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Happy New Year !

the SQUARE

healthcare bulletin

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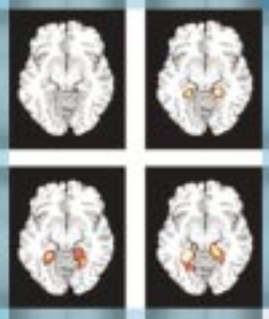

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Editorial

Dear Doctor :

Happy New Year !

Welcome to this edition of "*the SQUARE* " healthcare bulletin !

At first we express our heartiest gratitude for your encouraging response regarding "*the SQUARE* " ! Your inspiration motivate us to produce certain articles those are informative and also entertaining.

In this issue we have published a special feature on “Memory loss (amnesia)”, an unusual forgetfulness that can be caused by brain damage due to disease or injury, or it can be caused by severe emotional trauma. As this is very vast to describe, we condensed the best-published material on the topic focusing only the essentials.

We have also focused on “Infertility”, the inability or diminished ability to produce offspring. The extent of infertility varies among countries and even among different populations within a country. WHO estimates that there are 60-80 million infertile couple worldwide. In addition, we highlighted on “Hepatitis E virus (HEV)”, an enterically transmitted self-limited infection.

Besides, our regular features comprise "Product Profile", "*SQUARE* in International Business" and some fascinating news in the "Medical Breakthrough" section.

On behalf of the management of *SQUARE* , we wish you all a very healthy, happy and prosperous life.

Omar Akramur Rab

VOL 16 NO 1 January 2008

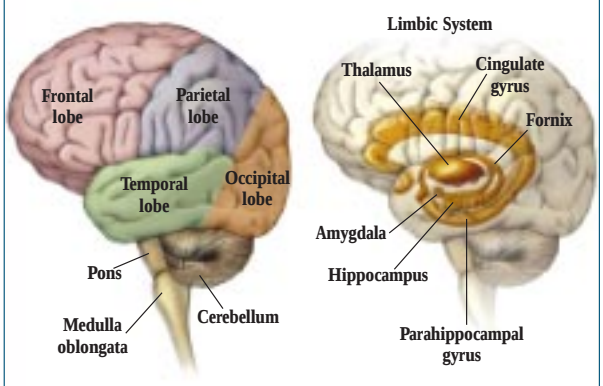
Memory Loss

Memory loss, also known as amnesia, is a state of unusual forgetfulness. This refers to a loss of the everyday sense of memory responsible for knowing facts, events, information and experiences. Also called 'amnestic syndrome', this memory loss can't be accounted for by problems with attention, perception, language, reasoning or motivation. People with amnesia typically are lucid and maintain a sense of self, but they face severe difficulties in learning new information and forming new memories. They may not be able to recall memories of past experiences and information.

It can be caused by brain damage resulting from diseases, such as Alzheimer's and Huntington's. It may result from an injury or severe emotional trauma. The normal aging process may lead to slower recall of information and greater difficulty in learning new material. In itself, however, aging will not dramatically affect one's memory.

Memory involves several different functions of the brain. Most students of the brain divide memory into two kinds, declarative and procedural. The procedural involves skills and habits. The declarative, on the other hand, involves strong facts. Memory processes can be itemized according to the time they take: very short-term memory, which lasts about 100 milliseconds; short-term memory, which is of a few seconds' duration; working memory, which stores recent experiences; and long-term memory, which houses verbal material that has been rehearsed and motor skills that have been practiced.

Anatomy of the Brain



One possible explanation of long-term memory is that it starts with activity in the front part of the brain. The information chosen for long-term memory passes as an electrical impulse to a part of the brain known as the hippocampus. Here a process called long-term potentiation enhances the neurons' ability to pass messages.

A different theory of memory stems from the idea that brain waves play a key part. Its proponents believe that regular oscillations of the brain's electrical activity, rather like the beat of a drum, help bind memories together and control the moment at which different brain cells are activated.

Researchers believe that the brain stores different aspects of memories in different places, each concept being linked to the area of the brain that specializes in perceiving it. Some parts of the brain certainly contribute to memory. The amygdala, a small almond-size clump of nerve cells close to the brain stem, processes memories of fear. The basal ganglia region is focused on habits and physical skills, and the cerebellum, at the base of the brain, concentrates on conditioned learning and reflexes. Here, it is believed, people store the skills of balance - for example, those they need to ride a bicycle.

There are at least three general types of amnesia :

- Anterograde. This form of amnesia follows brain trauma and is characterized by the inability to remember new information. Recent experiences and short-term memory disappear, but victims can recall events prior to the trauma with clarity.
- Retrograde. In some ways, this form of amnesia is the opposite of anterograde amnesia: the victim can recall events that occurred after a trauma, but cannot remember previously familiar information or the events preceding the trauma.
- Transient global amnesia. This type of amnesia has no consistently identifiable cause, but researchers have suggested that migraines or transient ischemic attacks may be the trigger. A victim experiences sudden confusion and forgetfulness. Attacks can be as brief as 30-60 minutes or can last up to 24 hours. In severe attacks, a person is completely disoriented and may experience retrograde amnesia that extends back several years. While very frightening for the patient, transient global amnesia generally has an excellent prognosis for recovery.

Causes of Memory Loss :

- Alcohol Abuse and Alcoholism
- Alzheimer's Disease
- Brain Tumor
- Creutzfeldt-Jakob Disease
- Dementia
- Depression
- Drug Abuse
- Encephalitis and Meningitis
- Epilepsy (Seizure Disorder)
- Human Immunodeficiency Virus

Memory Loss

- ❑ Parkinson's Disease
- ❑ Pick Disease
- ❑ Stroke

Other Causes of Memory Loss :

Cerebrovascular disease

- ❑ Head trauma
- ❑ Lewy body disease
- ❑ Malnutrition
- ❑ Medications
- ❑ Neurodegenerative diseases
- ❑ Neurosyphilis
- ❑ Normal pressure hydrocephalus
- ❑ Psychological/emotional disturbances
- ❑ Prolonged toxin exposure
- ❑ Sleep disorders
- ❑ Thyroid disease
- ❑ Transient ischemic attack (TIA)
- ❑ Vitamin deficiencies
- ❑ Wernicke-Korsakoff syndrome
- ❑ Wilson's disease

Common Causes

- ❑ Aging
- ❑ Alzheimer's disease
- ❑ Neurodegenerative illness
- ❑ Head trauma or injury
- ❑ Hysteria often accompanied by confusion
- ❑ Seizures
- ❑ General anesthetics such as halothane, isoflurane, and fentanyl
- ❑ Alcoholism
- ❑ Stroke or transient ischemic attack (TIA)
- ❑ Transient global amnesia
- ❑ Drugs such as barbiturates or benzodiazepines
- ❑ Electroconvulsive therapy (especially if prolonged)
- ❑ Temporal lobe brain surgery
- ❑ Brain masses (caused by tumors or infection)
- ❑ Herpes encephalitis
- ❑ Other brain infections
- ❑ Depression

The following may all be direct contributory factors in memory loss :

- ❑ Stress and anxiety
- ❑ ADHD
- ❑ Depression
- ❑ Metabolic diseases such as thyroid gland diseases, diabetes, and lung, liver, or kidney failure
- ❑ Alcoholism
- ❑ Vitamin B_{12} deficiency
- ❑ Infections
- ❑ Drugs, both prescription and over-the-counter
- ❑ Neurodegenerative illness
- ❑ Seizures
- ❑ Stroke
- ❑ Brain masses
- ❑ Herpes encephalitis

Sudden Memory Loss

Sudden memory loss is known medically as acute memory loss. It is a serious condition which may be caused by :

- Head injury
- Infection such as meningitis
- Long-lasting or repeating illness
- A change in blood flow to the brain
- Epilepsy

Short Term Memory Loss

The scientific term for short term memory loss is anterograde amnesia. In this form of amnesia, new events are not transferred to long term memory. Once a sufferer's attention has shifted, he/she will not be able to recall events which have only just happened. Different types of memories can be affected separately by the condition. A person may be able, for example, to recall new physical skills they have acquired, but not the events of the day.

Short term memory loss may be caused by damage to the hippocampus, fornix or mamilliary bodies. Damage to the basal forebrain as well as to a set of structures in the brain known as diencephalons can also cause the condition. Some medications, such as benzodiazepines and imidazo-pyradines have also been known to have an anterograde amnesiac effect. Heavy consumption of alcohol can also cause the condition.

A person with anterograde amnesia will still be able to remember things that happened before the onset of the condition.

Long Term Memory Loss

Long term memories are those that last for years or even decades. Long term memory differs structurally and functionally from short term and working memory. Short term memories move into long term memory via the process of long-term potentiation, the process of strengthening the connections between existing neurons to improve the effectiveness of their communication. Long term memories fade as part of the natural forgetting process, which increases with age, stress and illness. Serious loss of long term memory, however, is the result of either traumatic brain injury or a neurodegenerative disease.

Traumatic brain injury : Depending on what part of the brain has been affected, the ability to remember tastes, smells, appearances, or sounds may be affected. A head injury that causes swelling in the brain reduces the brain's ability to process incoming information. Additionally, once such incoming information is processed and stored in the appropriate area of the brain, the brain may have difficulty retrieving the information when needed. If someone suffer from traumatic injury to the head and forget where he had been or what he had been doing for a few days before the accident, he suffer from retrograde amnesia.

