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A PHARMACY CONTINUING EDUCATION PROGRAM
W-F Professional Associates, Inc. 400 Lake Cook Rd., Suite 207 Deerfield, IL 60015 847-945-8050

Nov/Dec 2005 "MS, ALS, HD" 707-000-05-011-H01

THIS MONTH
"ALS, MS & HD"

THIS IS THE FINAL DOUBLE LESSON FOR 2005. THIS YEAR'S DEADLINE FOR US TO RECEIVE QUIZZES (AND HAVE THEM APPEAR ON YOUR DEC 2005 CREDIT STATEMENT) IS NOVEMBER 30, 2005.

QUIZZES RECEIVED BETWEEN DEC 1, 2005 & DEC 31, 2005 WILL COUNT FOR 2005 CREDIT, BUT STATEMENTS FOR THAT CREDIT WILL NOT BE MAILED UNTIL AFTER JAN 1st.

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QUIZ DEADLINE FOR THIS YEAR = NOVEMBER 30, 2005.

Immunological and genetic diseases require both extensive clinical and interpersonal skills. Three of these are Multiple Sclerosis (MS), Amyotrophic Lateral Sclerosis (ALS) and Huntington's Disease (HD). Our goal is to take a brief look at the etiology/pathophysiology, symptoms, diagnosis, treatment and patient counseling. This lesson provides 2.50 hours (0.25 CEUs) of credit, and is intended for pharmacists in all practice settings.

The program ID # for this lesson is 707-000-05-011-H01.
Pharmacists completing this lesson by November 30, 2008 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Recognize symptoms of ASL, MS & Huntington's Disease (HD).
2. Discuss the pathophysiology & treatment options for these diseases.
3. Describe the pharmacist's role in counseling patients & family members regarding these diseases.

INTRODUCTION

Pharmacists deal with a variety of ailments in the course of their workday. While numerous diseases are particularly vexing, immunological and genetic diseases require both extensive clinical and interpersonal skills. Three of these are Multiple Sclerosis (MS), Amyotrophic Lateral Sclerosis (ALS) and Huntington's Disease (HD) or Chorea. Our goal is to take a brief look at the etiology/pathophysiology, symptoms, diagnosis, treatment and patient counseling.

MULTIPLE SCLEROSIS

Etiology/Pathophysiology

Multiple Sclerosis is a neurological disorder in which demyelination or deterioration of CNS (central nervous system) neuron structure occurs - resulting in disease. Often, axon (the axon is the thick branch of the neuron that sends messages) preservation is maintained in the disorder. The exact cause is unknown, but it is thought to be autoimmune and inflammatory in nature. CD8+ lymphocytes, a type of white blood cell, are believed to be involved with other inflammatory cells and cytokines (a part of the body's immune response) to cause degeneration of the myelin sheaths. Myelin sheaths aid in the conduction of neural transmissions. When these sheaths deteriorate, nerve transmission suffers. Think of an electrical wire that is frayed. The appliance connected to wire may work, but the wire can get hot or short circuit. Cerebral or spinal plaques are the pathological hallmark of MS. Under gross examination of the brain, various degrees of atrophy and ventricular dilatation are seen. Familial occurrence is typically between 3% to 23%. Sibling risk is 3% to 5%. If genetic incidence rates are less than 50%, then non-genetic factors obviously contribute.

Symptoms

Symptoms usually offer a nebulous diagnosis. Unless there are a key group of symptoms, differential diagnosis must occur before the clinician determines a definitive diagnosis. The problem is the symptoms could mimic other ailments. Here is a list of key symptoms:

- Optic neuritis (inflammation of the optic nerve) (common)
- Vertigo (common)
- Fatigue
- Impairment of facial sensation
- Intranuclear ophthalmoplegia (paralysis of eye muscles)
- Acute urinary retention (common)
- Lhermitte's Sign: electrical shock sensation upon flexion of the neck
- Limb weakness
- Sensory and vision loss/paresthesias
- Sexual Dysfunction

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Diagnosis

The following is insight into what a clinician might do in determining a clinical confirmation of MS. Patient history, as well as symptoms, is important in making the initial diagnosis of MS. The presenting signs are so highly variable that MS should be considered in any patient with new onset of neurological problems. Sensory manifestations can occur and include numbness, tingling (pins and needles in the extremities), coldness and/or swelling of the limbs. An intense unilateral itching sensation in the cervical area suggests MS.

