Multiple sclerosis is an autoimmune, inflammatory disease in which the body's immune system attacks the myelin covering of the axons in the central nervous system. It can present with a variety of neurological symptoms that may come and go, but the condition progressively worsens. Experts believe the disease develops in a genetically susceptible person following exposure to an environmental trigger.

Bob is a 29-year-old, hard-driving and aspiring attorney. He graduated top in his class from law school and never does things halfway. In his spare time, he enjoys outdoor sports, especially golf. Lately, however, his swing has been off and he's experienced tingling and weakness in his left leg, which seems to worsen during the hot part of the day. Over the weekend, Bob had gone with friends to the beach and after about an hour of lying on the sand he was so weak he could not get up without help. He went to see his doctor.

Bob's doctor performed a detailed neurological exam and found Bob did, in fact, have left leg weakness and an unsteady gait. There was also a mild sensory deficit over the dorsal aspect of his right hand. When the doctor asked Bob to look at picture of a grid to check his visual acuity, Bob's left eye was fine, but when using only his right eye, he reported several missing lines and segments of the grid. A careful history revealed that Bob has had at least two similar episodes in the past three years. Since Bob's previous symptoms had disappeared he had dismissed them as insignificant. Bob's doctor ordered a computerized tomography scan (CT) of Bob's brain. The CT findings were diagnostic of multiple sclerosis (MS).

The symptoms of multiple sclerosis present when the body's immune system attacks the myelin covering of the axons in the central nervous system.

- Myelin is a product of the oligodendrocytes and provides insulation for the axons.
- Oligodendrocytes are constantly renewing and regenerating the myelin wrappings around the axons.
- In MS, the damage occurs at a faster rate than the oligodendrocytes can replace the myelin, leaving the axon permanently exposed.
- Damage to the myelin impairs the nerve cell's ability to propagate a wave of depolarization; thus, there is poor communication between neurons.
- The breakdown in neuronal communication is what leads to the symptoms of MS.
- The term multiple sclerosis refers to the scars (scleroses, also known as plaques) that are left in the white matter of the brain and spinal cord after an episode of inflammation.

1. Myelin is critical to nervous system function since:
   A) it provides insulation for the neuronal axons and facilitates rapid propagation of neural impulses.
   B) it is the source of acetylcholine and thus critical to neuronal signal propagation.
   C) it is used by neurons as an emergency energy source during times of low blood glucose.

2. The cells of the nervous system that produce myelin are the:
   A) oligodendrocytes
   B) astrocytes
   C) unipolar neurons
   D) microglia
People with MS can experience neurological symptoms ranging from muscle weakness to tingling and numbness (hypoesthesia), visual defects, and even memory and cognitive impairment. The symptoms of MS may come and go, sometimes with months of remission, but the disease process continues. For reasons that are unclear, higher than usual ambient temperatures lead to an exacerbation of symptoms (Uthoff's phenomenon). Although relapses of symptoms can occur at any time, there are recognized triggers for acute attacks, among them: stress, viral infections, and pregnancy. Most researchers believe MS results from a combination of genetic and environmental factors. Genes that increase the risk have been identified. Regarding an environmental factor, an interesting geographical distribution has been observed. The further one gets from the equator, the greater the incidence (number of new cases) of MS.

Typically beginning in the early thirties MS progresses over a period of decades. Women are more often affected than men, and life expectancy of a person with MS is generally 5 to 10 years less than unaffected people. There is no cure for MS. Treatments are aimed at reducing the frequency and severity of attacks, recovering as much function as possible after an attack, and preventing or controlling long-term disability.

Because of Bob’s history of intermittent episodes with periods of remission, his condition was classified as relapsing remitting MS (as opposed to progressive forms, where there is a slow accumulation of symptoms over time). To treat his current episode, he was started on intravenous corticosteroids. Although helpful during an acute attack, steroids do not have a significant impact on long-term recovery. Bob and his doctor discussed long-term therapy and decided on a trial course of Fingolimod, an anti-inflammatory drug originally developed to prevent organ transplant rejection. In the case of MS, it seems to work by preventing immune cells from entering the central nervous system, and it might stimulate oligodentrocytes to repair the damaged myelin. Unfortunately, the medication is not without side effects, which include increased risk of infections, headaches, slow heart rate and certain kinds of skin cancer.

3. The symptoms of MS can come and go. This is because:
   A) the oligodendrocytes are constantly renewing the myelin sheathes, so they are able to temporarily repair some of the damage.
   B) the neurons themselves are making the myelin covering.
   C) the astrocytes take on the job of making the myelin.
   D) the neurons are able to temporarily adapt to the absence of the myelin and use an alternate system of propagating neural impulses.

4. Triggers of acute episodes of MS include:
   A) stress
   B) pregnancy
   C) infections
   D) all listed choices

5. Most researchers believe MS results from a combination of genetic and environmental factors. One peculiar observation regarding environment is the fact that the incidence increases as one gets further from the equator.
   A) True
   B) False
A 37-year-old female visits her doctor because of back pain and numbness and tingling in her legs. Sensory tests also show reduced ability to sense light touch and to feel a pinprick on both legs. X-rays show no abnormalities of the vertebrae or her spinal canal that might obstruct or damage nerve pathways. She is prescribed anti-inflammatory medication and sent home, and her symptoms gradually subside. Three months later she comes back to the clinic because her symptoms have returned. In addition to back pain and sensory disturbances in her legs, however, she now experiences double-vision and persistent dizziness. A sample of cerebrospinal fluid obtained by lumbar puncture shows the presence of an abnormally high concentration of disease-fighting proteins called antibodies. Magnetic resonance imaging (MRI) reveals the presence of several regions of damage (lesions) within her nervous system. Her condition is eventually diagnosed as multiple sclerosis.