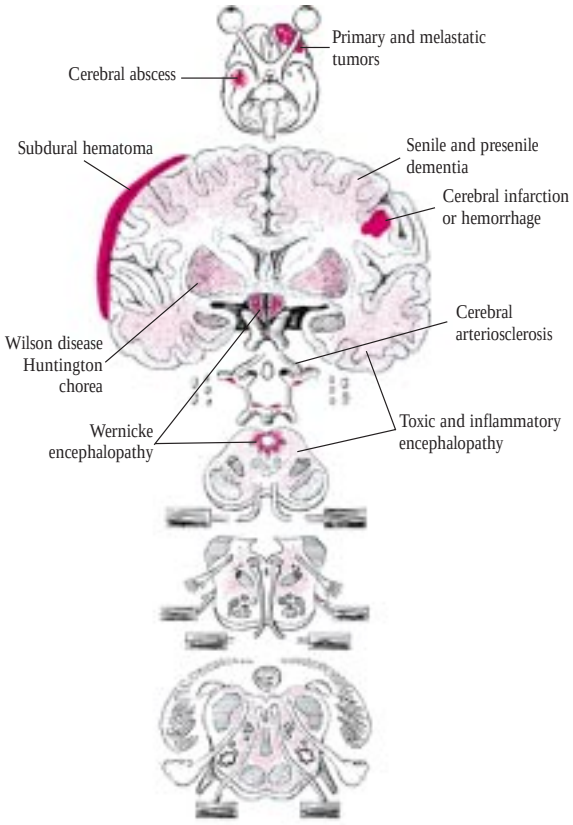
Memory Loss

Neurodegenerative Disease : the most prevalent neurodegenerative diseases that cause memory loss are Alzheimer's Disease, Dementia, Huntington's Disease, Multiple Sclerosis and Parkinson's Disease. Although none of these conditions act specifically on memory, memory deterioration is a casualty of general cognitive decline.

Memory Loss At Young Age

Childhood or infantile amnesia refers to a person's inability to remember specific events from childhood and infancy, typically prior to the age of four. Famed psychoanalyst Sigmund Freud believed childhood amnesia was a response to sexual repression. It has also been hypothesized that memories need to be stored conceptually and associated with words and meanings that people don't attain until about the age of four. It is also possible that the young child's brain does not have sufficient development to properly store memories. At birth babies have billions of brain cells, but there are relatively few connections between them.

Memory Loss And Dementia



Infant and childhood stress have been linked to memory decline at an early age. A 2005 study by the UC Irvine School of Medicine suggests that the emotional stress associated with parental loss, abuse or neglect may contribute to the type of memory loss during middle-age years that is normally seen in the elderly. The study involved limiting the nesting material in the cages of neonatal rats, which led to an increase in stress for these rats. In middle age, these same rats began to demonstrate deficiency in their ability to remember the location of objects they had seen before, as well to recognize objects they had seen on the previous day. These memory problems were far more pronounced than rats who had been raised for the first week of life under a typical nurturing environment. In the rats with impaired memory, the normal increase in brain communication through synapses, considered to the basis for memory, was found to be faulty.

Forgetfulness And Age-Associated Memory Impairment

Forgetfulness

It's quite normal to forget things occasionally. And as people grow older, they become more forgetful. Most people have forgotten the name of a person whose face is recognizable, have forgotten to switch the lights off or have turned back to make sure they turned off the stove or locked the door.

All of this is a normal part of growing older. Someone may not even remember when this change began; it just creeps up on him as he ages.

The question is, how much is too much to forget? Although scientists do not fully know the answer to this question, they have found some important differences between normal memory loss and memory loss that occurs with more serious conditions, such as dementia.

Age-Associated Memory Impairment

At the moment, researchers are studying senior citizens who suffer from mild memory loss that is greater than their peers. This condition is known as age-associated memory impairment

It is important to note that normal age-related memory loss does not indicate diminished intelligence or ability to learn. The brain may simply need more time to recall information from memory or to learn new information. Simple forgetfulness is not a disease.

It is also notable that memory loss does not always indicate dementia. Research is under way to determine whether those with age-associated memory impairment will eventually develop Alzheimer's disease.

Age-associated memory impairment generally affects people who are older than 50. It develops gradually. The most

common manifestations are difficulty remembering names, misplacement of objects, difficulty remembering a list of multiple items and problems with tasks that require multiple actions. There also may be difficulty remembering telephone numbers and zip codes. If the individual is distracted in some way, the problem is compounded, making it even harder to remember things-such as what was needed to buy or what the person meant to do.

Difference between age-associated memory impairment and Alzheimer's disease :

Activity	Age-associated memory impairment	Alzheimer's disease
Forgets	Parts of an experience	Whole experience
Remembers later	Often	Rarely
Follows written or spoken instructions	Usually able	Gradually unable
Is able to use notes	Usually able	Gradually unable
Is able to care for self	Usually able	Gradually unable

Adapted from Gwyther LP: Care of Alzheimer's Patients: A Manual for Nursing Home Staff. Chicago: Alzheimer's Association and American Health Care Association; 1985.

Researchers do not yet know the exact cause of age-associated memory impairment. However, there are things that contribute to memory change and/or loss.

Researchers used to think that age-associated memory impairment developed into Alzheimer's disease, but new research shows that this is not always true. Unlike Alzheimer's disease, age-associated memory impairment is not a progressive condition and is not as disabling as Alzheimer's disease.

Reversible Causes Of Memory Change

Certain factors and medical conditions can contribute to a change in memory function. Early diagnosis of these is a patient's best weapon and is of vital importance. If left unchecked and undiagnosed, these conditions can cause irreversible damage. The following is a list of factors to consider when assessing memory loss:

- Stress
- Sleep disorders
- Depression
- Metabolic disease, such as thyroid disease
- Alcoholism
- Vitamin B_{12} deficiency
- Infections
- Drugs

Fortunately, memory loss caused by illness or lifestyle choices can be prevented or remedied.

Stress

Everyone experiences a certain amount of stress, and how people cope with it is extremely important. Major life stress and/or prolonged stress can impair memory function and contribute to memory loss.

Sleep Disorders

At least six hours of sleep each night are essential for memory to perform at its peak. Regular sleep habits also make people less forgetful. Research shows a direct link between sleep deprivation and memory loss.

Depression

Sometimes, depression, particularly after the loss of a loved one, can mimic the signs of memory loss. People may become forgetful and less organized. Although there is evidence that depression can affect memory loss, by and large memory function should return to normal as depression lifts.

Metabolic Disease

Diseases of the thyroid gland affect one in 10 elderly people and can have a direct effect on memory function. However, the effects of thyroid problems on memory function are not limited to the elderly; people of any age can be affected. Certain other metabolic diseases, such as diabetes or failure of the lungs, liver or kidneys, are known to have an effect on memory function.

Alcoholism

It is known that alcohol abuse results in memory loss and possibly dementia. Initially, alcoholics develop short-term memory loss followed by amnesia, which results in the loss of long-term memory. Although each individual has a different threshold for alcohol tolerance, general guidelines identify "moderate" drinking as no more than two drinks per day for men and one drink per day for women. Some individuals have genetic factors that may predispose them to alcohol dependency.

Vitamin B_{12} Deficiency

Vitamin B_{12} is essential for optimal brain function. A lack of this vitamin actually can cause permanent damage to brain cells. If some one drink or smoke, he/she are at an even greater risk of having vitamin deficiencies (smoking and drinking leach nutrients from the body). Failure to treat this condition leads to worsening memory loss and progressive nerve damage.

Infections

There are many infections that can lead to a change in mental state, most notably meningitis and encephalitis-both

Memory Loss

infections that affect the meninges. After such an illness, patients may have memory loss that can continue for months. Chest, lung, urinary and other infections may lead to acute confusion, particularly in the elderly. Prompt identification and treatment of infection are essential and reduce the chance of long-term, permanent consequences.

Drugs

Both prescription and over-the-counter drugs can affect memory function, as can certain drug interactions. Certain classes of drugs are known to affect memory and brain function. These include sleeping pills, anti-anxiety medications, painkillers, antihistamines and antidepressants. As with vitamins, drugs are absorbed at varying rates. Any drug-related impairment is most often resolved, and memory returns to normal once the drug is discontinued.

Approach To The Diagnosis

A detailed medical history and neurological examination is essential. Recent, intermediate, and long-term memory may be tested. Once again, the presence or absence of other neurologic signs and symptoms is important. If one does not have the skills or the time for a complete neurologic examination, immediate referral is indicated. Next, a careful drug history is done. Withdrawal of all drugs may clear the dementia.

Diagnostic tests that may be performed include the followings :

1 Cerebral angiography
2 CT scan or MRI of the head
3 EEG
4 Blood tests (for specific diseases that are suspected)
5 Psychometric tests (cognitive tests)
6 Lumbar puncture

Other useful tests :

1. CBC (pernicious anemia)
2. Chemistry panel (uremia, liver disease, electrolyte disorder)
3. Serum B_{12} (pernicious anemia)
4. Urine thiamine afterload (Wernicke encephalopathy)
5. Drug screen (drug or alcohol abuse)
6. Neurology consult
7. HIV antibody titer (AIDS)
8. Schilling test (pernicious anemia)
9. FT4, S-TSH (hypothyroidism)
10. FTA-ABS test (neurosyphilis)

Preventing Memory Loss

To reduce the impact of age-related memory loss, it is important to stay healthy and fit. A well balanced diet which is low in fat and contains ample source of Vitamin B_{12} and folate will help to protect the nervous system. Drinking plenty of water will ward off dehydration, which can cause confusion and memory problems. Getting plenty of rest (8 hours per night), not smoking or using other tobacco products, engaging in regular aerobic and anaerobic exercise, and practicing stress reduction strategies will also beneficially affect memory.

Playing stimulating games, such as Scrabble, learning new things and reading different types of material will provide the brain with mental stimulation. Alcohol consumption should be strictly limited and illegal drugs should not be used. Research has shown that people who regularly get together with family or friends are less likely to lose mental function. Socializing also helps you stay connected with your community.