Here are some steps that clinicians take in determining MS.

1. Perform comprehensive physical and neurological exams.
2. Examine cranial nerves and fundi (base of the eye) for evidence of optic neuritis or brainstem involvement.
3. Perform eye exam for internuclear ophthalmoplegia.
4. Test for light touch, pain, vibration, and proprioception.
5. Examine deep tendon reflexes along with muscle tone and strength.
6. Test patient's stance and coordination.
7. Do an MRI, along with CBC (complete blood count) and analysis of cerebrospinal fluid.
8. Consider other conditions whose symptoms may be confused with MS, such as cancers, infections, hereditary disorders or systemic disorders.

Treatment

These are some generally accepted treatment strategies. The primary goal of treatment is to lengthen the times between MS exacerbations. With each exacerbation, there is a decrease in neurological body function.

Acute attacks involving significant neurological impairment such as loss of vision and/or motor impairment are often treated with high dose IV corticosteriods.

-Methylprednisolone IV 500-1000mg daily for 3 to 7 days (with or without
short prednisone taper).

Long-term medical therapy can be initiated after clinical disability has been assessed using the Kurtzke disability score or the expanded disability status score.

The Expanded Disability Status Scale

Score	Status
0	Normal neurologic exam
1.0	Patients fully ambulatory
1.5	No disability
2.0	Minimal disability in one of seven functional systems (FS)
2.5	Minimal disability in two FS
3.0	Fully ambulatory; moderate disability in one FS; or mild disability in three or four FS
3.5	Fully ambulatory; moderate disability in one FS and mild disability in one or two FS; or moderate disability in two FS; or mild disability in five FS
4.0	Fully ambulatory without aid, self-sufficient, active 12 hours a day despite relatively severe disability; able to walk without aid or rest for about 500 meters
4.5	Fully ambulatory without aid, active much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk without aid or rest for about 300 meters
5.0	Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities
5.5	Ambulatory without aid or rest for about 100 meters; disability severe enough to limit full daily activities

6.0	Intermittent or unilateral constant assistance (cane, crutch, or brace) required to walk about 100 meters with or without resting
6.5	Constant bilateral assistance (canes, crutches, or braces) required to walk about 20 meters without resting
7.0	Unable to walk beyond about 5 meters even with aid, essentially restricted to a wheelchair; wheels self in standard wheelchair and transfers alone; active in wheelchair about 12 hours a day
7.5	Unable to take more than a few steps; restricted to wheelchair; may need aid to transfer; wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair
8.0	Unable to walk at all, essentially restricted to bed, chair or wheelchair, but may be out of bed much of the day; retains many self-care functions; generally has effective use of arms
8.5	Essentially restricted to bed much of the day; has some effective use of arm(s); retains some self-care functions
9.0	Helpless bed patient; can communicate and eat
9.5	Totally helpless bed patient; unable to communicate effectively or eat/swallow
10	Death due to MS

Multiple Sclerosis Treatment Strategies

Disease course/disease stage	Treatment options
Monosymptomatic (e.g., optic neuritis)	IV methylprednisolone, 1000 mg daily for 5 days
Relapsing-remitting: no disease activity for several years and no MRI activity	IV steroids for attacks
Relapsing-remitting: current disease activity and/or MRI activity	IV steroids for attacks, plus: 1. INFß-1a: 30 mg IM weekly, or 2.INFß-1b: 1 mL SC every other day, or 3. Glatiramer acetate/copolymer 1: 20 mg SC daily
Relapsing-remitting: disease activity while on interferon or glatiramer acetate/copolymer 1	Add monthly bolus of IV methylprednisolone, consider increasing interferon dose
Relapsing-remitting: accumulating disability (interferon/glatiramer acetate/steroid nonresponders)	IV monthly cyclophosphamide (Cytoxan)/steroid pulse therapy, consider IV mitoxantrone (Novantrone)
Rapidly progressing disability	IV cyclophosphamide and steroid: 8-day induction, followed by pulse maintenance
Very rapidly progressing disability	Plasma exchange
Secondary progressive	1. IV steroid monthly pulses 2. IV cyclophosphamide/steroid monthly pulses 3. Methotrexate (Rheumatrex), oral or SC, 7.5-20 mg/week with or without monthly steroid pulses 4. Consider addition of an interferon if not currently prescribed 5. Consider IV immunoglobulin (Polygam) monthly
Primary progressive	1. IV steroid monthly pulses 2. Methotrexate, oral or SC, 7.5-20 mg/week with or without monthly steroid pulses 3. Cladribine (Leustatin), IV or SC4. IV immunoglobulin monthly 5. Consider mitoxantrone 6. Consider azathioprine (Imuran)