1. What does the presence of a high concentration of antibodies indicate?
   A) That there must be a virus present
   B) That there must be bacteria present
   C) That the immune system is attacking something
   D) That there is a genetic defect

2. In the disease multiple sclerosis, what is the target of the immune system's attack?
   The plasma membrane of neurons
   A) the meningococcus bacterium
   B) the myelin sheath that surrounds neurons
   C) the virus that causes rabies

3. Which of the following is most definitive in determining the diagnosis of multiple sclerosis?
   A) lesions within nervous tissue that increase in number and size over time
   B) numbness and/or tingling of the extremeties
   C) chronic pain that grows worse with time
   D) visual disturbances, like double vision
   E) increased antibody concentrations in cerebrospinal fluid

4. Which is NOT typically a symptom of multiple sclerosis?
   A) Weight gain
   B) Blurred vision
   C) Fatigue
   D) Decreased motor coordination
   E) Muscle weakness
Case Study C

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Wearing on Her Nerves: Exploring the Interrelation between the Nervous and Muscular Systems

Part I – Rise and Shine?
Kathy, a 20-year-old woman, awakens one morning to a tingling, numb sensation covering both of her feet. This has happened to her a number of times throughout the year. In the past, when experiencing this sensation, within a couple of days to a week the numbness would subside, and so she is not too concerned. About a week later, she notices that the numbness and tingling not only persists, but has also spread up to her knees. Again, she ignores the abnormal sensation. By the end of a month’s time, the numbness spreads to the midline of her body. At this point, she becomes alarmed.

Kathy sees the nurse at her college who tells her that she should see a doctor. Kathy calls her doctor’s office to schedule an appointment, but the soonest slot is in two weeks. She makes the appointment and goes about her daily routine. The next morning, Kathy wakes, but when she attempts to get out of bed, she comes crashing to the floor. Because she is still groggy from sleep, she doesn’t really understand what has just happened. As she tries to stand up, the muscles of her left leg engage, but as she also attempts pushing up with her right leg, she again falls to the floor. She sits in bewilderment as she tries to make sense of what has just happened and realizes that she has seriously scraped her knee in her fall. She does not feel the pain from her wound.

Kathy thinks about how odd this year has been. She remembers another medical issue she had earlier in the year when she had lost hearing in her right ear and wonders if there is a connection to her current condition. At that time, Kathy underwent extensive testing, but the ear, nose, and throat specialist remained baffled. He thought that a severe inner ear infection could have destroyed her ability to hear on that side, but there was no conclusive evidence to support this. In an attempt to recover any hearing he could, the doctor prescribed very high dosages of steroids; he told Kathy that she probably wouldn’t see a change, but there were rare occurrences where steroids helped. To both Kathy and her doctor’s surprise, after about a week of steroids, she completely regained hearing in her right ear. It was a “miracle.”

Kathy wonders whether she can count on a new miracle to heal her current medical issues.

1. What components of the nervous system are involved in physical sensation? How does sensory impulse move throughout the body?

2. What components of the nervous system are involved in skeletal muscle movement? How does motor impulse move throughout the body? What is a “motor unit”?

3. What movements are involved in the action of standing up? What muscles need to contract to perform these actions?

4. What are the different levels of organization of a muscle down to myofilaments? What is a “sarcomere” and how are its proteins organized?
5. Starting from the release of acetylcholine by the motor neuron, what are the steps in muscle contraction? How is contraction ended?

6. Are Kathy’s medical problems related to her sensory neurons, motor neurons, or both? What in Kathy’s medical history supports your answer?

Part II – Diagnosis and Treatment
Kathy realizes that she cannot wait until her appointment to receive medical care; she quickly goes to the emergency room. After a mountain of questions about Kathy’s symptoms and medical history, the doctors decide to admit her for further testing. She is transferred to the neurology unit and the doctors request she undergo a series of laboratory tests, including an MRI and a spinal tap. In the meantime, the doctors prescribe high dosages of steroids to help alleviate the symptoms.

Upon reviewing Kathy’s medical history and the results of the various laboratory tests, the neurologists diagnose her with Multiple Sclerosis (MS). They explain to Kathy that MS is an autoimmune disease and that her own immune system has been attacking the myelin sheath that surrounds the nerves of her central nervous system. She remains in the hospital for a week until sensation is fully recovered in her lower body and strength is restored in her legs. She is discharged from the hospital and schedules a follow up appointment with the neurologist.

When she returns to the neurologist, they discuss Kathy’s different options for treatment. Because there is no cure for the disease, options in medication vary greatly. She decides to try daily injections of Copaxone, a medication that is similar in structure to a protein found in myelin. Kathy continues to see the neurologist on a regular basis and gives herself an injection every evening. Over the course of seven months of therapy, she only experiences one occurrence of numbness, which subsides after a couple of days. She tries to stay positive and tries to minimize the disease’s impact on her life.

7. What is myelin and how does it affect the transmission of nerve impulses? Identify the cells responsible for the formation of myelin.

8. What are the “scleroses” in Multiple Sclerosis and where do they occur? How does this influence nerve transmission?

9. How do an MRI and spinal tap help confirm the diagnosis of Multiple Sclerosis?

10. Why did steroids help alleviate Kathy’s symptoms?

11. How does Copaxone work as treatment for Multiple Sclerosis? How do other types of medications differ?

12. Why did Kathy experience the altered sensation in her lower body? Was there something wrong with her skin? Why couldn’t she stand? Was there something wrong with the muscles of her right leg?

13. Did Kathy’s hearing loss have anything to do with the Multiple Sclerosis? Why/Why not?