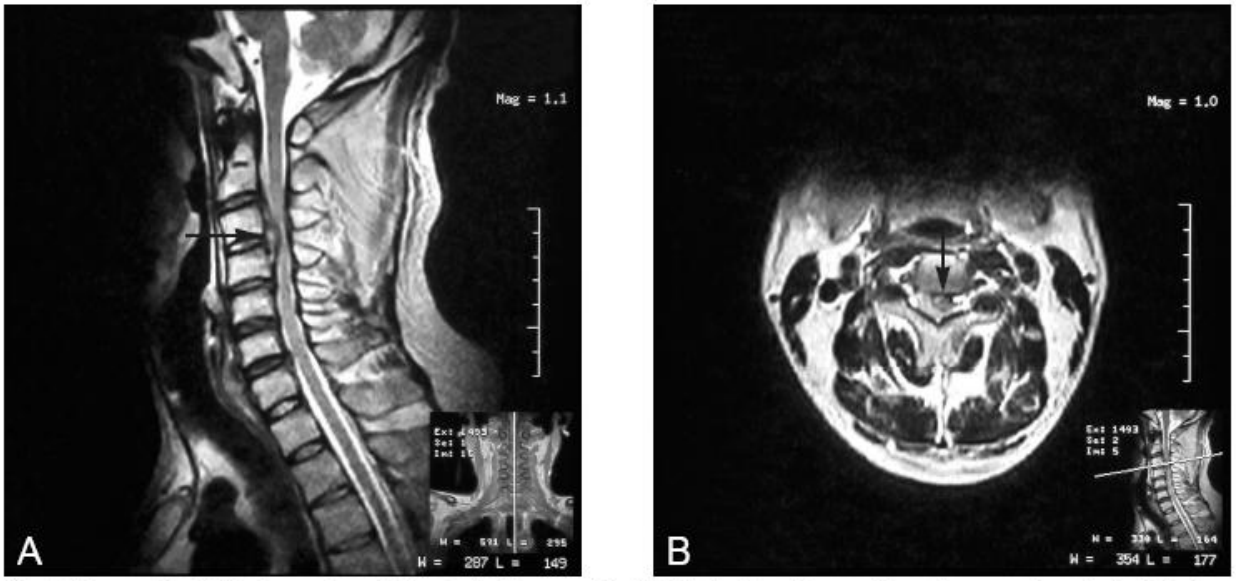

Fig. 1. Preoperative MRI shows a large left extradural paramedian C3-C4 disc herniation, with cord compression. A: Sagital view. B: Axial view.

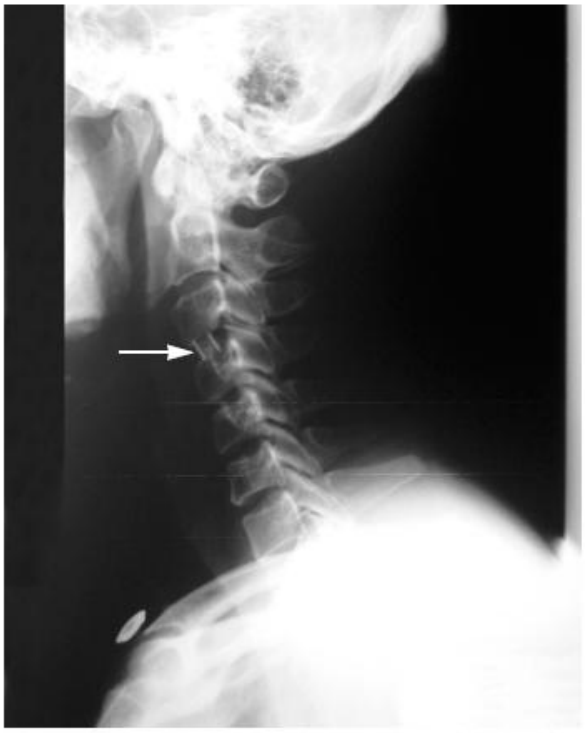

Fig. 2. Postoperative X-rays show interbody fusion with a polyetheretherketone (PEEK) cage.

performed with a polyetheretherketone (PEEK) cage (Stryker) containing a core of triosite (Zimmer) [1,2]. Before the closure of the superficial layers, an intraoperative lateral radiograph control was taken, and the correct position of the implant was checked. After the operation, the patient remained in a rigid cervical collar for 4 weeks.

The postoperative course was satisfactory. His weakness and both sensation of pain and temperature had recovered completely one month after surgery. The postoperative MRI and X-rays showed total decompression of the cord and roots and interbody fusion with the polyetheretherketone (PEEK) cage (Fig. 2).

DISCUSSION

Only a few cases of Brown-Sequard syndrome produced by cervical disc herniation have been published since 1928. However, cervical disc herniation is a common disorder. Large paracentral disc herniation with severe hemicord compression is also not unusual. We believe that Brown-Sequard syndrome produced by cervical disc herniation is not rare and is often underdiagnosed.

The first characteristic finding of discogenic Brown-Sequard syndrome is contralateral deficit in sensation of pain and temperature. This is an obscure perception and is often ignored by patients themselves. Without this chief complaint, physicians can detect the deficit only by very detailed neurological examination. However, there are many reasons why physicians

skip detailed neurological examininations to a brief one.

Hemiparasis without significant cervical symptoms is the first reason. In our patient, the initial presentation was hemiparasis without neck pain. This symptom pointed to a supratentorium cerebral vascular accident. However, when the brain MRI showed normal findings, we revised our neurological examination and found contralateral analgesia and thermanesthesia. Brown-Sequard syndrome caused by cervical lesion was suspected. Cervical MRI then confirmed the diagnosis of discogenic Brown-Sequard syndrome.

Severe and definite radicular sign is another reason. When patients come to the clinic with severe pain and parathesia of neck and limb, they are quickly diagnosed as having cervical disc herniation with radiculopathy after the cervical MRI. However, contralateral deficit in sensation of pain and temperature may coexist but is often disregarded. This is a special condition, which needs to be evaluated. In the literature, half of the cases of Brown-Sequard syndrome produced by cervical disc herniation (12 of 24) had preceded or accompanied radicular signs and symptoms [3-11]. Pure Brown- Sequard syndrome is rare. Fragments of the syndrome plus additional symptoms and signs are more common [11].

The second characteristic finding of discogenic Brown-Sequard syndrome is paracentral protrusion of the disc with cervical spinal stenosis. In the literature, the location of the cervical disc herniation was paracentral in the majority of cases (22 of 24) [6-15]. When a paracentral protrusion of the disc with cervical spinal stenosis is noted from cervical MRI, the sensation of pain and temperature showed be evaluated.

The number of reports of Brown-Sequard syndrome produced by cervical disc herniation is increasing because of the easy application of MRI. Accurate diagnosis has made rapid operation and promising recovery possible.

Brown-Sequard syndrome produced by a cervical disc herniation is presumably often underdiagnosed. Characteristic findings in most cases of discogenic Brown-Sequard syndrome are contralateral deficit in sensation of pain and temperature of more than a few levels below the level of cord compression and paracentral protrusion of the disc with cervical spinal stenosis. Outcomes are generally more favorable in patients for whom rapid diagnosis on MRI leads to spinal cord decompression treatment using surgical approach.