Modified from Weiner and Stazzone

Selected Symptomatic Treatments

Indication	Medications	Dosages
Spasticity	Baclofen (Lioresal)	5-20 mg t.i.d. or q.i.d.
	Tizanidine (Zanaflex)	4-12 mg q.d. -t.i.d.
	Dantrolene sodium (Dantrium)	25-100 mg q.d.
	Diazepam (Valium)	1-2 mg b.i.d or t.i.d.
	Botulinum toxin (Botox) injections	Dose as per selected muscle
	Baclofen implantable pump	Programmable dosing
Fatigue	Amantidine (Symmetrel)	100 mg b.i.d. or t.i.d.
	Pemoline (Cylert) a	18.75-37.5 mg b.i.d.
	Methylphenidate (Ritalin)	10-20 mg b.i.d. or t.i.d.
	Fluoxetine (Prozac)	10-20 mg/day
Bowel/bladder dysfunction	Oxybutynin (Ditropan)	2.5-5 mg q.d. -t.i.d.
	Propantheline (Pro-Banthine)	15 mg t.i.d. or q.i.d.
	Imipramine (Tofranil)	25-75 mg q.h.s.
	Desmopressin (DDAVP)	20-40 mg q.h.s.
	Tolterodine (Detrol)	2 mg b.i.d.
	Terazosin HCl (Hytrin)	2-5 mg q.d. or b.i.d.
	Bethanechol chloride (Urecholine)	10-50 mg t.i.d. or q.i.d.
	Self-catheterization	Intermittent
	Surgical diversion or drainage	
Depression	Selective serotonin reuptake inhibitors	Doses as per individual medication
	Tricyclic antidepressants	Doses as per individual medication
Tremor	Weighted wrist bracelets	
	Isoniazid + pyridoxine	800-1,200 mg/day + 100 mg/day
	Anticonvulsants	Doses as per individual medication
	Propanolol (Inderal)	20-40 mg t.i.d.
	Ondansetron (Zofran)	4-8 mg q.d. or b.i.d.
	Clonazepam (Klonopin)	0.5-2 mg q.d.-q.i.d.
	Surgical thalamotomy	
Motor improvement	3,4-Diamino pyridine	5-10 mg t.i.d. or q.i.d.
Pain, dysesthetic	Amitriptyline hydrochloride (Elavil)	50-200 mg q.h.s.
	Phenytoin (Dilantin)	200-600 mg/day
	Gabapentin (Neurontin)	100-600 mg t.i.d.
	Valproic acid (Depakote)	250-1,000 mg t.i.d.
Pain, paroxysmal	Carbamazepine (Tegretol)	100-300 mg b.i.d. or t.i.d.
	Phenytoin (Dilantin)	200-600 mg/day
	Misoprostol (Cytotec)	100-200 mg q.i.d. (trigeminal neuralgia)
Erectile dysfunction	Sildenafil (Viagra)	25-100 mg as needed
	Prostaglandin (MUSE system)	2 transurethral systems per week

[a] Because of the potential for hepatotoxicity, patients prescribed pemoline should have frequent liver-function tests.

Based on Kita [32]; Lindsey et al. [10]; Little [6]; Lynch [33].

Pharmacist Related Counseling

Counseling is critical for MS. Compentent, patient-friendly counseling can contribute to better therapeutic outcomes and also gives the patient awareness on how to handle side effects. To help the patient, the pharmacist needs to employ keen observation and use open-ended questions.

Corticosteriods: monitor for appearance of cataracts, check to see if patient has received liver function tests; patient should monitor salt and watch for fluid retention; monitor for evidence of immunodeficiency, impaired wound healing, skin atrophy, blood glucose changes, hypocalcemia, hypokalemia, osteoporosis with long term use.