The following 5 strategies have been proven beneficial in preventing memory loss :

1. **Exercise :** Physical fitness and mental fitness go hand in hand. Those who are aerobically fit have good lung function and good lung function appears to correlate to mental acuity. Exercise also reduces the risk for diabetes, high cholesterol, high blood pressure and stroke. All of these conditions can lead to memory loss. In addition, exercise increases the level of neurotrophins, substances that nourish brain cells and help protect them against damage from stroke and other injuries.
2. **Smoking :** It is unknown whether smoking directly impairs memory or is merely associated with memory loss because it causes illnesses that contribute to memory loss, such as stroke and hypertension. Smoking also damages the lungs and constricts the blood vessels to the brain, depriving it of oxygen and possibly harming neurons.
3. **Healthy Diet :** A memory nourishing diet is rich in fruits and vegetables as well as healthy fats from fish, nuts and whole grains. Saturated and trans fats should be avoided to keep arteries clear and cholesterol levels healthy. Healthy nuts are also beneficial for keeping your brain healthy.
4. **Learning :** A person who is an active, life-long learner will be less prone to memory loss. Reading regularly, keeping up with current affairs, learning a new hobby, and playing challenging games all exercise the mind and, therefore, help ward off memory loss.
5. **Sleep :** For maximum mental health it is vital that person get 6-8 hours of sleep each night. It is also important to establish and maintain a consistent sleep schedule and routine.

Nutrition **:**
It is very beneficial to consume foods that are high in antioxidants, such as the followings :

- Spinach
- Oranges
- Beets
- Avocados
- And especially blueberries or other berries

Vitamins For Memory
Neurotransmitters are the keys to the transmission of memories in the brain. Part of the constituent material that comprise neurotransmitters are vitamins, particularly those in the "B" group.

A group of researchers in the Netherlands decided to see what would happen if they added Vitamin B_6 to the diets of healthy older men. First the men were given a mental test that included things such as being able to remember different objects flashed on a screen and the names and occupations of people in a list. Then one group took 20 milligrams of B_6 a day, while the others took placebos.

At the end of three months, the men were tested again. The memories of those in the Vitamin B_6 group showed "modest but significant" gains, especially in long-term memory. The researchers believe that Vitamin B_6 helps create dopamine, serotonin and norepinephrine.

A deficiency in Vitamin B_{12} has also been identified as a factor in memory loss. Yet, nearly one-third of people over age 60 can't extract the Vitamin B_{12} they need from what they eat. That's because their stomachs no longer secrete enough gastric acid, the stuff that breaks down food and helps turn it into fuel for your brain and body. Doctors who suspect Vitamin B_{12} deficiencies in people with memory problems give them B_{12} shots, thus bypassing the faltering digestive system.

Eating small portions of dairy products or animal protein gives you enough Vitamin B_{12} . Virtually all animal products, such as milk, cheeses, yogurt and lean beef, contain Vitamin B_{12}. The Daily Value for B_{12} is six micrograms.

Treating Memory Loss
Treatment for amnesia focuses on techniques and strategies to help make up for the memory problem. A person with amnesia may work with an occupational therapist to learn new information to replace what was lost, or to use intact memories as a basis for taking in new information. Memory training may also include a variety of strategies for organizing information so that it's easier to remember and for improving understanding of extended conversation.

The treatment of memory loss depends on its cause. Sometimes it is as simple as treating the underlying illness that is causing it. For example, treating depression, thyroid disease or a sleep disorder should resolve any associated memory loss. Many people with amnesia find it helpful to use a personal digital assistant (PDA), such as a Palm Treo, or iPhone. With some training and practice, even people with severe amnesia can use these electronic organizers to help with day-to-day tasks. For example, they can program the PDA to remind them about important events or to take medications. Low-tech memory aids include notebooks, wall calendars, pill minders and photographs of people and places

At present, there is no drug that can prevent age-related memory loss or reverse it. Nor is there a pill for people who want to sharpen their memories, although experts believe that one day this might be possible.

However, self-help techniques and practical exercises, as described above, can be effective.

Drugs currently available for the treatment of memory loss
Various drugs and classes of drugs are currently available for the treatment of memory loss related to several types of illnesses. The following is a list of some of the drugs that are currently approved or under investigation for the treatment of memory loss.

Drugs in this section are used to treat several types of memory disorders including Alzheimer's disease, dementia due to Lewy bodies, vascular dementia and other types of memory loss.

The choice of drug depends on the condition and the physician's preference. Some physicians use one or more medications in combination.

- ❏ Tacrine
- ❏ Donepezil
- ❏ Rivastigmine
- ❏ Memantine
- ❏ Neotropin
- ❏ Nootropics
- ❏ Alpha-tocopherol
- ❏ Selegeline
- ❏ Non-steroidal Anti-inflammatory Agents
- ❏ Intravenous Immunoglobulin (IVIg)
- ❏ Gingko Biloba
- ❏ Estrogen Galantamine B-secretase inhibitors
- ❏ B vitamins
- ❏ Calcium channel blockers
- ❏ Cholesterol lowering agents
- ❏ Clioquinol, an earlier generation antibiotic

Tacrine, was the first drug approved by the Food and Drug Administration (FDA) for the treatment of Alzheimer's. It slows progression of Alzheimer's by increasing levels of the neurotransmitter acetylcholine. It needs to be taken four

times a day and blood tests for liver function need to be monitored. Up to six out of ten people are unable to reach the maximum dosage due to side effects.

Donepezil, was the second drug approved by the FDA to treat Alzheimer's. It works by raising the level of the chemical acetylcholine in the brain, slowing progression of some types of dementias. The dosing is once a day. Side effects include gastrointestinal discomfort.

Rivastigmine, was approved by the FDA to treat Alzheimer's. It also, increases levels of acetylcholine in the brain. It is given twice a day and side effects include gastrointestinal discomfort.

Galantamine, is last in the class of drugs that raise brain levels of acetylcholine. It has been approved by the FDA for treating Alzheimer's disease. It is given twice a day. Side effects include gastrointestinal discomfort.

Memantine, which prevents the harm to brain cells from excessive activity of the chemical glutamate. It was approved by the FDA for treating moderate to severe Alzheimer's dementia. Although approved for twice a day use, it may be given once a day.

Intravenous Immunoglobulin (IVIg), is derived from the pooled blood of thousands of donors. It is used for treating various autoimmune conditions and may have utility in treating Alzheimer's disease. For more information, please see the section on IVIg and Alzheimer's disease.

Neotropin, as the name suggests, is drug that possibly promotes the growth of nerve cell processes and maintains nerve cell viability. It is currently in clinical trials

Nootropics, the first class of agents used for treatment of memory loss have not been shown to be consistently effective.

Alpha-tocopherol, or vitamin E, in doses of 2000 international units has been shown to slow progression of Alzheimer's disease. The drug works as a free radical scavenger and promotes nerve cell viability.

Selegeline, is an agent that both raises the levels of certain neurochemicals and promotes nerve cell viability, has been used in the US for the treatment of Parkinson's disease. It has been shown to be effective for the treatment of Alzheimer's.

Non-steroidal anti-inflammatory agents, or NSAIDS, include drugs such as ibuprofen may have some utility in preventing Alzheimer's disease. However, NSAIDs were not effective in treating Alzheimer's.

Gingko biloba, a free radical scavenger and possible brain activator, is said to be the third most commonly prescribed drug for the treatment of dementia in Germany. Preparations of the drug in the US vary and the right dose of the right preparations may slow progression of some types of memory loss.

Estrogen, may increase or reduce risk for Alzheimer's disease in women, although data on this topic is exceptionally confusing and controversial.

B-secretase inhibitors, are the newest and most exciting class of drugs being developed for treating memory loss. These drugs stop formation of amyloid plaque and may halt progression of illnesses like Alzheimer's.

Vaccines, that dissolve plaques in the brain are also in development. A clinical trial using a vaccine developed by Elan was recently stopped because of possible side effects in some patients.

Certain classes of the B vitamins, are felt to be neuroprotective and are being used in clinical trials for treating memory loss.

Calcium channel blockers, a class of drugs used to treat illnesses like hypertension and migraine, have been used to treat memory loss.

Statins, a class of drugs used to lower cholesterol levels, may reduce amyloid plaque formation and thus may be helpful in some types of memory loss.

Clioquinol, an antibiotic withdrawn from the US market in the 1970s because of adverse effects may reduce plaque formation by binding to zinc and copper. A recent Swedish study found some benefit in patients with Alzheimer's disease.

Home Care

Family support should be provided. Reality orientation is recommended -- supply familiar music, objects, or photos, to help the patient become oriented. Support for relearning may be required in some cases.

Any medication schedules should be written down to avoid dependence on memory.

Extended care facilities, such as nursing homes, should be considered for people whose basic needs cannot be met in any other way, or whose safety or nutrition is in jeopardy.

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Infertility

Infertility is defined as the inability for a couple to become pregnant after a year of steady, unprotected intercourse. It affects approximately 6.1 million individuals throughout the United States. The male partner, the female partner, or both may have a fertility problem. A person who is infertile has a reduced ability to have a child. It usually doesn't mean a person is sterile -- that is, physically unable to ever have a child. For many couples, infertility is a crisis. It often comes with feelings of guilt or inadequacy. But a diagnosis of infertility is not necessarily a verdict of sterility. Fifteen percent of all couples are infertile but only 1%-2% are sterile. Half of couples that seek help can eventually bear a child, either on their own or with medical assistance.

Men and women are equally likely to have a fertility problem. In about one in five infertile couples, both partners have contributing problems and in about 15% no cause is found after all tests have been done (unexplained infertility).

Conception and pregnancy are complicated processes that depend upon many factors : 1) the production of healthy sperm by the man, 2) healthy eggs produced by the woman, 3) unblocked fallopian tubes that allow the sperm to reach the egg, 4) the sperm's ability to fertilize the egg when they meet, 5) the ability of the fertilized egg (embryo) to become implanted in the woman's uterus and 6) sufficient embryo quality. Finally, for the pregnancy to continue to full term, the embryo must be healthy and the woman's hormonal environment adequate for its development. When just one of these factors is impaired, infertility can result.

It is estimated that 10 - 20% of couples will be unable to conceive after 1 year of trying to become pregnant. It is important that pregnancy be attempted for at least 1 year. The chances for pregnancy occurring in healthy couples who are both under the age of 30 and having intercourse regularly is only 25 - 30% per month. A woman's peak fertility occurs in her early 20s. As a woman ages beyond 35 (and particularly after age 40), the likelihood of getting pregnant drops to less than 10% per month.