REFERENCES

1. Cho DY, Liau WR, Lee WY, et al. Preliminary experience using a polyetheretherketone (PEEK) cage in the treatment of cervical disc disease. *Neurosurgery* 2002;51:1343-50.
2. Cho DY, Lee WY, Sheu PC, et al. Cage containing a biphasic calcium phosphate ceramic (Triosite) for the treatment of cervical spondylosis. *Surg Neurol* 2005; 63:497-504.
3. Stookey B. Compression of the spinal cord due to ventral extradural cervical chondromas. Diagnosis and surgical treatment. *Arch Neurol Psychiatry* 1928;20:275-91.
4. Eisenberg RA, Bremer AM, Northup HM. Intradural herniated cervical disk: a case report and review of the literature. *AJNR Am J Neuroradiol* 1986;7:492-4.
5. Finelli PF, Leopold N, Tarras S. Brown-Sequard syndrome and herniated cervical disc. *Spine* 1992;17: 598-600.
6. Antich PA, Sanjuan AC, Girvent FM, et al. High cervical disc herniation and Brown-Sequard syndrome. A case report and review of the literature. *J Bone Joint Surg Br* 1999;81:462-3.
7. Clatterbuck RE, Belzberg AJ, Ducher TB. Intradural cervical disc herniation and Brwon-Sequard's syndrome. Report of three cases and review of the literature. [Review] *J Neurosurg* 2000;92(2 Suppl): 236-40.
8. Borm W, Bohnstedt T. Intradural cervical disc herniation. Case report and review of the literature. [Review] *J Neurosurg* 2000;92(2 Suppl):221-4.
9. Iwamura Y, Onari K, Kondo S, et al. Cervical intradural disc herniation. *Spine* 2001;26:698-702.
10. Kobayashi N, Asamoto S, Doi H, et al. Brown-Sequard syndrome produced by cervical disc herniation: report of two cases and review of the literature. [Review] *Spine J* 2003;3:530-3.

11. Mastronardi L, Ruggeri A. Cervical disc herniation producing Brown-Sequard syndrome: case report. *Spine* 2004;29:28-31.
12. Roda JM, Gonzalez C, Blazquez G, et al. Intradural herniated cervical disc. Case report. *J Neurosurg* 1982; 57:278-80.
13. Rumana CS, Baskin DS. Brown-Sequard syndrome produced by cervical disc herniation: case report and literature review. *Surg Neurol* 1996;45:359-61.
14. Kohno M, Takahashi H, Yamakawa K, et al. Postoperative prognosis of Brown-Sequard-type myelopathy in patients with cervical lesions. *Surg Neurol* 1999;51:241-6.
15. Schneider SJ, Grossman RG, Bryan RN. Magnetic resonance imaging of transdural herniation of a cervical disk. [Report] *Surg Neurol* 1988;30:216-9.

Issue for discussion

1. To discuss the structure and blood supply to the spinal cord.
2. Ascending and descending tracts in the spinal cord.
3. To discuss the effects of complete and incomplete transaction of spinal cord.

CASE 12

Malabsorption Syndrome

A 3 year old baby Radhika is referred by a primary physician to you. You are a leading gastroenterologist in the town. The mother of the child Mrs. Vedha, brings her to your office with a prior appointment with you. "Good morning Doctor" says Mrs. Vedha "Good morning Madam" please take your seat Mrs. Vedha sits down on the chair in front of you trying to hold Radhika on her lap. But Radhika is inpatient she gets down and starts moving around trying to explore the room. You glance at her while Mrs. Vedha starts "She is my 3 year old daughter. Doctor I have been referred by Dr. James who is our primary physician to get an expert opinion on her from you"! So saying she produces the referral letter from Dr. James to you. As you take a look at the letter, you observe that Radhika is sitting quietly on the floor silently observing the new environment. She looks thin and under nourished. Her hair is thin and brown. Now you start reading the letter from Dr. James "Dear Doctor, I am referring baby Radhika for your opinion. This is her case summary. She was born normally with a birth weight of 3.4kg. She first came to me when 8 months old with diarrhea. Since there she has been having recurrent diarrhea, vomiting and abdominal distention. I also noticed since then there has been a dip in her growth curve and that her growth was poor. She has also been having recurrent aphthous ulcers. I noticed that she was becoming paler and losing her hair. Her stools were sticky and greasy. I am suspecting that she may have some type of malasorption and need you expert opinion on her. I have enclosed the reports of the tests done on her. Kindly do the needful, with warm regards Dr. James. Slowly put time the letter aside you request Mrs. Vedha to bring Radhika to the examination couch. You then give a teddy bear to Radhika to play and observe her. She looks undernourished, with areas of fallen hair in her scalp. Her hands and legs look very thin. On weigh her on a weighing scale you observe that her weight falls below the 3rd centile for her age in the growth chart. You then pick up a torch and examine her eyes and mouth. You notice that her tongue pale, she has ulcers at the angle of her mouth and her dentitation is poor. Her ribcage looks prominent and seems to be covered by skin only. Her abdomen is distended. You rub your hands, make her lie down. Radhika now starts crying and refuses to lie down. You ask Vedha to make hold her in her lap and slowly palpate her abdomen. You go back to your desk and look through her reports. Her reports say that she was anemic and her peripheral smear showed dimorphic anaemia. Her stool examination report revealed that it was bulky and with more fat globules. Could it his gluten – enteropathy? .....

Points to be discussed

1. Anatomy and development of small and large instestine
2. Physiology of large intestine and the basis of the disease
3. Digestion and absorption of carbohydrates, proteins and fats
4. Steatorrhoea

Case 13

Case Records of the Massachusetts General Hospital

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

Case 10-2002

PRESENTATION OF CASE

First Admission

A 52-year-old right-handed woman was admitted to the neurologic clinic because of ataxia and fatigue.

The patient had been well until four months earlier, when she had had a "sinus infection" characterized by green nasal discharge. Radiographs of the paranasal sinuses were reported to be unremarkable. At about the same time, while she was performing aerobic exercises, there was a sudden sensation of "tilting," without diplopia; on walking shortly thereafter, she felt that she was veering to the left. She had an accompanying band of pain around the top of her head.

These symptoms persisted, and one week later she found that nausea occurred abruptly whenever she raised her head above the horizontal position. After two days, that symptom resolved but was followed by the development of profound fatigue and asthenia. The disequilibrium continued, as did the tendency to veer to the left on walking, although there was no frank vertigo or lightheadedness. The symptoms occurred as soon as she stood or sat up from a horizontal position, and they were not present when she was recumbent or even when she was turning over in bed. There was no associated tinnitus, deafness, nausea, or dysphagia, and the symptoms were not exacerbated in the darkness. She gradually became aware of impairment in her manual dexterity, in that she was able to type and to button her clothing only slowly. When she was fatigued, her speech was slightly slurred. During the next several weeks she began to sleep 16 to 18 hours daily and lost interest in eating, reading, and going to her clerical job.

Forty days before admission, a physician noted that the patient had an ataxic gait, with nystagmus and impaired rapid alternating movements in the right arm. During the month before admission she regained interest in eating and working and slept only eight hours nightly, although she still felt inadequately rested on awakening. For a few days there was fluctuating numbness of the tip of the left middle finger; it soon resolved completely. She was referred to this hospital.

The patient did not smoke and drank little alcohol. She had had oral ulcerations all of her life. She had had two uneventful pregnancies resulting in normal deliveries 31 and 28 years earlier, and she had undergone laparoscopic surgery for endometriosis 10 years before admission. She owned several cats but had never been scratched by them. There was a history of arthritis, which was limited to the fingers. She had visited Arizona two years previously. She had become menopausal during the preceding year and had terminated a trial of estrogen replacement six weeks before this examination. She did not use illicit drugs. Her father had died of lymphoma at the age of 80 years, and her mother had also died at the age of 80, of hepatic failure and breast carcinoma. Three younger siblings were well. There was no family history of psychiatric or neurologic disease. She was admitted to the neurologic clinic of this hospital.

