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كليـــة الصيدلـــة

Multiple Sclerosis

Multiple sclerosis (MS) is an immune-mediated inflammatory disease that attacks myelinated axons in the central nervous system, destroying the myelin and the axon in variable degrees and producing significant physical disability within 20-25 years in more than 30% of patients. The hallmark of MS is symptomatic episodes that occur months or years apart and affect different anatomic locations. In most cases, the disease follows a relapsing-remitting pattern, with short-term episodes of neurologic deficits that resolve completely or almost completely. A minority of patients experience steadily progressive neurologic deterioration.[1] Neuromyelitis optica (Devic disease), previously considered a variant of MS, is now recognized as a separate disorder.[2]

Pathophysiology

Localized areas of demyelination (plaques) occur, with destruction of oligodendroglia, perivascular inflammation, and chemical changes in lipid and protein constituents of myelin in and around the plaques. Axonal damage is possible, but cell bodies and axons tend to be relatively preserved. Fibrous gliosis develops in plaques that are disseminated throughout the CNS, primarily in white matter, particularly in the lateral and posterior columns (especially in the cervical regions), optic nerves, and periventricular areas. Tracts in the midbrain, pons, and cerebellum are also affected. Gray matter in the cerebrum and spinal cord can be affected but to a much lesser degree.[2]

Etiology

The cause of MS is unknown, but it is likely that multiple factors act in concert to trigger or perpetuate the disease. It has been hypothesized that MS results when an environmental agent or event (eg, viral or bacterial infection, exposure to chemicals, lack of sun exposure and low vitamin D levels) acts in concert with a genetic predisposition to immune dysfunction.[1]

Symptoms and Signs

MS is characterized by varied CNS deficits, with remissions and recurring exacerbations. Exacerbations

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average about 3 per year, but frequency varies greatly. Although MS may progress and regress unpredictably, there are typical patterns of progression:

- ***Relapsing-remitting pattern:*** Exacerbations alternate with remissions, when partial or full recovery occurs or symptoms are stable. Remissions may last months or years. Exacerbations can occur spontaneously or can be triggered by an infection such as influenza.
- ***Primary progressive pattern:*** The disease progresses gradually with no remissions, although there may be temporary plateaus during which the disease does not progress. Unlike in the relapsing-remitting pattern, there are no clear exacerbations.
- ***Secondary progressive pattern:*** This pattern begins with relapses alternating with remissions, followed by gradual progression of the disease.
- ***Progressive relapsing pattern:*** The disease progresses gradually, but progression is interrupted by sudden, clear relapses. This pattern is rare.[(2)]

The most common initial symptoms are the following:

- Paresthesias in one or more extremities, in the trunk, or on one side of the face
- Weakness or clumsiness of a leg or hand
- Visual disturbances (e.g., partial loss of vision and pain in one eye due to retrobulbar optic neuritis, diplopia due to ocular palsy, scotomas)

Other common early symptoms include slight stiffness or unusual fatigability of a limb, minor gait disturbances, difficulty with bladder control, vertigo, and mild affective disturbances; all usually indicate scattered CNS involvement and may be subtle. Excess heat (e.g., warm weather, a hot bath, fever) may temporarily exacerbate symptoms and signs.

Mild cognitive impairment is common. Apathy, poor judgment, or inattention may occur. Affective disturbances, including emotional lability, euphoria, or, most commonly, depression, are common. Depression may be reactive or partly due to cerebral lesions of MS. A few patients have seizures. [(2)]

Diagnosis

Multiple sclerosis (MS) is diagnosed on the basis of clinical findings and supporting evidence from ancillary tests, such as **magnetic resonance imaging (MRI)** of the brain and spinal cord and **cerebrospinal fluid examination**, **evoked potentials**, and **lab analysis of blood samples.**

Traditionally, MS could not be diagnosed after only a single symptomatic episode, as diagnosis required repeat attacks suggesting the appearance of lesions separated in time and space. In the past, treating physicians were content to "sit back and watch" after a single episode, as it was assumed the disease would "declare" itself. **The 2010 McDonald criteria** (developed in 2001 by an international expert panel and revised in 2005 and 2010, provide recommendations on the diagnosis of MS, including diagnosis after a single attack) allow diagnosis of MS even with a first clinical episode. Early diagnosis is important because there is growing evidence that early intervention is useful. It is known that axonal loss can be present, even in asymptomatic patients, early in the disease process. In addition, studies in patients with a first attack of neurologic symptoms suggestive of MS have demonstrated decreased disability and lower secondary relapse rates with interferon treatment.[(1)]