Symptoms and Signs

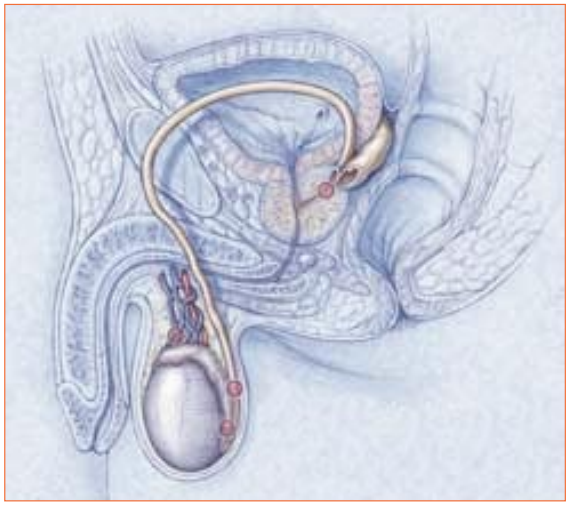
The history should include prior testicular insults (torsion, cryptorchidism, trauma), infections (mumps orchitis, epididymitis), environmental factors (excessive heat, radiation, chemotherapy), medications (anabolic steroids, cimetidine, and spironolactone may affect spermatogenesis; phenytoin may lower FSH; sulfasalazine and nitrofurantoin affect sperm motility) and drugs (alcohol, marijuana). Sexual habits, frequency and timing of intercourse, use of lubricants, and each partner's previous fertility experiences are important. Loss of libido and headaches or visual disturbances may indicate a pituitary tumor. The past medical or surgical history may reveal thyroid or liver disease (abnormalities of spermatogenesis), diabetic neuropathy (retrograde ejaculation), radical pelvic or retroperitoneal surgery (absent seminal emission secondary to sympathetic nerve injury), or hernia repair (damage to the vas deferens or testicular blood supply).

Female infertility occurs when the woman does not conceive after one year of attempting to become pregnant. Other signs and symptoms depend on the underlying cause of the woman's infertility.

Male Infertility

In men, the most common reasons for infertility are sperm disorders. These problems include:

- Low sperm count. This means there are too few or no spermatozoa in the ejaculate.
- Low sperm motility. This means that the sperm don't move as well as they should.
- Malformation of the sperm.
- Blocked sperm ducts.



The reasons that there may be a low sperm count or no sperm at all include one or more of the followings :

- A preexisting genetic condition
- Use of alcohol, tobacco or other illicit drugs
- A severe mumps infection
- A hormone disorder
- Exposure to poisonous chemicals
- Exposure to radiation
- Blockage caused from a previous infection
- Wearing restrictive or tight underwear

Another common problem is a temporary drop in sperm production. This happens when the testicles have been injured, as can happen when they have been too hot for too long or when the man has been exposed to chemicals or medications which affect sperm production. Spending a long

time in a hot tub, for example, or wearing underwear that holds the testicles too close to the body can increase the testicular temperatures and impair sperm production. Sometimes there is a physical reason. In the relatively common condition called varicocele, veins around the vas deferens (the duct that carries sperm from testicle to urethra) becomes dilated -- similar to a varicose vein in the leg. The pooling of blood in these veins keeps the temperature inside the scrotum too high. Certain lifestyles, like increased alcohol intake and smoking, can also have a negative effect on sperm count.

Male infertility also occurs when there are problems with ejaculation that prohibits the sperm from getting into the woman's vagina. Ejaculation problems include any of the followings :

- ❏ Premature ejaculation
- ❏ Retrograde ejaculation, which occurs when the semen is forced back into the bladder
- ❏ Erection dysfunctions
- ❏ A complication from radiation therapy or surgery

Diagnosis of Male Infertility

Potential male infertility will be assessed as part of a thorough physical examination. The exam. will include a medical history regarding potential factors that could contribute to infertility. Testing for male infertility is simple and routine. Male infertility is related to approximately 50% of all infertility cases, and male infertility alone accounts for approximately one-third of all cases. When a couple has been unsuccessful at getting pregnant over the course of one year, both need to go through a comprehensive physical and medical history.

Tests

A semen analysis is the most common testing procedure for determining if there is a male infertility factor. Sperm is collected into a specimen jar and presented to a lab to examines the sperm under a microscope to evaluate the count, shape, appearance, and mobility. For the sperm count, it will be checking to see whether the sperm concentration is above or below 20 million sperm cells per milliliter of ejaculation fluid. If the sperm count is low, test for blood testosterone, FSH, LH and prolactin levels will be needed.

A urinalysis may be used to look for white blood cells which may indicate an infection. The urinalysis will also determine if there is sperm in the urine, which would suggest that there is a problem with ejaculation known as retrograde ejaculation. If the medical history, physical examination and semen analysis are normal, attention should be directed to the female partner before further evaluation of the man. Further male factor evaluation is less likely to occur, but is sometimes needed. If so, additional laboratory and sperm analysis tests may be used. Here is a list of tests and a brief description of what each is examining:

Sperm agglutination : a laboratory test which examines sperm under a microscope to determine whether the sperm are clumping together. Clumping prevents sperm from swimming through the cervical mucus.

Sperm penetration assay : a laboratory test which uses hamster eggs to evaluate a sperms capability of penetrating the egg. This test is rarely used any more.

Hemizona assay : a laboratory test that involves cutting a non-usable human egg in half to see if the sperm can penetrate the outermost protective layer of the egg.

Acrosome reaction : a laboratory test which assess whether sperm heads can go through the chemical changes necessary to dissolve an egg's tough outer shell.

Hypo-osmotic swelling : a laboratory test that uses special sugar and salt solution to evaluate the sperm's tail and ability to penetrate the egg. The tails of healthy sperm tend to swell in this solution whereas dead or abnormal sperm do not swell.

Testicular biopsy : a small piece of tissue is removed from the tubules in the testes and examined to determine how well sperm are being produced.

Vasography : an x-ray exam. used to determine if there is blockage or leakage of sperm in the vas deferens.

Ultrasonography : an exam. used to locate damage or blockage in the male reproductive tract.

Female Infertility

Female infertility usually occurs when there is a problem with ovulation, a damaged fallopian tube or uterus, or there is a problem with the cervix. Age is a major factor of female infertility. In women, fertility declines with age, and even more so after the age of 35 years. Conception after age 45 is rare. Being overweight or underweight can also play a role. Women 40 and over often have decreased fertility. Age may also contribute to fertility struggles because as a women ages, her fertility decreases.

Ovulation problems may be caused by one or more of the followings :

- A hormone imbalance
- A tumor or cyst
- Eating disorders such as anorexia or bulimia
- Alcohol or drug use
- Thyroid gland problems
- Overweight
- Stress
- Intense exercise causing a loss of body fat
- Extremely short menstrual cycle

Damage to the fallopian tubes or uterus may be caused by one or more of the followings :

- Pelvic inflammatory disease
- A previous infection
- Polyps in the uterus
- Endometriosis or fibroids
- Scar tissue or adhesions
- Chronic medical illness
- Surgery to remove a tubal pregnancy
- A birth defect

Abnormal cervical mucus may be the cause of infertility. Abnormal cervical mucus may prevent the sperm from reaching the egg or make it more challenging for the sperm to penetrate the egg. Another reason for female infertility includes the inability of the fallopian tubes to carry eggs from the ovary to the uterus, usually due to scar tissue or a condition called *endometriosis*.

Rarely, in the uterus, fibroid growths, endometriosis, tumors, cervical problems or irregular uterine shape can keep the egg from implanting in the uterus. Fertilization may not happen if the cervical mucus damages sperm or impedes their progress.

Diagnosis of Female Infertility

Potential female infertility will be assessed as part of a thorough physical exam. The exam. will include a medical history regarding potential factors that could contribute to infertility. Usually the first question regarding female fertility is whether she is ovulating or not. The first test performed by fertility specialists involves measuring follicle stimulating hormone (FSH) and luteinizing hormone (LH) to establish a baseline. This is performed on the third day of cycle. This test is performed during first visit. And second visit will occur on the day of the LH surge, which is before ovulation in most cases.

Tests

During first cycle, it is common for fertility specialists to perform the following tests:

Cervical mucus tests : This involves a postcoital test (PCT) which determines if the sperm is able to penetrate and survive in the cervical mucus. It also involves a bacterial screening.

Ultrasound tests : This is used to assess the thickness of the lining of the uterus (endometrium), monitor follicle development and check the condition of the uterus and ovaries. An ultrasound may be conducted two to three days later to confirm that an egg has been released

Hormone tests : These tests are done to assess the various hormone levels that contribute to the reproductive process. These hormone tests include the followings :

- Luteinizing Hormone
- Follicle Stimulating Hormone
- Estradiol
- Progesterone
- Prolactin
- Free T3
- Total Testosterone
- Free Testosterone
- DHEAS
- Androstenedione

If both the semen analysis and the above testing return normal results, there is also additional testing that may recommend. These tests include any of the followings :

Hysterosalpingogram (HSG) : This is simply an x-ray of uterus and fallopian tubes. A blue dye is injected through the cervix into the uterus and fallopian tubes. The dye enables the radiologist to see if there is blockage or any other problems

Hysteroscopy : A procedure that may be used if the HSG indicates that there may be problems. The hysteroscope is inserted through the cervix into the uterus, which allows to see any abnormalities, growths or scarring in the uterus. The hysteroscope allows to take pictures which may be used for future reference.

Laparoscopy : A procedure which uses a narrow fiber optic telescope. The laparoscope is inserted through a woman's abdomen to look at the uterus, fallopian tubes, and ovaries. It is usually done to check for endometriosis, scar tissue, or other adhesions. It is important to confirm that the patient is not pregnant before this test is performed.