The vital signs, including the blood pressure, were normal. No rash was found except for lifelong acne rosacea. Heberden's nodes were present. The lungs and heart were normal. On neurologic examination, there was a very slight spastic dysarthria. Olfaction was normal, as were the optic fundi and visual fields. Ocular motor movements showed the normal generation of saccades, but saccadic pursuit was more prominent on the right side; in addition, symmetric, initially hypometric saccades may have been present. Facial sensation and jaw jerks were normal, and there was a symmetric grimace. The gag reflex and lingual movements were normal. Muscle tone was normal in both arms and both legs, without clonus. There was a five-degree pronating drift of the right hand. Motor power was 5/5 in all the muscle groups except the right wrist extensors, in which it was 4/5. The deep-tendon reflexes were ++ and symmetric; an equivocal Babinski sign was elicited in the left foot. There was a very mild, symmetric intention tremor on finger-to-nose testing. Fine finger movements were symmetric, with dysrhythmia, and the result of heel-to-shin testing was normal. There was a symmetric, 10 percent reduction in vibratory sensation at the toes. Pinprick sensation

and proprioception were preserved. The patient was unable to walk with a tandem gait and had a tendency to deviate to the left on walking.

Laboratory studies performed elsewhere showed a normal complete blood count and erythrocyte sedimentation rate. The total protein level was 8.2 g, and the albumin level 4.1 g per deciliter. The aspartate aminotransferase level was 42.1 U per liter (normal range, 11 to 40). The levels of electrolytes were normal except that the potassium level was 5.5 mmol per liter in a hemolyzed specimen. The levels of glucose, urea nitrogen, creatinine, bilirubin, calcium, alkaline phosphatase, and thyrotropin were normal. A test for antinuclear antibodies was negative on two occasions. Cranial magnetic resonance imaging (MRI), performed before and after the administration of gadolinium, revealed no abnormalities. Studies at this hospital disclosed normal levels of vitamin B_{12}, vitamin E, and angiotensin-converting enzyme. Tests for anti-Hu and anti-Yo antibodies and a serologic test for Epstein–Barr virus were negative. A lumbar puncture yielded clear, colorless cerebrospinal fluid that contained two red cells and four white cells per cubic millimeter; of the white cells, 82 percent were lymphocytes, 16 percent monocytes, and 2 percent nonhematic cells. The glucose level was 60 mg per deciliter (3.3 mmol per liter), the total protein level was 23 mg per deciliter, the albumin level was 15.6 mg per deciliter, and the IgG level was 2.7 mg per deciliter; no oligoclonal bands were detected.

Subsequent Evaluation

Two months later the patient returned to the clinic and reported that her symptoms had steadily improved and that she was "nearly normal." She said that she had resumed a normal manner of typing, writing, walking, and sleeping. She had resumed estrogen-replacement therapy one month before this visit and took no other medications.

On examination, she was alert and fully oriented. There still was mild saccadic breakdown on smooth pursuit. Motor power was 5−/5 in the left wrist extensors and in the left hip and left knee flexors. There was a very slight rebound phenomenon, more so in the left arm than in the right — that is, abrupt release of resistance to strong flexion of the arm resulted in sudden flexion that she could not inhibit. Finger-to-nose testing showed very slight ataxia bilaterally. The deep-tendon reflexes were ++++, with bilateral Hoffmann's reflexes and cross adductor signs. A few beats of clonus were noted at the left ankle, without a Babinski sign. The gait was slightly broad but was much more steady than on the initial evaluation, and she was able to walk with a tandem gait. No treatment was advised, and the patient did not return in six months for follow-up.

Second Admission

Two years and five months after the second evaluation at this hospital and after her retirement from work, the symptoms recurred and included word-finding difficulty, unsteadiness, and fatigue. Seventeen days before admission, neurologic examination revealed that she was fully alert and oriented, with normal memory and intellect but with slight word-finding difficulty. The cranial-nerve functions were preserved, except for strabismus with mild right esotropia. Sensation was normal. Motor power was 5/5 without drift, and muscle tone was normal. Rapid alternating movements and the result of finger-to-nose testing were slightly abnormal on the left side; the result of heel-to-shin testing was normal bilaterally. The gait was wide and slightly unsteady; Romberg's test was positive, with consistent backward falling; in addition, the patient was unable to walk with a tandem gait. The deep-tendon reflexes were ++ and symmetric, without abnormal reflexes.

A cranial MRI scan (Fig. 1), obtained elsewhere, showed an enhancing mass, approximately 1.5 by 1.2

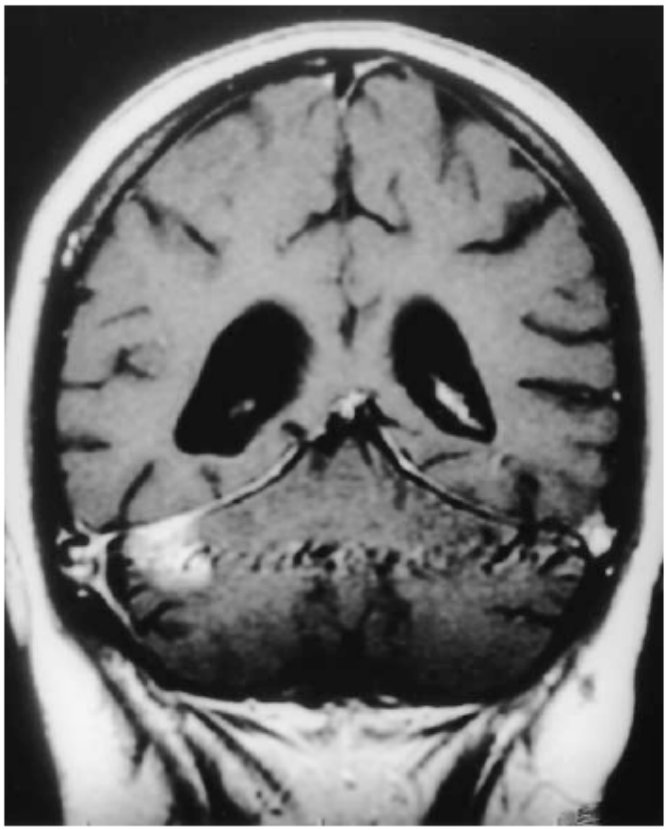

Figure 1. Coronal T_1-Weighted MRI Scan Obtained after the Administration of Contrast Material, Showing a 1.5-cm Enhancing Mass in the Right Cerebellar Hemisphere.

The mass abuts the right tentorium, and there is focal thickening of the tentorium at this site.

by 1.0 cm, in the right cerebellar hemisphere, with deviation of the fourth ventricle; the mass appeared to invade the right tentorium. A second mass, 8 mm in diameter, was adjacent to the left frontal horn of the ventricle, and a third lesion, 11 mm in its greatest dimension, was evident in the right corona radiata. A computed tomographic scan of the abdomen and pelvis was unremarkable except for a small density in the right ovary. Chest radiographs were clear.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

DR. LLOYD M. ALDERSON*: The striking feature of this patient's course is the long period between her initial neurologic illness, characterized by signs and symptoms referable to the cerebellum and brain stem, and her second illness, in which multiple enhancing brain lesions were seen. I prefer to make a single diagnosis that would account for both illnesses and shall therefore assume that they represent different manifestations of a single disease process. This process must therefore have elements of spontaneous recovery, a prolonged latency period, and enhancing parenchymal brain lesions.

The symptoms and signs of the initial illness suggest that the disease involves central nervous system structures in the posterior fossa. Disequilibrium and the presence of hypometric saccadic eye movements suggest dysfunction of the vestibulocerebellum.[1] Hypometric saccades may also be seen in patients with Parkinson's disease, progressive supranuclear palsy, or tumors involving the dorsal midbrain. The absence of vertigo argues that the vestibular nerve is not involved. Hypersomnia implies the presence of a lesion involving the hypothalamus and upper midbrain; the destruction of dopaminergic neurons in these areas eliminates inhibitory input to the dorsal raphe nuclei, which regulate sleep.[2] Hypersomnia and the indifference described in this patient are not localizing features and may also result from increased intracranial pressure or encephalitis.

May we review the MRI scans?