Treatment

Treatment of multiple sclerosis (MS) has 2 aspects: immunomodulatory therapy (IMT) for

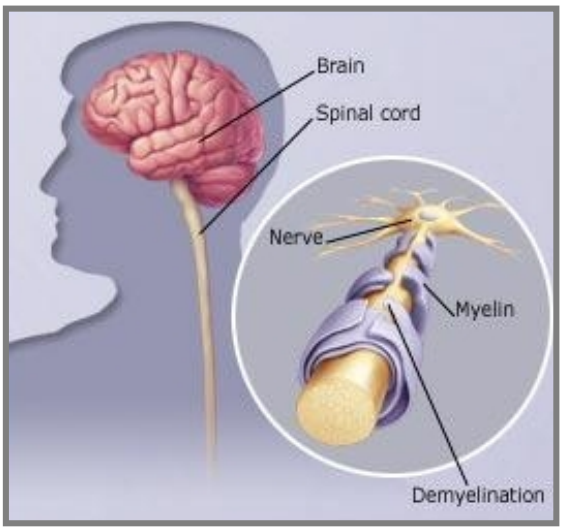
the underlying immune disorder and therapies to relieve or modify symptoms. IMT is directed toward reducing the frequency of relapses and slowing progression. Currently, most disease-modifying agents have been approved for use only in relapsing forms of MS. [(1)]

Strategies to treat attacks

- **Corticosteroids.** are mainly used to reduce the inflammation that spikes during a relapse. Examples include oral prednisone and IV methylprednisolone.
- **Plasma exchange (plasmapheresis).** Plasma exchange sometimes may be used to help combat severe symptoms of multiple sclerosis relapses in people who aren't responding to intravenous steroids.

Strategies to slow progress of the disease

- **Beta interferons.** These types of drugs — such as Avonex, Betaseron, Extavia and Rebif — appear to slow the progress of multiple sclerosis, reduce the number of attacks and lessen the severity of attacks.
- **Glatiramer acetate (Copaxone®).** May reduce the number of MS attacks. It's believed that glatiramer acetate works by blocking the immune system's attack on myelin. The drug is injected subcutaneously once daily.



- **Fingolimod (Gilenya®).** An oral medication given once daily, this works by trapping immune cells in lymph nodes. It may reduce attacks of MS and short-term disability.
- **Natalizumab (Tysabri®).** May reduce the number of MS attacks by interfering with the movement of potentially damaging immune cells from your bloodstream to your brain and spinal cord. Natalizumab generally is reserved for people who see no results from or can't tolerate other types of treatments. It increases the risk of progressive multifocal leukoencephalopathy (PML) - a usually fatal brain infection.

  A blood test helps detect whether a patient has been exposed to the JC virus, a virus that causes PML, before or while taking this medication. This virus, as well as other risks, may cause development of PML in people taking this medication.
- **Mitoxantrone.** This immunosuppressant medication can be harmful to the heart, and it's associated with development of blood cancers like leukemia. Because of these risks, it's usually only used to treat active severe, advanced multiple sclerosis, based on both clinical assessment and MRI studies.
- **Teriflunomide (Aubagio®).** This oral medication reduces attacks and lesions in people with MS. Liver function should be monitored, as it may cause serious liver damage. It can also cause serious fetal damage, and it must not be taken during pregnancy. The medication remains in the system for months. If there are complications, additional medications must be administered in order to help rapid elimination of the drug.

Strategies to treat symptoms

- **Physical therapy**
- **Dalfampridine (Ampyra®).** May improve walking speed in some people.

The major side effect is seizures.

- **Muscle relaxants.** Such as baclofen (Lioresal) and tizanidine (Zanaflex) may improve muscle spasticity.
- **Medications to reduce fatigue.** Such as amantadine may help reduce fatigue due to multiple sclerosis.
- **Other medications.** May be prescribed for depression, pain, and bladder or bowel control problems that may be associated with multiple sclerosis.