Endometrial biopsy : This is a procedure which involves scraping a small amount of tissue from the endometrium just prior to menstruation. This biopsy is performed to assess whether there is a hormonal imbalance or not. It is important to confirm that the patient is not pregnant before this test is performed.

Treatment

Treatment depends on the cause of infertility. Many times these treatments are combined. About two-thirds of couples who are treated for infertility are able to have a baby. It may involves-

1. Simple education and counseling

2. Medicines and/or surgery
3. Assisted reproductive technology

Doctors recommend specific treatments for infertility based on :

- ❏ test results
- ❏ how long the couple has been trying to get pregnant
- ❏ the age of both the man and woman
- ❏ the overall health of the partners
- ❏ preference of the partners

Infertility in men often treat in the following ways :

Sexual problems : If the man is impotent or has problems with premature ejaculation, doctors can help him address these issues. Behavioral therapy and/or medicines can be used in these cases.

Too few sperm : If the man produces too few sperm, sometimes surgery can correct this problem. In other cases, doctors can surgically remove sperm from the male reproductive tract. Antibiotics can also be used to clear up infections affecting sperm count.

Various fertility medicines are often used to treat women with ovulation problems. The following medications are used for ovarian stimulation :

Clomiphene citrate : This medicine causes ovulation by acting on the pituitary gland. It is often used in women who have Polycystic Ovarian Syndrome (PCOS) or other problems with ovulation. This medicine is taken by mouth. Potential side effects include :

- ❏ Increased incidence of multiple birth
- ❏ Increased incidence of miscarriage
- ❏ Hot flashes, nausea, and breast tenderness
- ❏ Headaches or blurred vision
- ❏ Depression and mood swings
- ❏ Ovarian cysts and pelvic discomfort

Synthetic Human Chorionic Gonadotropin (hCG) : Intramuscular injections used to induce the final maturational changes in the eggs and prepare them for retrieval. There are no known side effects.

Follicle Stimulating Hormone (FSH) : An injection given below the skin that bypasses the hypothalamus and pituitary glands to directly stimulate follicle growth in the ovaries. Potential side effects include:

- ❏ Increased incidence of multiple birth
- ❏ Increased incidence of miscarriage and premature delivery
- ❏ Breast tenderness, swelling, or rash at injection site
- ❏ Mood swings and depression
- ❏ Hyperstimulation syndrome which includes enlarged ovaries, abdominal pain and bloating

Human Menopausal Gonadotropins (hMG) : An injection that contains equal parts of FSH and LH (luteinizing hormone), or hCG as an LH substitute, given to stimulate the ovaries to produce multiple eggs during one cycle. Potential side effects include the same as noted above for FSH.

Bromocriptine and Cabergoline : Oral medications used to reduce the amount of prolactin released by the pituitary. Potential side effects include:

- ❏ Nausea, vomiting, nasal congestion
- ❏ Headache, dizziness, fainting
- ❏ Decreased blood pressure

Gonadotropin-Releasing Hormone (GnRH) : An injection used to stimulate the pituitary gland to secrete LH and FSH. Potential side effects include:

- ❏ Slight chance of multiple births
- ❏ Mild hyperstimulation which includes enlarged ovaries, abdominal pain, and bloating
- ❏ Headaches and nausea

Metformin : Doctors use this medicine for women who have insulin resistance and/or Polycystic Ovarian Syndrome (PCOS). This drug helps lower the high levels of male hormones in women with these conditions. This helps the body to ovulate. Sometimes clomiphene citrate or FSH is combined with metformin. This medicine is usually taken by mouth.

Assisted reproductive technology

Assisted reproductive technology (ART) is a term that describes several different methods used to help infertile couples. ART involves removing eggs from a woman's body, mixing them with sperm in the laboratory and putting the embryos back into a woman's body. Success rates vary and depend on many factors. Some things that affect the success rate of ART include :

- ❏ age of the partners
- ❏ reason for infertility
- ❏ clinic
- ❏ type of ART
- ❏ if the egg is fresh or frozen
- ❏ if the embryo is fresh or frozen

The U.S. Centers for Disease Prevention (CDC) collects success rates on ART for some fertility clinics. According to the 2003 CDC report on ART, the average percentage of ART cycles that led to a healthy baby were as follows:

- ❏ 37.3% in women under the age of 35
- ❏ 30.2% in women aged 35-37
- ❏ 20.2% in women aged 37-40
- ❏ 11.0% in women aged 41-42

ART can be expensive and time-consuming. But it has

allowed many couples to have children that otherwise would not have been conceived. The most common complication of ART is multiple fetuses. But this is a problem that can be prevented or minimized in several different ways. ART commonly practices are the followings :

In Vitro Fertilization (IVF)

IVF may help those with pelvic or tubal damage, or male infertility. It is the most commonly used Assisted Reproductive Technique (ART). The woman takes drugs to stimulate egg production, which are surgically removed. Then eggs and sperm (from her partner or a donor) are collected and combined outside the body, and inserted into her body to develop after fertilization takes place.

1. Eggs and sperm are harvested.
2. The collected eggs and sperm are combined in the laboratory.
3. Fertilized eggs are inserted directly into the uterus.

Gamete Intrafallopian Transfer (GIFT)

May help people with mild endometriosis, low sperm count, or sperm antibody problems. Similar to IVF, but the collected eggs and sperm (both are known as gametes) are placed beside each other in a woman's fallopian tube, which is where fertilization normally occurs.

1. Eggs and sperm are collected.
2. Eggs and sperm are inserted directly into the fallopian tube.

Zygote Intrafallopian Transfer (ZIFT)

Similar to GIFT, but the collected egg and sperm are first joined in the laboratory. The resulting zygotes (fertilized eggs) are then transferred to the woman's healthy fallopian tube, where one or more will travel to the uterus for implantation and development.

1. Eggs and sperm are collected.
2. The collected sperm is combined with the eggs.
3. Embryos are inserted directly into the fallopian tube.

Intercytoplasmic Sperm Injection (ICSI)

Each collected egg is injected, by hand, with one collected sperm, prior to insertion in the woman's body. This technique is used in ART procedures when patients have encountered difficulties with fertilization.

1. Eggs and sperm are harvested.
2. A single sperm is injected into each egg.
3. Fertilized eggs are inserted into fallopian tube or uterus.

Complications

Although infertility itself does not cause physical illness, the psychological impact of infertility upon individuals or couples affected by it may be severe. Couples may encounter marital problems, as well as individual depression and anxiety.

Prevention

Because infertility is frequently caused by sexually transmitted diseases, practicing safer sex behaviors may minimize the risk of future infertility. Gonorrhea and chlamydia are the two most frequent causes of STD-related infertility. STDs are often asymptomatic at first, until PID or salpingitis develops. These inflammatory processes cause scarring of the fallopian tubes and decreased fertility, absolute infertility or an increased incidence of ectopic pregnancy.

Mumps immunization has been well demonstrated to prevent mumps and its male complication, orchitis. Immunization prevents mumps-related sterility. Some forms of birth control, such as the intrauterine device (IUD), carry a higher risk for future infertility. However, IUDs are not recommended for women who have not previously had a child.

Women selecting the IUD must be willing to accept the very slight risk of infertility associated with its use. Careful consideration of this risk, weighed with the potential benefits, should be reviewed and discussed with both partners and the health care provider. Early diagnosis and treatment of endometriosis may decrease the risk of infertility.

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Hepatitis E

Introduction

Hepatitis is considered as one of the major public health issues in today's developing nations and Bangladesh shows no difference from that. The convergence of different forms of this particular viral infection (Hepatitis A, B, C, D & E virus) pose a serious health problem in this country especially in rural areas where there is lack of facilities for proper diagnosis and management. Among all forms of viral hepatitis, 'Hepatitis E' is the most common in Bangladesh and despite of high mortality in pregnant women, its sub-clinical nature underestimates the burden of the disease in the general population. All these reasons demand the necessity of evaluating the prevailing health condition due to hepatitis E virus and the recent advancement regarding treatment strategies for better handling of such condition in future.

Among the enterically transmitted viruses, Hepatitis E is the most common in Bangladesh. Infact, hepatitis E virus infections cause a substantial burden of sporadic and epidemic disease worldwide, specially in many developing countries in the south and south-east Asia. It is also recognized as the only cause of enterically transmitted non-A, non-B (ET-NANB) hepatitis. (The other enterically transmitted hepatitis is caused by Hepatitis A virus.) It is very recently realized that hepatitis E and not hepatitis A virus is the major cause of water-borne hepatitis spread by faeco-oral route in this sub-continent. The virus is thought to be endemic in many developing countries, although the greatest historical burden of disease has been confined to South and Southeast Asia.

Hepatitis E is basically a self-limiting viral disease with no documented chronic sequelae or carrier state. Even mortality from HEV is low in the general population (~1%). However pregnant women hospitalized for HEV disease in their 2nd and 3rd trimesters experience a case fatality rate of more than 20%. There is also proof that HEV can cause fulminant hepatitis and hepatic failure in the long run. Little is known about the burden of hepatitis E disease in Bangladesh because not many population-based researches have been conducted in either urban or rural populations. Although no outbreaks have yet been reported, there is both direct and indirect evidence that the virus contributes significantly to disease in Bangladesh.

History of Hepatitis E

It was not very long that Hepatitis E was recognized as a distinct human disease because there was no laboratory test invented to detect Hepatitis E virus in the affected population. HEV was first identified in 1980, when specific tests for antibody against hepatitis A were applied to the study an epidemic waterborne hepatitis in India. The results showed that the epidemics were not epidemics of hepatitis A and suggested existence of an additional water-borne hepatitis agent other than Hepatitis A. By 1983 this new form of hepatitis came to be known as Enterically transmitted non-A non-B hepatitis (ET-NANB), Epidemic non-A non-B hepatitis (ENANB), or Faecal-oral non-A non-B hepatitis. The agent was subsequently found to be the major cause of sporadic hepatitis cases in regions where the epidemic form was known to exist. Actually, very few epidemics of waterborne disease in developing countries of Asia and Africa have been linked to hepatitis A. Eventually the virus was identified and named Hepatitis E virus and the enterically transmitted disease itself was considered as Hepatitis E.