DR. R. GILBERTO GONZALEZ (Neuroradiology): Approximately two and a half years after MRI scans that showed no abnormalities were obtained, MRI was again performed. Axial T_2-weighted images through the posterior fossa showed a hypointense abnormality in the right cerebellar hemisphere. After the administration of contrast material, T_1-weighted coronal images (Fig. 1) showed intense enhancement of this abnormality. The lesion was approximately 1.5 cm in its greatest dimension; it abutted the tentorium, was contiguous with it, and may have invaded it.

Axial images obtained at the level of the third ventricle revealed an abnormal signal adjacent to the left frontal horn. After the administration of contrast material, the abnormal signal was enhanced, indicating breakdown of the blood–brain barrier. A third area of enhancement was seen in the right corona radiata, adjacent to the right lateral ventricle. After the administration of contrast material, this mass was intensely enhanced; it was approximately 11 mm in its greatest dimension.

DR. ALDERSON: I shall first discuss the possible causes of the patient's initial illness. Some causes of cerebellar ataxia are listed in Table 1. It is unlikely that this patient had an inherited disorder. Patients with inherited disorders generally have progressive disease, do not have spontaneous remissions, and do not have parenchymal brain lesions. Ataxia–telangiectasia, for example, is a congenital immunodeficiency syndrome that usually first appears in early childhood and that is characterized by telangiectasias, impaired intellect, and progressive ataxia.[3] Patients with ataxia–telangiectasia are predisposed to brain tumors, particularly primary lymphoma of the central nervous system. Although the brain lesions seen on the second MRI study in the current case are consistent with the presence of primary lymphoma of the central nervous system, there is little else to support a diagnosis of ataxia–telangiectasia.

Olivopontocerebellar atrophy is a progressive degeneration of the brain stem and cerebellum that affects adults in the fifth or sixth decade of life. In olivopontocerebellar atrophy, spontaneous remission is very un-

TABLE 1. POSSIBLE CAUSES OF CEREBELLAR ATAXIA IN ADULTS.

Inherited disorders
Friedreich's ataxia
Spinocerebellar ataxia
Type 1 (olivopontocerebellar atrophy)
Type 2 (Wadia's ataxia)
Type 3 (Machado–Joseph disease)
Type 4 (with sensory loss)
Dentatorubropallidoluysian atrophy
Dominant periodic ataxia
Ataxia–telangiectasia
Noninherited disorders
Olivopontocerebellar atrophy (spontaneous)
Stroke or transient ischemic attack
Multiple sclerosis
Paraneoplastic disorder
Alcoholic cerebellar degeneration
Tumor or abscess of the posterior fossa
Vitamin E deficiency
Exposure to toxins (lead, anticonvulsants, salicylates, aminoglycosides, sedatives)
Miller Fisher syndrome
Infection (viral encephalitis, human immunodeficiency virus infection, Creutzfeldt–Jakob disease)

*Department of Neurosurgery, Rhode Island Hospital; assistant professor of neuroscience, Brown University — both in Providence.

usual,[4] and MRI often shows some degree of cerebellar atrophy in patients who have symptoms. Without radiologic evidence, olivopontocerebellar atrophy is an unlikely diagnosis in this patient.

The acute onset of this patient's initial symptoms and her spontaneous recovery raise the question of stroke. Gait ataxia, headache, and nausea can reflect ischemic damage in a posteroinferior cerebellar artery or in a superior cerebellar-artery distribution. However, the absence of other cranial-nerve signs and the normal MRI scans of the brain in this case argue against infarction. In addition, this patient had no risk factors for atherosclerotic disease or cardioembolic stroke. Transient ischemic attacks due to vertibrobasilar insufficiency are a common cause of vertigo in older adults. Such attacks are usually abrupt in onset and episodic, lasting just minutes.[5] Associated symptoms include headache, diplopia, loss of consciousness, and weakness or numbness of the arms and legs. This patient's history does not support such a diagnosis.

Likewise, in multiple sclerosis, there may be an acute onset of signs and symptoms originating in the brain stem and cerebellum. Spontaneous recovery, quiescent periods, and recurrence with enhancing parenchymal brain lesions can all be features of this disease. In fact, the clinical history and examination results in this case — symptomatic lesions in the central nervous system separated in both time and space — meet the criteria for multiple sclerosis. Multiple sclerosis is about twice as common in women as in men, and the average age at the time of diagnosis is 30 years. This patient was a woman, but she was 52 years old at presentation.[6] Cerebellar dysfunction and lassitude (though not hypersomnia) are common features of multiple sclerosis at the time of presentation but are usually accompanied by internuclear ophthalmoplegia, which this patient did not have. The duration of an episode of multiple sclerosis is typically 6 to 8 weeks, and the interval between attacks is approximately 15 months. The timing of this patient's episodes is therefore consistent with a diagnosis of multiple sclerosis. However, the MRI studies do not support this diagnosis. In 90 percent of patients with multiple sclerosis, there are abnormalities on MRI,[7] whereas this patient's initial MRI scans were normal. Although there are several discrepancies between a classic presentation of multiple sclerosis and this patient's presentation, the timing of her symptoms prevents me from ruling out this diagnosis.

Neurosarcoidosis is another disease with a relapsing and remitting course, and it may produce enhancing brain lesions. Inflammatory cells, particularly CD4 lymphocytes, congregate and produce cytokines that can promote the formation of granulomas in a variety of tissues, including those of the lungs, skin, eyes, brain, cerebrospinal fluid, and peripheral nerves.[8] Neurologic manifestations include cranial neuropathies, mass lesions in the brain, aseptic meningitis, encephalopathy, and myopathy. Evaluation of the cerebrospinal fluid can reveal elevated pressure, increased total protein, hypoglycorrhachia, and mononuclear pleocytosis. After the administration of contrast material, cranial MRI frequently shows hyperintense lesions on T_2-weighted images. In the current case, the factors that argue against a diagnosis of neurosarcoidosis are the absence of systemic involvement (90 percent of patients with sarcoidosis have lung involvement) and the essentially normal findings on examination of the cerebrospinal fluid.

A paraneoplastic disorder is an important consideration in this case because of the tendency of these disorders to affect the cerebellum and because of the enhancing lesions seen on the patient's MRI scans at the time of the second admission; those lesions could represent a metastatic neoplasm. The first point to remember when considering this diagnosis is its rarity: paraneoplastic disorders occur in fewer than 1 percent of all patients with cancer.[9] Paraneoplastic cerebellar degeneration is most often associated with lymphomas and tumors of the breast, lung, and female reproductive tract.[10] In patients with paraneoplastic cerebellar degeneration, cancer has a more indolent course than it does in patients without the degeneration, and the neurologic symptoms precede the diagnosis of cancer. Clinically, patients with paraneoplastic cerebellar degeneration present with unrelenting truncal and appendicular ataxia, dysarthria, and nystagmus that progresses over a period of weeks or months to a severe pancerebellar dysfunction. MRI scans of the brain are normal in the early stages of paraneoplastic cerebellar degeneration. In this patient, the 24-month interval during which neither the autoimmune neurologic disease nor the underlying cancer was symptomatic would be atypical for paraneoplastic cerebellar degeneration, making this diagnosis very unlikely.

Toxins and drugs are a more common cause of ataxia, particularly in association with transient symptoms. Patients with alcoholic cerebellar degeneration present with progressive ataxia of the gait and appendicular ataxia, without dysarthria or nystagmus.[11] In that disease, MRI may show atrophy of the vermis of the cerebellum. We are not given a history of alcohol ingestion in this case, and the parenchymal brain lesions seen later in the patient's course would have had to represent a separate disease. Similarly, the possibility of ataxia associated with other environmental toxins or drugs is not supported by the history.