A number of other medications and procedures to treat multiple sclerosis are under investigation. For example, stem cell transplantation is being studied. (3)

References:

1) L. Christopher. Multiple Sclerosis [Internet]. Medscape Reference, Drugs, Diseases &Procedures; Feb 20, 2013 [cited Feb, 2013]. Available from: http://emedicine.medscape.com/article/1146199-overview#aw2aab6b2b2

2)Merck Sharp & Dohme Corp. Multiple Sclerosis(MS) [Internet]. The Merck Manual for Health Care Professionals; Feb 2012 [cited Feb 2013]. Available from: http://www.merckmanuals.com/professional/neurologic_disorders/demyelinating_disorders/multiple_sclerosis_ms.html?qt=multiple%20sclerosis&alt=sh

3) Mayo Clinic Staff. Multiple Sclerosis [Internet]. Mayo Clinic, Mayo Foundation for Medical Education and Research; Dec 2012 [cited Feb, 2013]. Available from: http://www.mayoclinic.com/health/multiple-sclerosis/DS00188

Terminology

Akathisia

Akathisia or **Restless leg syndrome** is a syndrome characterized by unpleasant sensation of inner restlessness that manifests through the inability to sit still or not moving. It can be a side effect of medication, many neuroleptic antipsychotics especially the phenothiazines (aschlorpromazine and perphenazine) tioxantenele (as flupentixol and zuclopentixol), butyrophenones (haloperidol), piperazines, antiemetics (metoclopramide and promethazine) and stimulants (amphetamines and antidepressants). Akathisia can be caused by Parkinson's disease and associated syndromes. But more likely is due to drugs used in treatment of disease than itself.

Akathisia has been found to involve high levels of the neurotransmitter norepinephrine, which is associated with mechanisms that regulate aggression, alertness and arousal.

Reference: http://www.transhumanmedicine.com/2011/08/24/akathisia-inner-restlessness/

FDA News

FDA approves *Octaplas* to treat patients with blood clotting disorders

The U.S. Food and Drug Administration Jan. 17, 2013 approved **Octaplas**, a pooled plasma (human) blood product for the replacement of clotting proteins (coagulation factors) in certain medical conditions where patients have insufficient levels. Clotting protein deficiencies can cause excessive bleeding or excessive clotting.

Octaplas is a sterile, frozen solution of pooled human plasma from several donors that has been treated with a solvent detergent process. This process kills certain viruses and thereby minimizes the risk of serious virus transmission. The plasma used to manufacture **Octaplas** is collected from U.S. donors who have been screened and tested for diseases transmitted by blood, and determined to be suitable donors.

Like Fresh Frozen Plasma, **Octaplas** should be matched to the recipient's blood group to help avoid transfusion reactions. An additional benefit to **Octaplas** is that each lot is tested for composition of key clotting factors and is only released if the levels are within acceptable ranges.

Octaplas has been used extensively in Europe and other countries. A previous generation of **Octaplas** was first marketed in 1992, and the current version has been marketed since 2009. All generations of the product have had similar manufacturing processes and comparable ingredients and properties. In total, more than 2 million patients have been treated with over 7 million doses of **Octaplas** outside of the United States. The licensing of **Octaplas** was primarily based on clinical studies conducted in patients with liver disease, liver transplant, heart surgery and TTP. Additional data supporting the safe use of **Octaplas** for the U.S. market came from prior use of the products in Europe and other approved markets. Use of the product in Europe was not associated with transfusion-related acute lung injury, an uncommon but serious risk of transfusion with single units of plasma.

The most common adverse reactions observed in clinical studies included shortness of breath, dizziness, chest discomfort, skin itchiness and rashes, headache and tingling sensations. The product is manufactured by Octapharma, Vienna, Austria.
Source:http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm336009.htm

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Test Your Knowledge

1) Benzodiazepines appear to act as anxiolytics by:
A) altering the sodium ion influx into the CNS
B) potentiating the effects of GABA
C) altering the calcium ion influx into the CNS
D) interfering with the amine pump
E) inhibiting the action of monoamine oxidase

2) The age range for a neonate is considered to be:
A) birth to 1 month B) 1 month to 6 months
D) birth to 1 week E) 1 year through 5 years

3) Parenteral solutions that are isotonic with human red blood cells have an osmolality of approximately how many mOsm/L?