Betaseron ®(Interferon Beta 1B) is a biotechnology drug used in treating MS: patient may experience flu like symptoms such as fever, chills, or muscle aches, headache, asthenia, injection site pain and irritation. Monitor CBC, LFTs (liver function tests) at 1, 3, and 6 months after initiation of therapy; thyroid function tests should be done every 6 months.

Copaxone® (Glatiramer Acetate) - another biotechnology drug used in MS treatment: Patient may experience anxiety, asthenia (lack or loss of strength or energy); hypertonia (rigidity and spascity of muscles); joint pain, transient chest pain; vasodilation; nausea; hypertension is frequent; palpitations; pain and edema at the injection site.

Methotrexate: Patient may experience photosensitivity, rash, alopecia, anoxeria, nausea, vomiting, and diarrhea. Monitor baseline CBC with differential and platelet count, LFTs and renal function every 1 to 2 months. Severe reactions can occur and include: cirrhosis and acute renal failure.

With this disease as well as other diseases discussed in this lesson, in addition to explaining adverse effects, going over asceptic technique and storage is important. In addition to minimizing the chance of an infection, proper counseling reduces the chance of incorrectly storing, preparing and administering the dose. These drugs are quite expensive and have controlled distribution. Therefore, missing dosings could adversely affect therapeutic outcome.

Cyclophosphamide: Common side effects are leukopenia (impaired immunity), amenorrhea in females, alopecia, nausea and vomiting, bleeding from thrombocytopenia. Monitor CBC at baseline and a urinalysis for red blood cells.

Leustatin®: Common side effects include fatigue, headache, nausea, and injection site reactions such as rash or edema. Monitor CBCs periodically during the first 4 to 8 weeks post-treatment. Also monitor LFTs and renal function.

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Etiology/Pathophysiology

ALS, also known as "Lou Gehrig's Disease", is a progressive, degenerative disease that affects neurons in the CNS, especially the spinal cord alpha motor neurons. The disease is believed to be inherited in an autosomal (chromosome) dominant matter where people that are heterozygous (containing two different forms of the same gene) for the trait are both carriers and inflicted by the disease. The chromosomal aberration has been localized to chromosome 21 and encodes the superoxide dismutase (SOD) enzyme present in all somatic cells, especially in cells of neutral crest origin (neurons, endocrine glands, glands of the GI tract). The lack of superoxide neutralizng function of the enzyme contributes to the destruction of the neurons; however, recent evidence indicates that the mutant protein may be cytotoxic to motor neurons specifically. This type of ALS that is inherited is called FALS-familial amyotrophic sclerosis. Although most cases of ALS arise sporadically with the afflicted person having no other family member with the disease. This may indicate that gene defects in the SOD gene may not be the only factor in the development of the disease.

Symptoms

- Increasing muscle weakness, especially in the arms and legs
- Problems with speech, swallowing and breathing (most common complication)
- Inability to control the use of arms and legs
- Muscle twitching

- Fatigue
- Muscle cramps at night and usually at later stages of the disease
- Pain

Note: The first sign of ALS may be slight weakness in one leg, one hand, face or tongue.

Diagnosis

A physical exam of the nervous system that evaluates muscle and nerve function and also motor reflexes should be performed. These tests include electromyography (EMG) and nerve conduction studies. The EMG helps measure how well and how quickly the nerves and muscles function, while the nerve conduction studies test nerve function. Additional tests may be conducted to rule out other possible nerve system disorders. These tests include blood tests, a muscle biopsy and imaging tests such as a CT scan or MRI.

Treatment

Treatment for ALS is two-fold: nonpharmalogical and pharmalogical.

Nonpharmacological

- Physical and occupational therapy to help maintain strength and residual function
- Speech therapy to help maintain the ability to communicate
- Emotional counseling should also be provided to help minimize psychological problems
- As recommended by The American Academy of Neurology, acupuncture can also be used by neurologists to help patients with breathing difficulties

Pharmacological

- To relieve muscle stiffness, spasms and twitching: Baclofen (lioresal), Zanalfex (tizanidine), Dantrium (dantrolene) or a benzodiazepine such as Valium (diazepam).
- To relieve muscle cramps: Quinine, Dilantin (phenytoin sodium), Neurontin (gabapentin) or a benzodiazepine
- To decrease breathing problems, morphine is often used
- To relieve anxiety caused by breathing problems: Ativan (lorazempam) or Valium (diazepam)
- Antidepressants are also useful in managing this disease. They help not only with depression, but also with sleeplessness, poor appetite, fatigue and they decrease the production of saliva
- Pain relievers are also used in later stages of the disease

The only current medication that specifically treats ALS is Rilutek® (riluzole) 50mg given every 12 hours. Normal pediatric dose: safety and efficacy has not been established in the pediatric population. Renal and hepatic dosing adjustments: no established recommendations at this time. NOTE: ALS is not curable.