Infectious and postinfectious neurologic disorders can remit spontaneously and may explain this patient's initial illness. In children, infection with coxsackievirus or echovirus can result in acute cerebellar ataxia, a benign disease in which symptoms resolve spontaneous-

ly over a period of weeks or months.[12] However, this syndrome is rare in adults. Epstein–Barr virus is another agent associated with cerebellar dysfunction[13] and is of particular concern in this patient because of its association with neoplasms that can involve the brain (e.g., lymphoma and nasopharyngeal carcinoma). In the current case, however, negative titers for Epstein–Barr virus make this diagnosis unlikely. Another herpesvirus similar to Epstein–Barr virus, human herpesvirus 8, has been found in most of the tumor samples obtained from both immunocompetent and immunodeficient patients with primary lymphoma of the central nervous system.[14] Although this virus is not associated with cerebellar or brain-stem symptoms, the lesions seen on the patient's second series of MRI scans are consistent with those seen in primary lymphoma of the central nervous system.

Acute infection with the human immunodeficiency virus (HIV) may cause a mononucleosis-like syndrome, with headache, fever, altered mental status, cranial neuropathies, and abnormal findings in the cerebrospinal fluid, such as lymphocytic pleocytosis and an elevated protein level. Patients with HIV infection are susceptible later in the course of the disease to primary lymphoma of the central nervous system and to toxoplasmosis, both of which can produce enhancing brain lesions. Cerebellar degeneration has also been described in HIV-infected patients.[15] This patient's course is not typical of acute HIV infection, however, and the brain lesions associated with primary lymphoma of the central nervous system or with toxoplasmosis in patients with the acquired immunodeficiency syndrome are frequently ring-enhancing, unlike the homogeneously enhancing lesions seen in this patient.[16]

A postinfectious syndrome may also have some of the features of this patient's course. Patients with the Miller Fisher syndrome, which is a variant of the Guillain–Barré syndrome, present with ataxia, ophthalmoplegia, and loss of reflexes.[17] The symptoms may develop suddenly, and there may be a recent history of gastrointestinal or respiratory tract infection. The symptoms plateau two to three weeks later and are followed by a recovery phase that often lasts months. This patient was not evaluated at the onset of her symptoms, but the examination four months later did not show a loss of reflexes; moreover, the level of protein in the cerebrospinal fluid, which is frequently elevated in Guillain–Barré syndrome, was normal. Although this syndrome remains a viable explanation for the patient's initial illness, it does not explain her subsequent illness.

If I assume that this patient's two illnesses are somehow linked, I must try to explain the 24-month period during which she had no symptoms. Tumors can have prolonged dormant periods and then recur years after the initial presentation. Such dormancy may be a feature of almost any tumor but is common in lymphoma and cancer of the breast and kidney.

In this patient, the initial presentation has characteristics of an infectious or immune-mediated disease, and the second has features more consistent with those of a neoplasm. If these two illnesses were separate, then the differential diagnosis of the enhancing brain lesions is large. Many cancers can metastasize to the brain and appear as enhancing lesions similar to those seen in this case on the second MRI study. If a neoplasm can explain this patient's complete clinical course, we must consider the possibility of a lesion in the cerebellum or brain stem that spontaneously regressed. Spontaneous regression has been described in primary lymphoma of the central nervous system,[18] and that is what I believe is the most likely diagnosis here.

Primary lymphoma of the central nervous system is a form of extranodal non-Hodgkin's lymphoma, usually of the diffuse large-cell or immunoblastic subtype.[19,20] Immunocompetent patients commonly present in the sixth decade of life with an intracranial mass lesion. In cases of primary lymphoma of the central nervous system, tumors are rarely seen outside of the central nervous system or the eyes. Specifically, the vitreous is involved in 20 percent of the cases, and the cerebrospinal fluid is involved in 33 percent. The radiographic appearance of primary lymphoma of the central nervous system is consistent with the findings on this patient's second series of MRI scans. The lesions are multiple in 60 percent of the cases and have a tendency to occur in the white matter adjacent to an ependymal surface.[21] The size of the lesions ranges from 0.9 to 5.0 cm, with an average of 2.1 cm. On MRI scans of immunocompetent patients, the lesions are homogeneously enhanced on T_1-weighted images after the administration of gadolinium and are isointense relative to gray matter on T_2-weighted images. The latter characteristic reflects the high degree of cellularity often seen on biopsy. Although these characteristics are not highly specific, they are all evident on this patient's second MRI study.

The case history is similar in many ways to that of patients with the sentinel lesions of primary lymphoma of the central nervous system. An atypical form of multiple sclerosis is possible, but less likely. The diagnostic procedure was most likely a brain biopsy.

CLINICAL DIAGNOSIS

Primary lymphoma of the central nervous system.

DR. LLOYD M. ALDERSON'S DIAGNOSIS

Primary lymphoma of the central nervous system, with sentinel lesions.

PATHOLOGICAL DISCUSSION

DR. IVANA DELALLE (Neuropathology): A biopsy of the left frontal lobe performed at another hospital showed atypical lymphocytes surrounding intraparenchymal vessels and diffusely infiltrating white matter, findings consistent with the presence of a diffuse large-B-cell lymphoma. As stated by Hochberg and Miller,[20] a diagnosis of primary lymphoma of the central nervous system can be made if two criteria are met. First, the patient must present with a neurologic symptom originating from a lesion proved to be lymphoma, either on biopsy or on autopsy; second, at the time of initial evaluation, there must be no evidence of lymphoma at any site except the brain, leptomeninges, spinal cord, or eye. According to a recent statistical analysis, primary lymphoma of the central nervous system represents about 10 percent of all primary tumors of the central nervous system and thus has a prevalence exceeded only by those of meningioma and low-grade astrocytoma.[22]

The most common type of primary lymphoma of the central nervous system is large-B-cell lymphoma, characterized by large cells with a high nuclear-to-cytoplasmic ratio, vesicular chromatin, and prominent nucleoli. These cells uniformly express the B-cell markers CD19, CD20, CD22, and CD79a (Fig. 2) and variably express the surface or cytoplasmic immunoglobulin CD5 or CD10 (or both). Other, relatively rare types of primary lymphoma of the central nervous system include peripheral T-cell lymphoma, anaplastic large-T-cell lymphoma, and plasmacytoma.

The main clinical characteristic of this patient's lymphoma was the series of remissions that were spontaneous or associated with corticosteroid treatment, mimicking the presentation of a demyelinating disease. Several cases of large-B-cell lymphoma in which there was at least one episode of spontaneous remission have been reported.[18,23,24] The term "sentinel" lesion has been proposed for those cases of primary lymphoma of the central nervous system in which lesions regress spontaneously or regress with corticosteroid treatment.[18] All the patients in the reported cases, like this patient, were immunocompetent women with diffuse large-B-cell lymphoma.

DR. ROBERTO CIORDIA (Neuro-oncology): After the diagnosis of primary lymphoma of the central nervous system was established, the patient was treated with high-dose methotrexate. Despite treatment, her disease progressed, and she died eight months after the diagnosis was made.

DR. DELALLE: An autopsy was restricted to the brain. Gross examination showed a coiled aneurysm in the right anterior communicating artery; old, bilateral linear infarcts in the medial prefrontal lobes; and a lesion that resembled an infarct in the left lateroventral prefrontal cortex. On microscopical examination, this lesion appeared to be a scar infiltrated by many lymphocytic cells, some of which appeared atypical. Gliotic scars adjacent to the prominent infiltrates of lymphoma were found in several areas of the brain. These scars probably represented "burned-out" lymphoma — that is, the lesions that caused the initial neurologic symptoms, which subsided when the lymphoma spontaneously regressed.

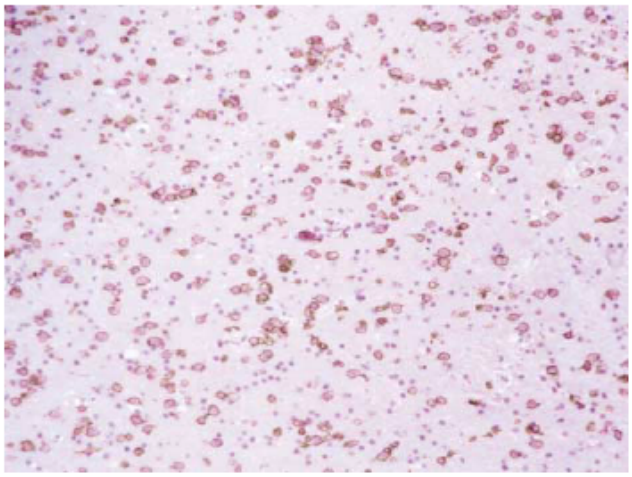

Figure 2. Large, Atypical Lymphoid Cells That Express CD20, a B-Cell Marker (Hematoxylin and Eosin, ×125).