A) 20 B) 40 C) 50 D) 150 E) 300

4) The pharmacist should advise a patient that he or she may experience dizziness and syncope after taking the first dose of:
A) trandolapril B) fosinopril C) clonidine
D) terazosin E) labetalol

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center!

Enquiry received from: Dr. AbdElmoatamed Ali, AbdElmoatamed Pharmacy- Assiut.
Enquiry: How is Ibuprofen overdose treated?

Summary of Answer:

In general, patients with NSAID overdose are asymptomatic or have mild gastrointestinal upset (nausea, vomiting, abdominal pain, sometimes hematemesis). Occasionally patients exhibit drowsiness, lethargy, ataxia, nystagmus, tinnitus, and disorientation. With the more toxic agents **oxyphenbutazone, phenylbutazone, mefenamic acid,** or **piroxicam** and with massive **ibuprofen** overdose, seizures, coma, renal failure, and cardiorespiratory arrest may occur. Hepatic dysfunction, hypoprothrombinemia, and metabolic acidosis are also commonly reported. A summary of managing NSAIDs overdose is as follows:

A. Emergency and supportive measures

1. Maintain an open airway and assist ventilation if necessary. Administer supplemental oxygen.

2. Treat seizures, coma, and hypotension if they occur.

3. Antacids may be used for mild gastrointestinal upset. Replace fluid losses with intravenous crystalloid solutions.

B. Specific drugs and antidotes. There is no antidote. Vitamin K may be used for patients with elevated prothrombin time (PT) caused by hypoprothrombinemia.

C. Decontamination

1. Prehospital. Administer activated charcoal if available. Ipecac-induced vomiting may be useful for initial treatment at the scene (eg, children at home) if it can be given within a few minutes of exposure.

2. Hospital. Administer activated charcoal. Gastric emptying is not necessary for most ingestions if activated charcoal can be given promptly. Consider gastric lavage for massive overdoses.

D. Enhanced elimination. NSAIDs are highly protein bound and extensively metabolized. Thus, hemodialysis, peritoneal dialysis, and forced diuresis are not likely to be effective.

1. Charcoal hemoperfusion may be effective for **phenylbutazone** overdose, although there are limited clinical data to support its use.

2. There are no data on the use of repeat-dose activated charcoal therapy.

Refrences:1) Keller K. 1999. Nonsteroidal Anti-Inflammatory Drugs. In: Olson K.Poising and Drugs Overdose. 3rd ed.Connecticut : Appleton & Lange. Pp237-239.
2) Lacy F. 2001-2002.Charles Drugs information handbook 9th ed. Ohio: Lexi-comp. p 627

What Are The Top 10 Healthy Foods?

The following ten foods are generally considered to be the healthiest.

1) Apples are an excellent source of antioxidants, which combat free radicals. Some animal studies have found that polyphenols found in apples might extend life spans. Another study found that adult females who regularly ate apples had a 13% to 22% lower risk of developing heart disease.

2) Almonds are rich in nutrients, including iron, calcium, vitamin E, fiber, riboflavin, and magnesium. Almonds as a food may help maintain healthy cholesterol levels.

The fatty acid profile of almonds, which is made up of 91-94% unsaturated fatty acids, may partly explain why it helps maintain healthy cholesterol levels.

3) Broccoli is rich in fiber, folate, potassium, calcium and phytonutrients. Phytonutrients are compounds which reduce the risk of developing heart disease, diabetes and some cancers. Broccoli also contains beta-carotene, an antioxidant, as well as vitamin C.
If the enzyme myrosinase is not destroyed during cooking, broccoli can also reduce the risk of developing cancer. The best way to cook broccoli and to preserve the myrosinase is to steam the vegetable lightly. Another ingredient, sulforphane, which exists in broccoli, is also said to have anti-cancer as well as anti-inflammatory qualities. Broccoli powder does not contain myrosinase.

4) Blueberries are rich in phytonutrients, antioxidants and fiber.According to a study carried out at Harvard Medical School, elderly people who eat plenty of blueberries (and strawberries) are less likely to suffer from cognitive decline, compared to other people of their age who do not.Blueberries were found to help in curbing obesity. Plant polyphenols, which are abundant in blueberries, have been shown to reduce the development of adipogenesis, while inducing the breakdown of lipids and fat.Regular blueberry consumption can reduce the risk of suffering from hypertension by 10%, because of the berry's bioactive compounds, anthocyanins, Blueberry consumption has also been associated with a lower risk of artery hardening, and/or intestinal diseases. The fruit has also been linked to stronger bones in animal studies.