Pharmacist Related Counseling

In regards to Rilutek® (riluzole), take on an empty stomach, one hour before or two hours after meals. Some common side effects are abdominal pain, anorexia, diarrhea, joint pain, dizziness, somnolence, vertigo, hypertension, tachycardia, nausea, vomiting and pneumonia. Advise patient to monitor serum ALT levels every month during the first three months of treatment and every three months during the remainder of the first year and periodically thereafter. Discontinue treatment if ALT exceeds 10 x ULN (upper limits of normal) or if jaundice develops. Also CBC and renal function should be monitored.

HUNTINGTON'S DISEASE OR HUNTINGTON'S CHOREA

Etiology/Pathophysiology

Discovered in 1872, Huntington's disease (HD) was originally called Huntington's Chorea for the Greek word "chorea," meaning dance. This is a reference to the twisting, spastic movements associated with the disease. Dr. George Huntington, who discovered the disease, described the affliction as a degenerative disorder of the Central Nervous System (CNS) causing progressive degeneration.

HD is due to a mutation in a gene transmitted as an autosomal dominant trait. Each child of a parent who is carrying a defective gene for HD has a 50% risk of inheriting the disease gene. In addition, although HD usually runs in certain families, the disorder may sometimes occur as the result of a spontaneous (sporadic) change in the gene for HD.

The gene responsible for HD, known as IT15, is located on chromosome 4. The IT15 gene regulates, controls, or "encodes" production of a protein known as Huntington. The protein is found in neurons throughout the brain. Mutations of the IT15 gene result in abnormally long repeats of DNA instructions. These instructions include unusual, repeated sequences of certain basic chemicals known as cytosine, adenine, and guanine or CAG trinucleotide repeats. These expanded CAG sequences result in the production of abnormal Huntington Protein.

Individuals who do not have HD tend to have about 20 CAG repeats in the IT15 gene (ranging from about 9 to 29). In contrast, those with the disorder may have about 36 to 121 CAG repeats. The length of the expanded CAG repeats is thought to have some relation to the age at symptom onset (large number of repeats tend to develop symptoms at an earlier age).

Expanded CAG repeats are not stable and tend to expand from generation to generation. This phenomenon is known as "genetic anticipation." Evidence suggests that CAG repeats are unstable when the disease gene is inherited from the father. Therefore, individuals with HD who inherit the disease gene from their fathers may tend to develop symptoms at an earlier age.

The basal ganglia is usually the first structure affected by the disease. Later the disease progresses to the frontal lobes where symptoms of inattention and lack of motivation appear. HD is classified as a frontal-subcortical (beneath the cerebral cortex – the part of the brain where thought takes place) disease. The disease goes largely untreatable except for measures taken to ease the symptoms and discomfort.

Throughout Europe and North America, the incidence of HD is approximately five to eight per 100,000. About 30,000 Americans have HD symptoms and another 150,000 have a 50% risk of carrying the gene that is responsible for the disease. All of those who carry the gene will show signs of the disease by the third or fourth decade of life.

Symptoms

Symptoms of Huntington's disease vary but may mimic the progression of Parkinson's disease—initial motor effects and eventual effects on frontal lobe functioning. Cognitive deficits affect the portion of the brain called the caudate nucleus in its mental rather than its motor functions. HD is classically associated with progressive emotional, cognitive, and motor disturbances. Early symptoms may precede outright disease onset by several years. Initial characteristic signs may include:

- Slight personality changes
- Forgetfulness
- Clumsiness
- Gradual development of random, brief, "fidgeting" movements of the fingers or toes

Emotional or behavioral disturbances tend to develop gradually over time and may become apparent before or concurrent with the motor manifestations of HD. Initial symptoms of HD may include personality changes such as:

- Increased irritability
- A tendency to easily find fault with others
- Constant complaining
- Suspiciousness
- Impulsiveness

- Lack of self-control
- Lack of interest in acts that previously provided pleasure (anhedonia)

Behavioral, emotional, or psychiatric disturbances may also become apparent including:

- Anxiety
- Depression
- Mania
- Depression accompanied by mania
- Obsessive-compulsive behaviors
- Agitation
- Hostile outbursts
- Sleep disturbances
- Increasing social withdrawal

Severe distortions in thinking may also occur— false beliefs or delusions. In addition, hallucinations may develop, such as the perception of sounds, sights, or other sensations in the absence of external stimuli.

HD is often characterized by progressive dementia or gradual impairment of the mental processes involved in comprehension, reasoning, judgment, and memory. Early signs of cognitive decline may include:

- Forgetfulness
- Difficulty maintaining focus and attention

As HD progresses, additional symptoms may develop including:

- Increased difficulty concentrating
- Inability to absorb and understand new information
- Impaired ability to engage in problem solving
- Diminished memory retrieval
- Progressively impaired judgment and impulse control
- Diminished language skills with disorganized speech
- Increasingly impaired ability to plan, initiate, or perform certain purposeful movements (apraxia)

Communication difficulties may include problems expressing thoughts in words, initiating conversations, or comprehending others' words and responding appropriately. Early motor signs of HD typically include:

- Gradual onset of clumsiness
- Balance difficulties
- Brief, random, "fidgeting" movements
- Frequent, irregular, purposeless, jerky motions

Many HD patients develop a distinctive manner of walking (gait) that may be unsteady, disjointed, or lurching. The gait has also been described as "dance-like" in nature. As the disease progresses, other findings may include:

- Clumsy fine motor movements
- Postural instability
- Inability to sustain certain voluntary movements
- Poor control of the tongue and diaphragm
- Difficulty swallowing (dysphagia)
- Poorly articulated, slurred speech
- Strained, hoarse, inappropriately loud voice
- Impaired control of voluntary eye movements
- Muscle stiffness

Diagnosis

Diagnosis is based on a thorough personal and family medical history, physical examination (including neurological exam), and a series of laboratory tests. The physician will ask about recent changes in intellectual or emotional function, which may be an early indicator of Huntington's disease.

Genetic Testing

Genetic testing involves taking a blood sample for DNA analysis to determine whether the distinct mutation for HD has occurred in gene IT-15. During this testing, the number of CAG repeats within the IT15 gene region is estimated. A sample of DNA also may be required from a closely related affected relative (parent is ideal). This helps confirm the diagnosis of HD and is important if the family's history is in any way unclear, uncertain, or unusual. Persons who test positive and are considering pregnancy are advised to seek genetic counseling.

Family-Based Linkage Studies

Before identification of the IT15 gene, investigators characterized DNA that was closely linked to the gene (DNA linkage analysis) and typically inherited with it as a unit. This discovery enabled researchers to map the gene to the short arm (p) of chromosome 4. This led to the development and availability of presymptomatic testing. Numerous DNA markers closely linked to the HD gene have since been identified in different families affected by the disease.

DNA linkage analysis detects the inheritance of DNA potentially linked to the gene as opposed to the presence of the mutated gene itself. Therefore, this testing is much less specific than the direct mutation analysis previously described. DNA linkage testing necessitates the analyses of blood samples from multiple unaffected and affected family members (preferably from two generations)—and may have only a certain degree of accuracy. Linkage analysis is no longer used for diagnosis of HD but for confirmation.

Computed Tomography (CT Scan)

Painless diagnostic procedure produces computer-generated images of the brain's internal structures. Patients with HD often show shrinkage in the caudate nuclei and putamen of the brain. There is also an enlargement within the ventricles of the brain. The presence of these structural changes is not conclusive for HD nor does the absence rule it out. MRI done in combination with CT scan may be more beneficial to view convex bulge of the caudate nucleum.

Testing Guidelines

A positive test result impacts both the patients and their families. Anyone contemplating genetic testing should obtain testing guidelines from the testing center or from an organization devoted to the interests of Huntington's disease patients and their families. Guidelines include:

- Counseling provided before and after test and before known results.
- Test results are disclosed only in person to the individual being tested.
- To protect the interests of minors, including confidentiality, testing should not be conducted for persons under 18 without a compelling medical reason, such as the appearance of HD symptoms in a child.