ANATOMICAL DIAGNOSIS

Primary lymphoma of the central nervous system.

REFERENCES

1. Hotson JR. Cerebellar control of fixation eye movements. Neurology 1982;32:31-6.
2. Markand ON, Dyken ML. Sleep abnormalities in patients with brain stem lesions. Neurology 1976;26:769-76.
3. Sedgwick RP, Boder E. Ataxia-telangiectasia. In: Vinken PJ, Bruyn CW, eds. The phakomatoses. Vol. 14 of Handbook of clinical neurology. Amsterdam: North-Holland Publishing, 1972:267-339.
4. Berciano J. Olivopontocerebellar atrophy: a review of 117 cases. J Neurol Sci 1982;53:253-72.
5. Grad A, Baloh RW. Vertigo of vascular origin: clinical and electronystagmographic features in 84 cases. Arch Neurol 1989;46:281-4.
6. Rolak LA. Multiple sclerosis. In: Samuels MA, Fiske S, eds. Office practice of neurology. New York: Churchill Livingstone, 1996:350-3.
7. Francis GS, Evans AC, Arnold DL. Neuroimaging in multiple sclerosis. Neurol Clin 1995;13:147-71.
8. Stern BJ, Krumholz A, Johns C, Scott P, Nissim J. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42:909-17.
9. Jaeckle KA. Paraneoplastic neurologic diseases. In: Levin VA, ed. Cancer of the nervous system. New York: Churchill Livingstone, 1996:361-72.
10. Dalmau J, Graus F. Paraneoplastic syndromes of the nervous system. In: Black PM, Loeffler JS, eds. Cancer of the nervous system. Cambridge, Mass.: Blackwell Science, 1997:674-702.
11. Victor M, Adams RD, Mancall EL. A restricted form of cerebellar cortical degeneration occurring in alcoholic patients. Arch Neurol 1959;1:579-688.
12. Weiss S, Carter S. Course and prognosis of acute cerebellar ataxia in children. Neurology 1959;9:711-21.
13. Ito H, Sayama S, Irie S, et al. Antineuronal antibodies in acute cere-

bellar ataxia following Epstein-Barr virus infection. Neurology 1994;44: 1506-7.
14. Corboy JR, Garl PJ, Kleinschmidt-DeMasters BK. Human herpesvirus 8 DNA in CNS lymphomas from patients with and without AIDS. Neurology 1998;50:335-40.
15. Tagliati M, Simpson D, Morgello S, Clifford D, Schwartz RL, Berger JR. Cerebellar degeneration associated with human immunodeficiency virus infection. Neurology 1998;50:244-51.
16. Cordoliani Y-S, Derosier C, Pharaboz C, Jeanbourquin D, Schill H, Cosnard G. Primary cerebral lymphoma in patients with AIDS: MR findings in 17 cases. AJR Am J Roentgenol 1992;159:841-7.
17. Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 1956;255:57-65.
18. Alderson LM, Fetell MR, Sisti M, Hochberg F, Cohen M, Louis DN. Sentinel lesions in primary CNS lymphoma. J Neurol Neurosurg Psychiatry 1996;60:102-5.
19. Maher EA, Fine HA. Primary CNS lymphoma. Semin Oncol 1999; 26:346-56.
20. Hochberg FH, Miller DC. Primary central nervous system lymphoma. J Neurosurg 1988;68:835-53.
21. Johnson BA, Fram EK, Johnson PC, Jacobowitz R. The variable MR appearance of primary lymphoma of the central nervous system: comparison with histopathologic features. AJNR Am J Neuroradiol 1997;18:563-72.
22. Nuckols JD, Liu K, Burchette JL, McLendon RE, Traweek ST. Primary central nervous system lymphomas: a 30-year experience at a single institution. Mod Pathol 1999;12:1167-73.
23. Al-Yamany M, Lozano A, Nag S, Laperriere N, Bernstein M. Spontaneous remission of primary central nervous system lymphoma: report of 3 cases and discussion of pathophysiology. J Neurooncol 1999;42:151-9.
24. Sugita Y, Shigemori M, Yuge T, et al. Spontaneous regression of primary malignant intracranial lymphoma. Surg Neurol 1988;30:148-52.

Issue for discussion:

1. Discuss the anatomy, histology and blood supply of the cerebellum
2. Functional division and connection of the cerebellum
3. Cerebullar function test and Cerebullar disorders

CASE 14

A Case of Cerebrovascular Accident

by
David F.Dean, Department of biology, Spring Hill college

Case Presentation:

Samuel Dexter is a 52-year-old African-American man who is both a husband and father. He is moderately obese (BMI of 32), and has smoked two packs of cigarettes a day for the past 38 years. He awakes one morning with weakness on his right side. He is a bit confused, sees double, and his speech is slurred. When he attempts to walk to the bathroom, he stumbles a few times and falls once. His wife suspects that he has suffered a stroke and calls 9II. Emergency personnel arrive within minutes of her call and transport Samuel to the emergency room of the nearest hospital.

Upon examination by the emergency room physician, Samuel is found to have right hemiparesis and diminished pinprick and two-point discrimination on the right side of his head and arm. His deep tendon reflexes are hyperactive on the right and there is a positive Babinski reflex on the right. He has difficulty articulating answers to the questions he is asked, speaking only a few words and frequently responding with just a verb or a noun.

His ability to respond to complicated verbal commands, whether spoken or written, is not impaired. In addition, his systemic blood pressure was found to be 160/100. A serum lipid profile was performed and the results are shown in the table below.

Table 1. Serum Lipid Profile Results	
Triglycerides	220 mg/dl
Total Cholesterol	280 mg/dl
LDL	210 mg/dl
HDL	30 mg/dl

Questions

1. Name and discuss the descending motor fibres.
2. Discuss the origin, course and termination of the pyramidal tract.
3. Discuss the features of UMN lesion.
4. Define the terms ischemia and infarction
5. What is a stroke?
6. Define the terms ipsilateral and contralateral as they apply to the functionality of the central nervous system.
7. Explain the significance of the findings of hyperactive deep tendon reflexes and babinski sign positive on the affected side of Samuel's body.
8. Based upon the historical and physical exam findings, what specific area(s) of Samuel's brain have been damaged as the result of his stroke?

CASE 15

A 64 year old male presented with an one year history of slowly progressive tremor of the right hand. During this time he had also noticed a change in his handwriting. He would start off a sentence with well-formed characters that, however, would progressively deteriorate into smaller and smaller script. He was not hypertensive or diabetic.

On examination he was elderly appearing. He was oriented to place time and person. He was attentive with a digit span of 6 digits forward. He had recall of 4items at 5 minutes. Speech was fluent with good naming, comprehension and repetition. Verbal responses were slow accurate. He was hypophonic. Visuospatial constructions were well organized. His drawing and handwriting were however affected by a tremulous motion of the right hand. Cogwhell rigidity was evident in both upper extremities, more marked on the right. Strength was normal in all four extremities. DTRs were normal (2) in upper and lower extremities. The jaw jerk was not increased and a snout reflex was not present. Plantar reflexes were flexor. Sensory examination was normal to primary and cortical modalites. His posture was stooped forward. There was moderate retropulsion and he walked with a shuffling gait. Romberg testing was steady eyes open and closed.