5) Oily fish Examples of oily fish include salmon, trout, mackerel, herring, sardines and anchovies. These types of fish have oil in their tissues and around the gut. Their lean fillets contain up to 30% oil, specifically, omega-3 fatty acids. These oils are known to provide benefits for the heart, as well as the nervous system. Oily fish are also known to provide benefits for patients with inflammatory conditions, such as arthritis.Oily fish also contain vitamins A and D. Prostate cancer progression was significantly slowed when patients went on a low-fat diet with fish oil supplements.

6) Leafy green vegetables High intake of dark-leafy vegetables, such as spinach or cabbage may significantly lower a person's risk of developing diabetes type 2. Spinach, for example, is very rich in antioxidants, especially when uncooked, steamed or very lightly boiled. It is a good source of vitamins A, B_6, C, E and K, as well as selenium, niacin, zinc, phosphorus, copper, folic acid, potassium, calcium, manganese, betaine, and iron.

7) Sweet potatoes are rich in dietary fiber, beta carotene, complex carbohydrates, vitamin C, vitamin B_6, as well as carotene.

8) Wheat germ
Wheat germ is high in several vital nutrients, such as vitamin E, folic acid (folate), thiamin, zinc, magnesium, phosphorus, as well as fatty alcohols and essential fatty acids. Wheat germ is also a good source of fiber.

9) Avocados Many people avoid avocados because of its high fat content; they believe that avoiding all fats leads to better health and easier-to-control body weight - this is a myth. Approximately 75% of the calories in an avocado come from fat; mostly monosaturated fat. Weight-for-weight, avocadoes have 35% more potassium than bananas. Avocados are also very rich in B vitamins, as well as vitamin K and vitamin E. Avocados also have a very high fiber content of 25% soluble and 75% insoluble fiber. Studies have shown that regular avocado consumption lowers blood cholesterol levels.

Avocado extracts are currently being studied in the laboratory to see whether they might be useful for treating diabetes or hypertension.
Researchers from Ohio State University found that nutrients taken from avocados were able to stop oral cancer cells, and even destroy some of the pre-cancerous cells.

10) Oatmeal is meal made from rolled or ground oats, or porridge made from ground or rolled oats. Interest in oatmeal has increased considerably over the last twenty years because of its health benefits. Studies have shown that if you eat a bowl of oatmeal everyday your blood cholesterol levels, especially if they are too high, will drop, because of the cereal's soluble fiber content. In 1997, the FDA agreed that foods with high levels of rolled oats or oat bran could include data on their labels about their cardiovascular heart benefits if accompanied with a low-fat diet. Oats is rich in complex carbohydrates, as well as water-soluble fiber, which slow digestion down and stabilize levels of blood-glucose. Oatmeal porridge is very rich in B vitamins, omega-3 fatty acids, folate, and potassium. *Source:http://www.medicalnewstoday.com/articles/245259.php*

Answers:
Q1: (B) Benzodiazepines are believed to act by potentiating the effects of gamma-aminobutyric acid (GABA), an inhibitory amino acid.
Q2: (A) Neonates have an age span from birth to 1 month of age. Infants are 1 month to1 year, early childhood is 1 through 5 years, and late childhood is 6 through 12 years.
Q3: (E) Osmolarity, expressed as mOsm/L, is included on the labels of large-volume parenteral (LVPs). Those injections with a value of approximately 300 mOsm/L will be isoosmotic and presumably isotonic with the blood.

Q4: (D) Terazosin is an alpha1-adrenergic blocker that causes peripheral vasodilation Side effects of therapy may include precipitous fall in blood pressure, possibly accompanied by tachycardia and syncope following the first dose.

Uses: Chemotherapy nausea, chemical exposure.
Ingredients:
1 tsp. Siberian Ginseng - fresh or dried
1 tsp. Caraway seed
2 cups water
➢ Bring the water and the herbs to a boil, cover. Lower the heat and simmer for 10 minutes. Strain the herbs. Drink 1 cup of tea every 3-4 hours or as needed
Source: *The Herbal Pharmacy CD, By Hale Software, Inc 1997.*

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