Hepatitis E virus

Hepatitis E virus is a non-enveloped, spherical, positive-stranded RNA virus. Several different strains have been isolated, partially characterized and molecularly cloned. The virion is composed entirely of viral protein and RNA. The diameter of the virion is 27-34 nm. Electron microscopy analyses show spherical particles of possible icosahedral symmetry, with indefinite surface substructure, resembling the caliciviruses.

Morphologically, HEV is similar to Norwalk virus, a member of the calicivirus family and thus initially been classified into the caliciviridae family from 1988 to 1998. Because the phylogenetic analysis of non-structural regions of the virus did not support the classification of HEV but most closely resembles the sequence of rubella virus, a togavirus, and beet necrotic yellow vein virus, a plant furovirus HEV now is classified into the separate genus Hepatitis E-like viruses. At least four major genotypes have been identified but only one serotype of HEV is recognized.

The hepatitis E genome consists of a linear, single-stranded, positive-sense RNA (mRNA) containing a 3' poly(A) tail and short 5' and 3' noncoding (NC) regions. Three overlapping open reading frames (ORFs) exist, and all three coding frames are used to express different proteins.

ORF1 encodes a polyprotein of about 1690 amino acids that probably undergoes post-translational cleavage into multiple nonstructural proteins required for virus replication, including a methyltransferase, a putative papain-like cystein protease, an RNA helicase and an RNA-dependent RNA polymerase.

ORF2 does not overlap with ORF1 and encodes the principal and probably only structural protein. It is a capsid protein of 660 amino acids (71 kDa).

ORF3 begins with the last nucleotide of ORF1. It overlaps extensively with ORF2 and is the shortest of the open reading frames, encoding a small immunogenic 123 amino acid phosphoprotein (14.5 kDa) which associates with the cytoskeleton, suggesting a possible role in the assembly of virus particles.

Serologic tests for anti-HEV based upon expressed ORF2 sequences are more sensitive for detecting IgM and IgG anti-HEV than are tests based upon antigens containing ORF3

sequences. In fact, proteins expressed from ORF2 measure antibodies that correlate with protection against hepatitis E.

Transmission

HEV is spread by the faeco-oral route. Consumption of faecally contaminated drinking water has given rise to epidemic cases. This enterically transmitted virus has been implicated in several food and waterborne outbreaks. There is also evidence of increase hepatitis E following flood.

However, intact HEV particles are present in patient's stool in low amount thus accounts for the generally lower rate of person-to-person transmission of hepatitis E in comparison with that of hepatitis A.

Naturally acquired HEV antibodies have been detected in primates, rodents and swine. Human hepatitis E has been transmitted under laboratory conditions to various species of primates, domestic pigs, lambs and laboratory rats. Since monkeys, pigs, cows, rodents, sheep and goats are susceptible to infection with HEV a zoonotic spread of HEV is not excluded.

There is no evidence for sexual transmission or for transmission by transfusion of blood or blood products.

Prevalence

HEV and HAV are highly endemic in Bangladesh, implying that there might be a constant source of infection, such as water supply contamination. Bangladesh, the largest delta of the world, is basically a plain land with a large number of rivers crisscrossing the area and flooding in the rainy seasons is almost inevitable. Thus the geographical features and climatic conditions of the country is ideal for such a contamination.

Luckily the population has a high percentage of immunity and a sudden epidemic outbreak of waterborne hepatitis is unlikely. However a higher rate of sub-clinical infection with HEV and possible superinfection in other form of hepatitis makes the population vulnerable. It has been acknowledged in a number of studies that hepatitis E occurs as a superinfection in HBsAg carriers.

About 7.3% of the apparently healthy population had been undergoing a state of subclinical HEV infection reflects the alarming level of endemicity of the disease at Dhaka. A similar study in 1995 on

Bangladeshi peacekeepers participating in the United Nations Mission in Haiti (UNMIH) was undertaken after the diagnosis of acute HEV infection in four soldiers. A serosurveillance study on 105 Bangladeshi soldiers revealed asymptomatic HEV infection in 7%. In another study on UNMIH peacekeepers the seroprevalence of HEV IgG in the South Asian contingents were found 62% in Pakistani soldiers, 37% in both Indian and Nepalese and 27% in Bangladeshi soldiers. The figures of Indian and Nepalese contingent might be considered as average taking hygienic conditions and food habit of the subcontinent into consideration. However in healthy Bangladeshi population, seroprevalence of HEV IgG have been found as high as 60%.

Hepatitis E outbreaks are associated with rainy seasons, floods and overcrowding. All of the factors are well incorporated with Bangladeshi population. Hepatitis E virus is also the principal cause of acute hepatitis on the Indian subcontinent, in South-eastern and central Asia, in the Middle East, in Mexico, and in parts of Africa. Recent outbreaks have occurred in Iraq, Chad, Sudan, and India.

The disease

The clinical presentation of hepatitis E is comparable to hepatitis A. The disease may range in severity from subclinical to fulminant hepatic failure. The incubation period following exposure to HEV ranges from 3 to 8 weeks, with a mean of 40 days. Typical signs and symptoms of hepatitis include jaundice, anorexia, hepatomegaly, abdominal pain and tenderness, nausea and vomiting and fever. The severity of an HEV infection is generally greater than the severity of an HAV infection.

Peak viremia and peak shedding of HEV into the faeces occurs during the incubation period and early acute phase of disease. Detection of HEV antigens in the liver generally parallels viremia and faecal shedding of virus.

The highest rate of clinically evident disease is typically observed in young to middle-age adults. Highest incidence of the disease ranges from 15 years to 40 years. Lower disease rates in younger age groups may be the result of anicteric or/and subclinical HEV infections.

The course of infection has 2 phases termed prodromal and icteric. Prodromal-phase symptoms includes myalgia, arthralgia, fever with mild temperature elevations, anorexia, nausea or vomiting, weight loss (typically 2-4 kg), dehydration, right upper quadrant pain that increases with physical activity.

Icteric-phase symptoms comprise jaundice (serum bilirubin level is greater than 3 mg/dl), scleral icterus, dark urine, light-colored stools (20-40%), pruritus (50%),

Other features consist of urticarial rash, diarrhea, rapidly increasing serum amino transferase levels that peak within 4-6 weeks of onset and gradually decrease to normal within 1-2 months, viral excretion in stool persisting 14 days from onset. Common symptoms of other hepatitis are also present.

Physical signs include right upper quadrant tenderness, possible enlarged liver (usually palpable edges), possible splenomegaly, and possible transient spider angiomata.

Investigations

As hepatitis E is not clinically distinguishable from other types of acute viral hepatitis, diagnosis is made by biochemical assessment of liver function. Usual laboratory evaluation of urine bilirubin and urobilinogen, total and direct serum

bilirubin, ALT and AST, alkaline phosphatase, prothrombin time, total protein, albumin, IgG, IgA, IgM, complete blood count is done. Acute hepatitis E is diagnosed when the presence of IgM anti-HEV is detected.

Hepatitis E should be suspected in outbreaks of waterborne hepatitis occurring in developing countries, especially if the disease is more severe in pregnant women, or if hepatitis A has been excluded. If laboratory tests are not available, epidemiologic evidence can help in establishing a diagnosis.

HEV RNA can be detected in acute phase faeces by polymerase chain reaction (PCR) tests in approximately 50% of cases. Immune electron microscopy is positive in only about 10% of cases. The viral proteins pORF2 and pORF3 have been expressed in various recombinant systems and form the basis for diagnostic tests and vaccine studies. To confirm the results of Enzyme Immuno-Assays (EIA) or ELISA tests, Western blot assays to detect IgM and IgG anti-HEV in serum can be used, along with PCR tests for the detection of HEV RNA in serum and stool, immunofluorescent antibody blocking assays to detect antibody to HEV antigen in serum and liver, and immune electron microscopy to visualize viral particles in faeces.

Western blot and enzyme immunoassays detect anti-HEV antibodies by using the antigenic domains from ORF-2 and ORF-3. However, assays of ORF-2 are more sensitive.

Testing to detect anti-HEV immunoglobulin M (IgM) and immunoglobulin G (IgG) differentiates acute and chronic infection. The IgM titer falls rapidly after infection, becoming virtually undetectable within 6 months. Anti-HEV IgG persists for longer than 6 months, although its actual duration of positivity is unknown. IgG anti-HEV appears to afford protection against reinfection.

Aminotransferase levels (AST, ALT) are elevated several days before the onset of symptoms but generally return to normal within 1- 2 months after the peak severity of the disease has passed. Elevations can be associated with underlying liver disease or exposure to other hepatotoxins. Whether the magnitude of elevation correlates with the histological severity is not clear.

Serum bilirubin elevations occur in both the total and direct fractions. Hemolysis is unusual. In most cases, bilirubin levels take longer to return to normal than aminotransferase levels.

Many patients develop a mild leukocytosis. If associated with fever, bacteremia should be suspected. More commonly, WBC counts are decreased. Differential counts may show atypical cells and lymphocytosis.

Imaging Studies

Abdominal radiographs have no role in evaluating acute viral hepatitis unless the physical examination suggests a perforated viscus.

Abdominal ultrasonography is recommended. It helps rule out biliary obstruction in cases with significant nausea, vomiting, or fever. It can demonstrate the presence of an enlarged liver; echo texture is heterogeneous and coarsened. It can demonstrate splenomegaly, if present.

Other Tests

Perform blood cultures if the patient is febrile and hypotensive with an elevated WBC count. Determine serum acetaminophen levels if overdose is suspected.

Procedures

Liver biopsy usually is not necessary. Typical histological Findings includes cholestatic pathology with stasis of canalicular bile and marked proliferation of intralobular bile ductules. The cholestasis is most notable within the centroacinar regions. Parenchymal changes are less severe and include swollen hepatocytes, foam cells, and acidophil bodies. Inflammatory infiltrate of mononuclear cells is present, resulting in expanded portal areas and possible piecemeal necrosis.