Diagnostic evaluation may include a series of tests to eliminate other disorders with similar symptoms. For example, certain autosomal dominant neurodegenerative disorders closely mimic HD. These include neuroacanthocytosis and dentatorubropallidoluysian atrophy. HD must also be differentiated from other disorders or conditions associated with chorea, such as Wilson disease; drug-induced tardive dyskinesia; Sydenham's chorea; systemic lupus erythematosus; or senile chorea, a symptom complex primarily characterized by the development of chorea after age 60. Although some patients with senile chorea may have neurodegenerative changes of the caudate nuclei, there is typically no family history of HD.

Treatment/Patient Counseling

Pharmacological

The treatment of HD patients requires an integrated, multidisciplinary approach including symptomatic and supportive medical management; psychosocial support (physical, occupational, or speech therapy; genetic counseling) or additional supportive services. No medications are approved by the Food and Drug Administration (FDA) to treat the symptoms of HD. However, medications may help manage or alleviate certain neurobehavioral or movement abnormalities associated but do not alter the progressive decline of HD.

Dopamine Antagonists

These include haloperidol, tetrabenazine, and other phenothiazines used to suppress choreic movement and control psychiatric abnormalities such as severe agitation, hallucination, and delusion. Side effects include extrapyramidal effects, blurred vision, constipation, dry mouth, nasal congestion, dizziness, drowsiness, and photosensitivity.

Anti-Viral

Amantadine may worsen choreic movements in most patients. However, the treatment of juvenile HD may include administration of amantadine to try to control extra movements by increasing dopaminergic activity in the peripheral and central nervous system in the later stages of the disease. Common side effects & adverse reactions reported most frequently (5 to 10%) are: nausea, dizziness, insomnia, depression, anxiety, hallucinations, confusion, anorexia, dry mouth, constipation, ataxia, orthostatic hypotension, and headache.

Benzodiazepines

These include clonazepam & diazepam. They may be used to reduce choreiform movement. It is an alternative to haloperidol, and should only be used when a patient's condition is functionally disabling. Side effects include aggravation of seizures, dizziness, behavior problems, drowsiness, depression, increased saliva, and respiratory depression.

Investigational Treatments

Research is ongoing to learn more about the inheritance patterns, pathophysiology, symptoms, and progression of HD and develop new or improved therapies. Investigators are evaluating whether excessive activation of glutamate may be reduced by blocking receptors of N-methyl-D-aspartate (NMDA), a similar neurotransmitter, possibly helping to halt abnormal nerve cell death. Studies are being conducted to assess the potential symptomatic and neuroprotective effects of riluzole (Rilutek®), an agent that is thought to moderate the effects of glutamate.

There has been some evidence to suggest that Co-Enzyme Q10 may minimally decrease progression of the disease by having a protective effect on striatal nerve cells (neurotrophic growth factors). However, much is still to be learned about basic biochemical pathways and metabolism and bioavailability of Q_{10} and herbal products are not FDA regulated, which cause a great deal of concern in recommending the use of an herbal supplement.

Medical management may also include administration of agents to help alleviate depression, anxiety, or obsessive-compulsive behaviors potentially associated with HD. It is important to note the adverse effects associated with certain medications may be difficult to differentiate from signs of HD. Any medication regimen needs to be assessed on a regular basis to determine the benefits and possible adverse effects of specific therapies and evaluate the need for continued treatment.

Non-pharmacological Treatment

Some Huntington's disease patients need a lot of time for meals because the loss of coordinated movement can make it difficult for them to swallow or feed themselves. Food can be cut into small pieces, softened, or pureed to make swallowing easier. Swallowing therapy can help if started before there is serious difficulty. Avoid dairy products because they tend to increase the secretion of mucus, which can increase the risk for choking. Patients should consume enough calories to maintain adequate body weight. The number of daily meals may have to be increased and vitamins and nutritional supplements may be recommended. If eating and dietary problems become severe, families and caregivers may need to consider the use of a feeding tube. HD patients require large quantities of fluid to avoid dehydration. In cases where the patient's muscular capability is severely weakened, water may have to be thickened with additives to the consistency of syrup before drinking is possible. It is important for Huntington's disease patients to be as physically fit as their condition permits. Daily exercise promotes physical and mental well being.