Issue for discussion:

1. Name the various nuclei & connections of the Basal ganglia.
2. What are the features of Parkinsonism?
3. Discuss their pathophysiology?
4. The pharmacophysiology of drugs used in this disorder.
5. Name the other disorders of Basal ganglia.

SESSION / TIME	TOPIC/OBJECTIVES 2016
Session 1 8-9 am	**Neurology as a specialty** Students should know about • Eliciting the history • Clinical exam • correlating transfer diagnosis • Investigations of the clinical diagnosis
Session 2A 9-11 am	**Reaction of protein –Gelatin (B)** At the end of the session the students should be able to Perform the tests to identify gelatin in the given sample
Session 3 11-12 noon	**Case Introduction (Brown Sequard Syndrome) - Spinal Cord** The student should know the extent, meningeal coverings, arterial supply, and venous drainage, transverse section of the spinal cord and important sensory tracts and motor tracts
Session 4 1-2 pm	**Introduction and causes of cerebrovascular diseases (CM)** At the end of the session the student should be able to List out the causes of cerebrovascular diseases
Session 5 2-4 pm	**Dissection – Spinal cord** At the end of session students should know the external features of spinal cord. Small group demonstration
Session 6 8-9 am	**Digestion & absorption of lipids** At the end of the session the students should be able to • The role of bile acids in the process of emulsification of lipids • The enzymes involved in the digestion of lipids • Absorption of digested lipids • Disorders associated - steatorrhea
Session 2B 9-11 am	**Histology of spinal cord** The students should understand the microanatomy of spinal cord.
Session 7 11-12 noon	**Medulla-I** At the end of the session the students should know the external features of medulla oblongata
Session 8 1-2 pm	**Medulla – II** Students should know at the end of the session: The various structures present at sensory decussation and mild olivary level sections of medulla
Session 9 2-4 pm	**Dissection – Spinal cord** At the end of session students should know the external features of spinal cord/ histology of spinal cord
Session 10 8-9 am	**Fatty acid synthesis, acylglycerol, lipd storage disorders** The student should know at the end of the session • The biomedical importance of fatty acid synthesis. • De novo synthesis of fatty acids. The mechanisms that regulate lipogenesis.
Session 11a	**Reaction of protein –Casein (B)** At the end of the session the students should be able to
Session 12 11-12 am	**Pons** The student should know the external features and internal features of pons at two levels (upper and lower level).
Session 13 1-2 pm	**Community Medicine** At the end of the session the students should be able to
Session 14 2-4 pm	**Medulla Dissection** The students should be able to identify the external features of medulla, blood supply and applied anatomy of it.

Session 15 8-9 am	**Introduction - Receptor, generator potential & properties** At the end of the session students should be able to • Describe Structure and function of receptors. • Classify receptors. • Explain Properties of the receptors. Explain the Experimental evidences to study the properties of receptor.
Session 11b 9-11 am	**COMMUNITY MEDICINE**
Session 16 11-12 noon	**Classification of Nerve, Nerve Injury, Wallerian degeneration and regeneration** Students should know at the end of the session: 1. Classification of neurons. Nerve injuries, Wallerian degeneration and regeneration.
Session 17 1-2 pm	**Synapse - I** Students should know at the end of the session: 1. Synapse-Types, 2.structure, 3.mechanism of transmission, 4.properties and Neurotransmitters
Session 18 2-4 pm	**Pons - Dissection** The students should know the external features important cranial nerve nuclei situated, blood supply and applied anatomy of pons
Session 19 8-9 am	**Synapse - II** Students should know at the end of the session: 1. Synapse-Types, 2.structure, 3.mechanism of transmission, 4.properties and Neurotransmitters
Session 20a 9-11 am	**General Examination (P)** At the end of the session the students should be able to
Session 21 11-12 noon	**Reflexes – I** Students should know at the end of the session: 1. Reflex arc 2. Muscle spindle structure and functions Monosynaptic reflex
Session 22 1-2 pm	**Reflexes – II** Students should know at the end of the session: Polysynaptic Reflex, 2. Properties of Reflex.
Session 23 2-4 pm	**Osteology** The student should know at the end of the session: • Base of skull, Norma frontals, Norma verticalis, Norma occipitals, Norma lateralis. **Teaching Method :** Small group teaching and learning
8-12	**PTA**
Session 24 1-2 Pm	**Spinal cord – I Descending tracts** Students should know at the end of the session: Descending Tracts – Pathways and their Functions
Session 25 2-3 Pm	**Mid brain** The Students should know the external and internal features of midbrain, its blood supply and applied anatomy.
Session 26 3-4 Pm	**Mid brain - Dissection** The Students should know the external and internal features of midbrain, its blood supply and applied anatomy.
Session 27 8-9 am	**Spinal cord - II Ascending tracts** Students should know at the end of the session: 1. Ascending Tracts, their pathways and functions. Clinical features of Hemiplegia
Session 20 B 9-11 am	**General Examination (P)** At the end of the session the students should be able to

Session 28 11-12 noon	**Spinal Cord III - Transection of spinal cord/ hemi/ Complete** Students should know at the end of the session: 1. Causes of transection of Spinal Cord. Features of Complete / Hemisection of the Spinal Cord.
Session 29 1-2 pm	**Case Introduction (Cerebellar disease)cerebellum** The student should know at the end of the session about parts, features, subdivisions, nuclei, connections and functions of cerebellum.
Session 30 2-4 pm	**Dissection – Cerebellum** The student should know the important gross anatomical features of cerebellum along with its blood supply and applied anatomy.
Session 31 8-9 am	**Cerebellum -I** Students should know at the end of the session: Nuclei and connections of Cerebellum
Session 32 A 9-11am	**Physiology Tutorial** At the end of the session the students should be able to
Session 33 11-12 noon	**Embryology- Development of Brain** At the end of the session the students should be able to describe the embryological development of brain
Session 34 1-2 pm	**Cerebellum -II** Students should know at the end of the session: 1. Functions of cerebellum and effect of lesion. Cerebellar function tests.
Session 35 2-4 pm	**Dissection – Cerebellum** At the end of the session the students should be able to identify parts nuclei and blood supply
Session 36 8-9 am	**Fourth ventricle** At the end of the session students should know the structures forming the roof, floor and openings in the Fourth ventricle. Students should know at the end of the session: 1. The Structure, Connections and Functions of Reticular Formation. The structure and functions of ARAS
Session 32 B 9-11 am	**Examination of sensory system – Physiology** Students should know at the end of the Session: 1. To elicit the various sensory functions of the nervous system.
Session 37 11-12 noon	**Cerebrum -I** Students should know at the end of the session: Sulcs & gyrus and blood supply
Session 38 1-2 pm	**Brain stem-reticular formation, ARAS** Students should know at the end of the session: 1. The Structure, Connections and Functions of Reticular Formation. The structure and functions of ARAS
Session 39 2-4 pm	**Dissection – Fourth Ventricle** The students should able to identify the structures in the floor, roof of the fourth ventricle
Session 40 8-9 am	**Case 14: Hemiplegia Introduction,Cerebral cortex – I** The student should know at the end of the session: Mapping of cortical areas, Localization of functions, pathophysiology of speech.
Session 41 A 9-11am	**Examination of unknown protein**
Session 42 11-12 pm	**Cerebrum -II** Students should know at the end of the session: **1.** Functional areas of various surface
Session 43 1-2 pm	**Fatty acid oxidation – all types** At the end of the session the students should be able to
Session 44 2-4 pm	**Cerebrum Dissection** The students should be able to identify the sulcus, gyrus functional areas of various surface