Complications and chronicity

In general, hepatitis E is a self-limiting viral infection followed by recovery. Occasionally, a fulminant form of hepatitis develops, with mortality rates ranging between 0.5% - 4.0% of the overall population of patients. Fulminant hepatitis cases in pregnancy may reach a mortality rate of 20% in the 3rd trimester. Premature deliveries with high infant mortality of up to 33% are also observed. The reason for this high mortality is not clear yet. Some of the complications of pregnancy are toxemia with hypertension, proteinuria, edema, and kidney lesions. By directly or indirectly affecting the kidneys, HEV might precipitate eclampsia and lead to increased mortality in pregnant women. Common cholestatic jaundice can persist for several weeks.

Fulminant hepatitis (FH) is a serious complication of acute liver disease characterized by massive hepatocellular necrosis and encephalopathy. In the Western countries, hepatotoxic drugs and toxins have been increasingly related to FH, but viral infection remains the most frequent cause worldwide. All the hepatitis viruses have been implicated in the cause. In advanced countries where cases of enterically transmitted hepatitis are rare, HBV has been considered a major cause of infection related FH. In developing countries where all types of viral hepatitis prevail, a predominance of HEV infection has been observed.

Immune prophylaxis and vaccination

There is no available immunoglobulin (IG) prophylaxis at present. IG prepared from donors in non-HEV-endemic countries does not prevent infection and the efficacy of IG prepared from donors in HEV-endemic areas is unclear, although convalescent human sera have given promising preliminary results for passive protection, especially in pregnant mothers.

Experimental immune prophylaxis against HEV based on recombinant antigens appears to confer short term protection

and may be useful for pregnant women in endemic areas and travellers coming into these regions. At present, no commercially available vaccines exist for the prevention of hepatitis E. However, several studies for the development of an effective vaccine against hepatitis E are in progress.

A recombinant HEV-derived ORF2 protein has been used to vaccinate rhesus monkeys against different strains of hepatitis E. Although primates could still be infected, the vaccine protected them from the symptoms of disease. This form of vaccine however is not ready to be used in human.

The direct intramuscular injection of purified plasmid DNA containing the full-length ORF2 of HEV has induced a prolonged humoral immune response (>12 months) to the expressed structural protein ORF2 in 80% and 100% of two separate groups of challenged mice, respectively. This form of sub-unit vaccine is under trial in human and has been showed better efficacy in the long run. There is strong possibility that sub-unit vaccine will be used in the future for HEV vaccination.

The development of an attenuated or killed vaccine is not currently possible because of lacking an efficient cell culture system for replication of HEV.

Prevention

As almost all HEV infections are spread by the faeco- oral route, good personal hygiene, high quality standards for public water supplies and proper disposal of sanitary waste have resulted in a low prevalence of HEV infections in many well developed societies.

For travelers to high endemic areas, the usual elementary food hygiene precautions are recommended. These include avoiding drinking water and/or ice of unknown purity and eating uncooked shellfish, uncooked fruits or vegetables that are not peeled or prepared by the traveler.

Prevention of viral diseases remains the most important weapon for control since antivirals have never been as successful for the treatment of viral infections as antibiotics have been for the treatment of bacterial infections,

Surveillance and control procedures should include

- ❒ Provision of safe drinking water and proper disposal of sanitary waste
- ❒ Monitoring disease incidence
- ❒ Determination of source of infection and mode of transmission by epidemiologic investigation
- ❒ Detection of outbreaks
- ❒ Spread containment

Treatment

No specific therapy is capable of altering the course of acute hepatitis E infection so prevention is the most effective approach against the disease. As with hepatitis A, hepatitis E patients generally do not require hospitalization. Admission is required for fulminant hepatitis and should be considered for infected pregnant women. Supportive treatment with adequate hydration and electrolyte repletion should be added in hospital care. Hospitalization may also be indicated for patients unable to maintain oral intake.

The acute illness may result in anorexia, nausea, and vomiting, predisposing patients to dehydration. These symptoms tend to be worse in the afternoon or evening. Patients should attempt to ingest significant calories in the morning. As they improve, frequent small meals may be better tolerated. Neither multivitamins nor specific dietary requirements are required.

Guidelines for epidemic measures

1. Determination of mode of transmission.
2. Identification of the population exposed to increased risk of infection.
3. Elimination of common source of infection.
4. Improvement of sanitary and hygienic practices to eliminate faecal contamination of food and water.

Conclusion

HEV, especially, is an unrecognized problem of national significance in Bangladesh, which likely contributes to population morbidity as well as to the high level of maternal and neonatal mortality documented in Bangladesh.

Public health measures such as the provision of safe drinking water, improvement of sanitary and sewerage systems, and development of mass awareness to the prevailing situation are absolutely necessary.

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Test Yourself - 23

Correct Answers :

1. b d 2. a d 3. c 4. a c 5. a c 6. b d

CONGRATULATIONS!

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Test Yourself - 24

1. All the followings are true for 'Infertility' except:
- a. Men and women are not likely to have a infertility problem.
- b. A women's peak fertility occurs in her early 20s.
- c. The most common reasons for male infertility are sperm disorders.
- d. Female infertility occurs when there is a problem with ovulation only.

2. The following points are true for 'Hepatitis-E' except:
- a. HEV was first identified in 1980.
- b. The incubation period following exposure to HEV ranges from 2-8 weeks.
- c. Peak shedding of HEV into the faeces occurs during the incubation period.
- d. Highest incidence of the disease ranges from 10-50 years.

3. All the followings are correct for 'Memory loss' except:
- a. The 'procedural' memory involves storing facts in the brain.
- b. There are at least three general types of amnesia.
- c. Dementia, Depression, Alxheimer's disease, Drug abuse are the only causes of 'memory loss'.
- d. Stress, anxiety, ADHD, Vitamin B-12 deficiency are among the direct contributory factors in 'memory loss'.

4. All the followings are true for 'Infertility' except:
- a. The first test performed for female infertility involves FSH & LH to establish a baseline.
- b. IVF may help those with male infertility only.
- c. IVF is the most commonly used Assisted Reproductive Technique.
- d. Gonorrhea and Chlamydia are the two most frequent causes of STD related infertility

5. The followings are true for 'Hepatitis-E' except:
- a. Acute hepatitis-E is diagnosed when the presence of IgM anti HEV is defected.
- b. AST, ALT are elevated after onset of symptoms.
- c. Abdominal ultrasonography has no role to rule out biliary obstruction.
- d. Fulminating hepatitis (FH) is a serious complication of acute liver disease.

6. All the followings are true for 'Memory loss' except:
- a. Normal age related memory loss does not indicate diminished intelligence or ability to learn.
- b). Sleep disorders, Depression, Stress are among the irreversible causes of 'memory change'.
- c. Cerebral angiography, CT scan or MRI of head, EEG are among the diagnostic tests for the 'memory loss'.
- d. A deficiency of Vitamin B_6 has also been identified as a factor for 'memory loss'.

Soon our officials will be visiting you with a token of our appreciation

The British High Commissioner Inaugurated SQUARE's First Shipment to UK

On September 25, 2007 H.E. Mr. Anwar Choudhury, the British High Commissioner to Bangladesh, visited *SQUARE* Pharmaceutical's Kaliakoir facility. Mr. Kevin Ringham, Director of Trade and Investment and other officials accompanied the High Commissioner.

Mr. Samson H. Chowdhury, Chairman *SQUARE* Group and other Senior Officials of *SQUARE* Pharmaceutical's received the dignitaries. *SQUARE* Pharmaceutical's is the first company from Bangladesh to get the UK MHRA

(Medicines and Healthcare Products Regulatory Agency) Certification and also the first to export pharmaceuticals to United Kingdom.

The High Commissioner and his entourage visited the Manufacturing and Quality Assurance facilities of *SQUARE* Pharmaceuticals Ltd. and *SQUARE* Cephalosporins Limited. He was impressed by the level of manufacturing excellence at the plants and also expressed his great satisfaction on the quality commitments.

Later His Excellency inaugurated the first shipment of *SQUARE* manufactured pharmaceuticals for UK by receiving a token pack of products being shipped to UK from Mr. Samson H. Chowdhury, Chairman *SQUARE* Group. The first shipment contains two cardiovascular drugs.

The UK MHRA certification of *SQUARE* Pharmaceuticals followed by its first shipment of products to UK opened a new era in the history of Pharmaceuticals exports from Bangladesh. This certification will open the door for Pharmaceuticals exports to other EU countries for *SQUARE* and the company is actively pursuing the opportunity.

Product Profile-Carbizol®

Carbizol®

Composition

Carbizol® : Each film coated tablet contains Carbimazole BP 5 mg.

Pharmacokinetics

Carbimazole is an anti-thyroid substance which depresses the formation of thyroid hormone. It reduces the uptake and concentration of inorganic iodine by the thyroid but its main effect is to reduce the formation of di-iodotyrosine and thyroxine. Carbimazole is absorbed rapidly from the gastro-intestinal tract and is widely distributed throughout the body. Carbimazole is completely metabolised to methimazole and it is the metabolite that is responsible for its clinical activity.

Carbimazole readily crosses the placental barrier and also attains a high concentration in the milk of lactating patients.

Excretion in the urine is rapid. The elimination half-life of methimazole may be increased in hepatic and renal impairment.

Indication

Carbizol® is indicated in the management of hyperthyroidism, thyrotoxicosis (including thyroid storm), and also for the preparation of patients for thyroidectomy.

It can also be used in combination with radio-active ablative therapy.

Dosage & Administration

Adults :

The initial dose: 20 – 60 mg, in 2-3 divided doses until the patient is euthyroid. Daily dosage should be divided.

Maintenance regimen: Dose is gradually reduced to maintain a euthyroid state. Final dosage is usually in the range of 5 – 15 mg/day which may be taken as a single daily dose.

Neonates & Children below 12 years: The usual initial dose is 250 mcg /Kg/day in divided doses.