Patients should walk as much as possible, even if assistance is necessary. Caregivers should keep the patient's surroundings free of hard, sharp objects because patients are prone to falls. Small weights worn around the ankles and sturdy, well-fitting shoes that slip on and off easily can help improve a patient's stability.

Social Activity

Unless and until the disease's progression prohibits it, people with HD should participate in outside activities, socialize, and pursue hobbies and interests. These activities also give family members and caregivers valuable time for themselves.

Support Groups

Support groups for patients & families affected by Huntington's Disease are available. See the Huntington's Disease Society of America website for local information: http://www.hdsa.org/.

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THIS IS THE FINAL DOUBLE LESSON FOR 2005. THIS YEAR'S DEADLINE FOR US TO RECEIVE QUIZZES (AND HAVE THEM APPEAR ON YOUR DECEMBER 2005 CREDIT STATEMENT) IS NOVEMBER 30, 2005.

QUIZZES RECEIVED BETWEEN DEC 1, 2005 & DEC 31, 2005 WILL COUNT FOR 2005 CREDIT, BUT STATEMENTS FOR THAT CREDIT WILL NOT BE MAILED UNTIL AFTER JAN 1st.

Some of the topics that we'll be presenting in 2006:

Review of Diabetes	New Drugs for Erectile Dysfunction
Peptic Ulcer Disease & Its Treatment	Obesity Management
Skin Exposure to the Sun	Update on Medication Errors
Pharmacy Law Update	HIV / AIDS Update
Diarrhea/Constipation Management	Jaundice Control

Fill in the information below, answer questions and return **Quiz Only** for certification of participation to:
CE PRN®, 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.

NAME_____(ID # 1st line on label)_____

ADDRESS_____CITY_____-_____STATE_____ZIP_____

CHECK IF NEW ADDRESS ❑ **ARE YOU LICENSED IN FLORIDA? IF YES FL LIC _____**

EMAIL Address (we need this)_____

LESSON EVALUATION

Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?
   - Recognize symptoms of ASL, MS & Huntington's Disease — Yes No
   - Discuss the pathophysiology & treatment options for these diseases — Yes No
   - Describe the pharmacist's role in counseling patients & family members regarding these diseases — Yes No
2. Was the program independent & non-commercial? — Yes No

	Poor			Average			Excellent
3. Relevance of topic to your practice	1	2	3	4	5	6	7
4. Author's ability to communicate	1	2	3	4	5	6	7

5. What did you like most about this lesson?_____
6. What did you like least about this lesson?_____
7. How would you improve this lesson?_____
8. Further comments or suggestions for future programs_____

(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

1. Multiple sclerosis occurs when the axon deteriorates.
   A. True
   B. False
2. The following symptoms help a clinician diagnose multiple sclerosis:
   A. Optic neuritis
   B. Bell's palsy
   C. Fatigue
   D. All of these
   E. A &C
3. In MS the scale that classifies disability is called the _____scale. The higher the number, the_____ disease progression.
   A. Kurtzke, more severe
   B. EMI, less severe
   C. MS, More severe
   D. None of these
4. Which neuron does ALS affect?
   A. Alpha beta motor neurons
   B. Alpha motor neurons
   C. Beta motor neurons
   D. None of these
5. What is the incidence of HD in Europe & North America?
   A. 100 per 100,000
   B. 30 per 100,000
   C. 5 to 8 per 100,000
   D. 60 per 100,000
6. What are some patient counseling guidelines for riluzole?
   A. Take on empty stomach
   B. Make patient aware that abdominal pain may occur
   C. Exercise when possible
   D. A & B
7. The gene responsible for HD is:
   A. R87
   B. IT 15
   C. IT 14
   D. CAG
8. ALS is not curable. What drugs are used to treat symptoms?
   A. Lioresal
   B. Tizanidine
   C. Dantrolene
   D. Riluzole
   E. All of these
9. Symptoms of Huntington's Disease include:
   A. Slight personality changes
   B. Forgetfulness
   C. Clumsiness
   D. Fidgeting movements in fingers & toes
   E. All of these
10. When counseling patients, keen observation & open-ended questions are helpful.
    A. True
    B. False

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