Session 45 8-9 am	**Cerebral cortex II** The student should know at the end of the session: Sensory, Motor, Association, Prefrontal Areas and Functions.
Session 41 B 9-11 am	**Examination of sensory system Revision – Physiology** Students should know at the end of the Session: 1. To elicit the various sensory functions of the nervous system.
Session 46 11-12 noon	**Embryology- Development of Brain** At the end of the session the students should be able to describe the embryological development of brain
Session 47 1-2pm	**Osteology** The student should know at the end of the session: • Base of skull, Norma frontals, Norma verticalis, Norma occipitals, Norma lateralis. **Teaching Method :** Small group teaching and learning
Session 48 2-4 pm	**Physiology Tutorials II(P)** At the end of the session the students should be able to
Session 49 8-9 am	**Biochemistry Block II Charts (B)** At the end of the session the students should be able to
Session 50 A 9-11 am	**Physiology Tutorials III(P)** At the end of the session the students should be able to
Session 51 11-12 noon	**White matter - I** The student should able to classify white matter, parts, connections, functions and the clinical significance.
Session 52 1-2 pm	**White matter -II** The student should know the different fibres of white matter, parts, connections, functions and the clinical significance.
Session 53 2-4 pm	**Lateral ventricle & White matter** The students should clearly understand the parts, location, relations, extension and communications of the lateral ventricle. And able to classify white matter parts , connections and blood supply
Session 54 8-9 am	**CSF, BBB, Circum Ventricular Organ** Students should know at the end of the session: 1. Circulation of CSF 2. Role of BBB The Circum ventricular organs
Session 50 B 9-11 am	**Examination of motor system** Students should know at the end of the session: Examine and grade the strength of various individual and groups of muscles
Session 55 11-12 am	**Surface Marking** At the end of the session the students should be able to mark sulcus , gyrus and ventricular system
Session 56 1-2 pm	**Physiology theory Revision CNS –I** At the end of the session the students should be able to
Session 57 2-4 pm	**III Ventricle – Dissesction** At the end of the session the students should be able to identify the parts connection and relations
Session 58 8-9 am	**Lateral ventricle** The students should clearly understand the parts, location, relations, extension and communications of the lateral ventricle.
Session 59 A 9-11 am	**Reaction of unknown protein (B)** At the end of the session the students should be able to
Session 60 11-12 noon	**Inter peduncular fossa / Review of brainstem histology**

	At the end of the sessions the students should be able to know the bounderies, contents of Inter peduncular fossa
Session 61 1-2 pm	**Thalamus** Students should know at the end of the Session: Structure – Nuclei and connections, functions and effect of lesion in Thalamus.
Session 62 2-4 pm	**Lateral ventricle & Thalamus Dissection** The students should be able to identify the parts, location, relations, extension and communications of the lateral ventricle. And also identify the Nuclei and connections, functions and effect of lesion in Thalamus.
Session 63 8-9 am	**Thalamus** Students should know at the end of the Session: Structure – Nuclei and connections, functions and effect of lesion in Thalamus.
Session 59 B 9-11 am	**Examination of motor system - Revision** Students should know at the end of the session: Examine and grade the strength of various individual and groups of muscles
Session 64 11-12 noon	**Pain & analgesic system** Students should know at the end of the session: Pain pathway and central analgesic system, Referred pain
Session 65 1-2 pm	**Hypothalamus I** Students should know at the end of the session: The nuclei and connections of hypothalamus
Session 66 2-4 pm	**Case 11,13,14 Resolution** At the end of the session the students should be able to
Session 67 8-9 am	**Hypothalamus - II** Students should know at the end of the session: The functions and Effect of lesion In Hypothalamus. Theories and disorders of sleep.
Session 68 A 9-11 am	**Histology Revision** At the end of the session the students should be able to identify the micro anatomy of brain at various levels
Session 69 11-12 noon	**EEG, sleep** Students should know at the end of the session: 1. The electro physiology of EEG
Session 70 1-2 pm	**Case 15 Introduction - Basal ganglia l** The students should know the basal ganglia nuclei, their connections and applied aspects
Session 71 2-4 pm	**Physiology Tutorial IV**
Session 72 8-9 am	**Basal ganglia I** Students should know at the end of the session: Structure - Nuclei and connections of basal ganglia.
Session 68 B 9-11 am	**Cerebellar Function Test** At the end of the session the students should be able to
Session 73 11-12 noon	**Basal ganglia II** **Case 15 resolution (Parkinsons Large group)** Students should know at the end of the session: Functions and disorders of basal ganglia.
Session 74 1-2 pm	**Arterial supply to Brain** Students should know at the end of the session: Identify the important arteries and the areas supplied by them
Session 75 2-4 pm	**Dissection – Blood supply of Brain – I** The students should be able to identify the arteries and the area supplied by them
Session 76 8-9 am	**Cerebral circulation and regulation** Students should know at the end of the session: Blood flow to the brain, special features, regulation and applied aspects
Session 77 A	**Physiology Tutorial V**

9-11 am	At the end of the session the students should be able to
Session 78 11-12 noon	**Metabolism of Ketone bodies** The student should know at the end of the session • Importance of Ketone bodies • Formation & utilization of Ketone bodies • Regulation of Ketogenesis • Diabetic keto acidosis and starvation ketoacidosis
Session 79 1-2 pm	**Venous drainage brain** Students should know at the end of the session: Superficial and deep veins of the brain
Session 80 2-4 pm	**Dissection – Blood supply of Brain – II** At the end of the session the students should be able to identify the superficial and deep veins of the brain
Session 81 8-9 am	**Limbic system Learning and memory conditioned reflexes** Students should know at the end of the session: • Components and functions of limbic system • Learning – Types, conditioned reflex Memory – Types, Mechanism and applied aspects
Session 77 B 9-11 am	**Superficial & deep reflexes - Revision** At the end of the session, the student should be able to do clinical examination of superficial & deep reflexes. **Teaching Method** PPT presentation followed by Small group demonstration
Session 82 11-12 noon	**Metabolism of cholesterol, bile acids, enterohepatic circulation** The student should know at the end of the session • Names of the Primary & Secondary bile acids, synthesis of bile acids & its regulation. • Role of bile acids in absorption & digestion of fats – micelle formation • Enterohepatic circulation of bile acids Steatorrhea • Biomedical importance of cholesterol • Synthesis of cholesterol • Regulation of cholesterol synthesis Modes of lowering plasma cholesterol
Session 83 1-2 pm	**Metabolism of CM & VLDL** The student should know at the end of the session: • The structure & classification of lipoproteins • Metabolism of chylomicrons (C M) • Metabolism of VLDL • Metabolism of LDL • Fatty liver
Session 84 2-4 pm	**Osteology Revision** At the end of the session the students should be able to identify the Base of skull, Norma frontals, Norma verticalis, Norma occipitals, Norma lateralis. **Teaching Method :** Small group teaching and learning
Session 85 8-9 am	**Metabolism of HDL & Dyslipoproteinemia** • Metabolism of HDL & reverse cholesterol transport • Reference values for lipid profile • Dyslipoproteinemias & classification, clinical and biochemical features • Atherosclerosis – Pathogenesis

Session 86 A **9-11 am**	**Block III Charts & Estimation of cholesterol** Students should know at the end of the session : To estimate the amount of cholesterol in the given sample
Session 87 **11-12 noon**	**Anatomy Theory Revision** Theory revisions of Block III portions
Session 88 **1-2 pm**	**Posture Equilibrium & Vestibular Apparatus** Students should know at the end of the session: • Role of nervous system in maintenance of posture Vestibular apparatus – pathway, functions and applied aspects
Session 89 **2-4 pm**	**Physiology Charts** At the end of the session the students should be able to
Session 90 **8-9 am**	**Physiology Revision** At the end of the session the students should be able to
Session 86 B **9-11 am**	**Superficial & deep reflexes - Revision** At the end of the session, the student should be able to do clinical examination of superficial & deep reflexes. **Teaching Method** PPT presentation followed by Small group demonstration
Session 91 **11-12 noon**	**Physiology Theory Revision** At the end of the session the students should be able to
Session 92 **1-2 pm**	**Biochemistry Revision** At the end of the session the students should be able to
Session 93 **2-4 pm**	**Biochemistry Tutorial** At the end of the session the students should be able to