Duration of treatment: 18 to 24 months

Contraindication

Hypersensitivity to Carbimazole or other thiourea antithyroid agents.

Precaution

Carbimazole should be given with the utmost caution, or not at all, if there is any degree of tracheal obstruction, as high dosages may produce thyroid enlargement and obstructive symptoms may become marked.

Pregnancy and Lactation

Carbimazole may be given during pregnancy to a thyrotoxic patient, but the smallest effective dose should be used least overdosage adversely affects the foetus. Carbimazole crosses the placenta and is excreted into the breast milk. Carbimazole may, therefore, cause foetal or neonatal hypothyroidism and goitre.

Drug Interaction

Carbimazole may interact adversely with other medicines. Iodine or iodine excess may decrease the response to Carbimazole, requiring an increase in dosage or longer duration of therapy with antithyroid agents.

As thyroid and metabolic status of patient decreases toward normal, response to oral anticoagulants may decrease, however, if thioamide-induced hypoprothrombinemia occurs, anticoagulant effects may be enhanced. Adjustment of oral anticoagulant dosage on the basis of prothrombin time is recommended. Serum concentrations of digoxin and digitoxin have been reported to increase as the thyroid and metabolic status of patients taking antithyroid agents decreased, reduction in dosage of any digitalis glycoside may be necessary as patients become euthyroid.

Adverse reactions

Side-effects may include rash, pruritis, skin pigmentation, paraesthesias, urticaria, headache, arthralgia, and gastro-intestinal disturbances (including nausea, vomiting and gastric discomfort), and abnormal hair loss. Drug fever, a lupus-like syndrome, vasculitis and nephritis, and hepatic disorders, most commonly jaundice, and taste disturbances following Carbimazole therapy have been reported.

Overdosage

Overdosage or accidental poisoning may result in hypothyroidism and goitre. If blood dyscrasias occur, the drug should be immediately withdrawn. Further treatment is symptomatic and supportive.

New Technology To Test Live Toxicity Of Drugs

One of the main reasons that drugs are pulled off the market is because of liver toxicity. The problem is researchers have no way to accurately measure how the liver will respond to drugs. In the past, they have relied on liver cells from rats, but they do not always respond the same as human liver cells. Now, researchers from Massachusetts Institute of Technology (MIT) have created tiny colonies of living human liver cells that model the full-sized organ.

In order to build these model livers, MIT researchers use micropatterning technology. This is the same technology used to place tiny copper on computer chips. Essentially, the technology precisely arranges human liver cells on a plate. Because the cells are arranged so precisely, the micro-liver mimics the behavior of a human liver. Investigators tested the function of their model liver and found it does closely resemble the human liver. Then they found a way to mass produce the miniature liver models using soft lithography. This technique is done using a reusable stencil which allows the patterning of over 888 miniature model livers in a matter of minutes.

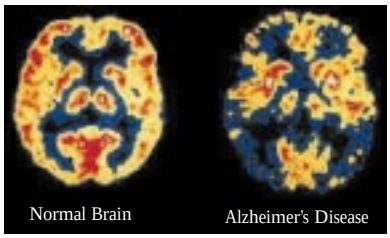
Study authors then tested their model livers by testing drugs with known toxicity levels. For example, they tested troglitazone which is a drug that was taken off the market because of liver toxicity. Researchers say their test showed toxicity levels higher than other similar drugs.

Researchers say they hope this new technology will make drugs safer, cheaper and better labeled.

SOURCE : Nature Biotechnology, November 2007

New Alzheimer's Treatments !

One of the characteristics of Alzheimer's disease is the clumping of amyloid beta proteins that turn to plaque. These toxic plaques kill neurons in the brain and are common in Alzheimer's patients. Two new studies have found ways to prevent the transformation of amyloid beta protein to the toxic plaque. For the first time, researchers say an interaction with another protein called cystatin C can prevent the killing of neurons in animals.



PET scan of brain

Study authors caution that a lot of research still needs to be done, but they are very optimistic that this will lead to new treatments for Alzheimer's disease. One of the research teams has already begun work on a drug that will mimic the ability of the protein cystatin C. They say cystatin C is protective against of variety of factors that cause cell death in the brain.

The studies were both done on mice. The mice were genetically engineered to produce human cystatin C as well as amyloid beta plaques in their brains. The cystatin C stopped the amyloid beta from depositing in the brain.

Study authors say this new research suggests that even small modifications of cystatin C protein levels could affect amyloid beta accumulation and deposition in the brain. This could lead to the first treatment to slow the progression of Alzheimer's disease.

SOURCE : Nature Genetics, November 2007

Low B_{12} Tied To Faster Mental Decline With Age

Low levels of vitamin B_{12} could speed mental decline in older people, a new study suggests.

Among a group of men and women aged 65 and older, those whose levels of two B_{12} activity markers indicated higher blood levels of the vitamin had a slower drop-off in cognitive function over 10 years than their peers, researchers found.

Folic acid and vitamin B_{12} supplements can reduce levels of homocysteine, a protein that has been tied to Alzheimer's disease, suggesting that supplementing with these B vitamins could ward off dementia, the researchers explain in the American Journal of Clinical Nutrition. However, folic acid can mask B_{12} deficiency, and some studies have linked low levels of B_{12} and high folic acid consumption with faster mental decline.

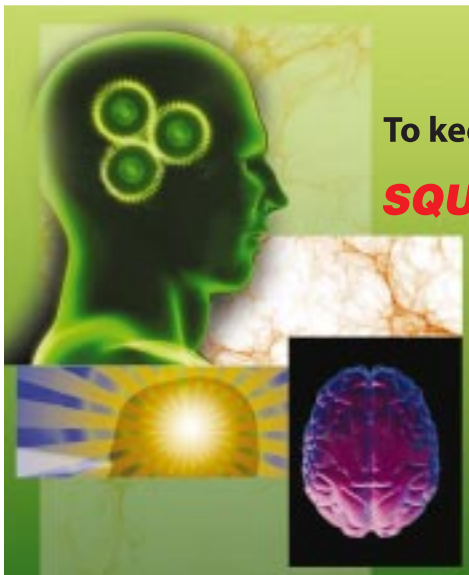
To better understand the relationship among homocysteine, folic acid, B_{12} and cognitive function, the researchers of the University of Oxford in the United Kingdom and colleagues followed 1,648 men and women 65 and older whose mental function was tested at least three times over a 10-year period.

The researchers checked levels of the biologically active portion of vitamin B_{12}, holotranscobalamin, as well as methylmalonic acid, a marker for B_{12} function. Testing for B_{12} itself has a "poor predictive value," they note.

There was no association between homocysteine or folate levels and cognitive function, the researchers found. However, lower holotranscobalamin levels and higher methylmalonic acid levels- both of which are markers for low levels of vitamin B_{12}-were each independently linked to faster mental decline. Higher folate levels along with low B_{12} levels did not accelerate mental decline.

The findings suggest that doubling a person's vitamin B_{12} levels by taking oral supplements could slow cognitive decline by one third, according to the researcher.

SOURCE : American Journal of Clinical Nutrition, November 2007.



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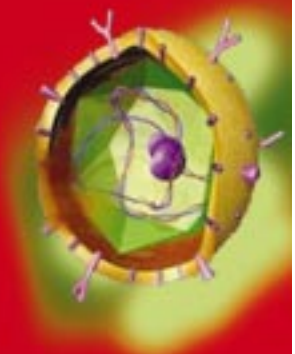
A burning global health care issue



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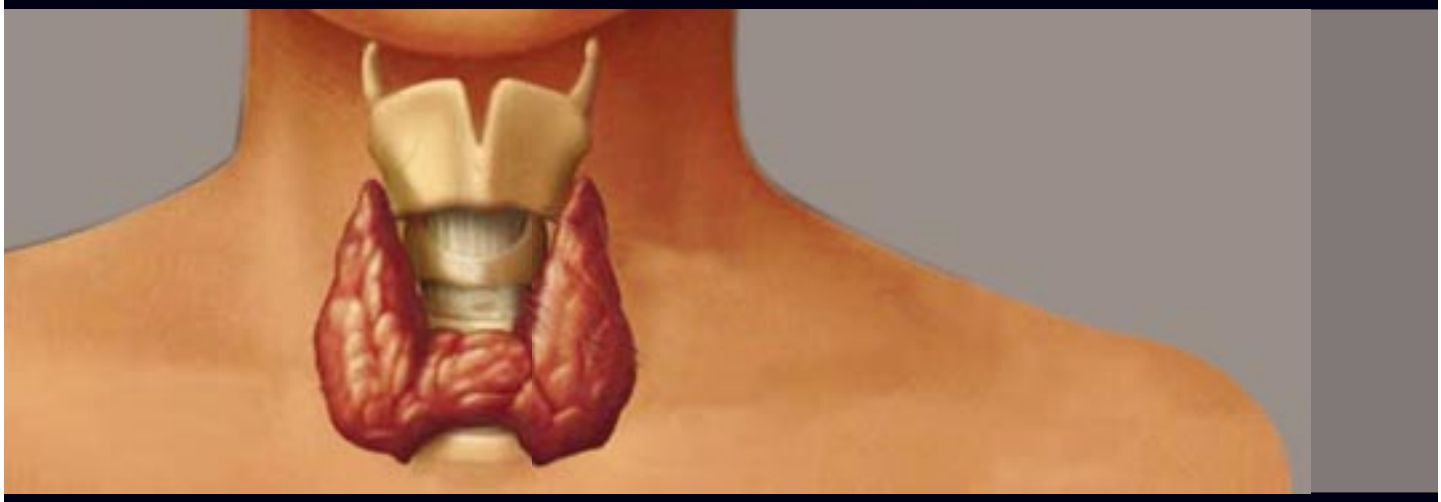
Undiagnosed and untreated hyperthyroidism can increase the risk of its fatal complications.



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- **Provides a spontaneous remission, thereby avoiding lifelong treatment**
- **Significantly improves symptoms in Graves' disease**
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