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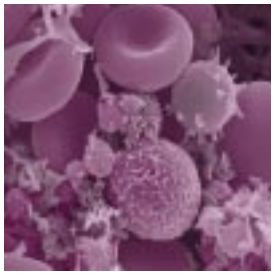

Test yourself 25

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Contents

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Editorial

Dear Doctor :

Hello again and welcome to this edition of "the *SQUARE* " healthcare bulletin !

This issue features a variety of articles including “Anxiety Disorders” that range from feelings of uneasiness to immobilizing bouts of terror. These disorders are the most common of all mental health problems. Research into their origins continues, but it is believed they are caused by a combination of biological factors and an individual's personal circumstances, much like other health problems, such as heart disease or diabetes. You will also find an article on “Bleeding Disorder” which is an acquired or inherited tendency to bleed excessively. In this issue we also emphasized on “Lactose Intolerance” which is a condition the vast majority of the world's population suffer from to some degree, particularly adults. What's more is, whilst lactose intolerance is so common, and some people may suffer terribly with it, the majority of sufferers do not know they are lactose intolerant, and are unaware it is lactose which is causing their bodies distress. Besides, our regular features comprise "*SQUARE* in International Business" and one of the product profiles.

We believe you will enjoy reading this publication and that the contents provided will prove helpful towards your goal of optimum health!

We welcome your feedback regarding "the *SQUARE* "! Your valuable feedback will assist us to better meet your needs and to improve this service!

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

Omar Akramur Rab

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Anxiety Disorders

Anxiety is a normal human emotion that everyone experiences at times. Many people feel anxious or nervous when faced with a problem at work or before taking a test or making an important decision. Anxiety disorders, however, are different. They can cause such distress that it interferes with a person's ability to lead a normal life.

An anxiety disorder is a serious mental illness. For people with anxiety disorders, worry and fear are constant and overwhelming and can be crippling.

These disorders are the most prevalent of psychiatric disorders, yet less than 30% of individuals who suffer from anxiety disorders seek treatment. Prevalence of anxiety disorders is difficult to pinpoint since even small changes in diagnostic criteria, interview tools or study methodology affect results.

Anxiety Disorders affect about 40 million American adults age 18 years and older (about 18%) in a given year causing them to be filled with fearfulness and uncertainty. Unlike the relatively mild, brief anxiety caused by a stressful event (such as speaking in public), anxiety disorders last at least 6 months and can get worse if they are not treated. Anxiety disorders commonly occur along with other mental or physical illnesses including alcohol or substance abuse, which may mask anxiety symptoms or make them worse. In some cases, these other illnesses need to be treated before a person will respond to treatment for the anxiety disorder. Despite the high prevalence rates of these anxiety disorders, they often are underrecognized and undertreated clinical problems.

Pathophysiology

Anxiety disorders appear to be caused by an interaction of biopsychosocial factors including genetic vulnerability which interact with situations, stress or trauma to produce clinically significant syndromes. In the central nervous system, the major mediators of the symptoms of anxiety disorders appear to be norepinephrine and serotonin. Other neurotransmitters and peptides such as corticotropin-releasing factor may be involved. Peripherally, the autonomic nervous system especially the sympathetic nervous system mediates many of the symptoms.

Mortality/Morbidity

- Anxiety disorders may contribute to morbidity and mortality through neuroendocrine and neuroimmune mechanisms or by direct neural stimulation eg. hypertension or cardiac arrhythmia.
- Severe anxiety disorders may be complicated by suicide with or without secondary mood disorders (eg. depression). Anxiety disorders have high rates of comorbidity with major depression and alcohol and drug abuse. Some of the increased morbidity and mortality associated with anxiety disorders may be related to this high rate of comorbidity. Two major studies in the United States have estimated the prevalence rates for a variety of anxiety disorders. These 2 studies are the Epidemiological Catchment Area (ECA) study and the National Comorbidity Survey (NCS) study. The ECA study found that panic disorder was associated with suicide attempts (odds ratio=18 compared to populations without psychiatric disorders). How much of the association of panic disorder with suicide is mediated through the association of panic disorder with mood and substance abuse disorders is unclear. Acute stress may play a role in producing suicidal behavior. Suicide attempts can be precipitated by adverse life events such as divorce or financial disaster. The effects of acute stress in producing suicidal behavior are increased in those with underlying mood, anxiety and substance abuse problems.
- Chronic anxiety may be associated with increased risk for cardiovascular morbidity and mortality.

Race

- The ECA study found no difference in rates of panic disorder among white, African American or Hispanic populations in the United States.
- Some studies have found higher rates of Post-Traumatic Stress Disorder (PTSD) in minority populations. Some of this association may be due to higher rates of specific traumatic events (eg. assault) in minority populations.

Sex

- The female-to-male ratio for any lifetime anxiety disorder is 3:2.

Age

- Most anxiety disorders begin in childhood, adolescence and early adulthood. Separation anxiety is an anxiety disorder of childhood that often includes anxiety related to going to school. This disorder may be a precursor for adult anxiety disorders. Panic disorder demonstrates a bimodal age of onset in the NCS study in the age groups of 15-24 years and 45-54 years. The median age of onset of social phobia in the NCS study was 16 years. The age of onset for Obsessive-Compulsive Disorder (OCD) appears to be in the mid 20s to early 30s. New-onset anxiety symptoms in older adults should prompt a search for an unrecognized general medical condition, a substance abuse disorder or major depression with secondary anxiety symptoms

Five major types of anxiety disorders are:

- Generalized Anxiety Disorder
- Obsessive-Compulsive Disorder (OCD)
- Panic Disorder
- Post-Traumatic Stress Disorder (PTSD)
- Social Phobia (or Social Anxiety Disorder)

Generalized Anxiety Disorder (GAD)

People with generalized anxiety disorder (GAD) go through the day filled with exaggerated worry and tension, even though there is little or nothing to provoke it. They anticipate disaster and are overly concerned about health issues, money, family problems or difficulties at work. Sometimes just the thought of getting through the day produces anxiety. GAD sometimes runs in families but no one knows for sure why some people have it, while others don't. When chemicals in the brain are not at a certain level it can cause a person to have GAD.

GAD is diagnosed when a person worries excessively about a variety of everyday problems for at least 6 months. People with GAD can't seem to get rid of their concerns even though they usually realize that their anxiety is more intense than the situation warrants. They can't relax, startle easily and have difficulty concentrating. Often they have trouble falling asleep or staying asleep. Physical symptoms that often accompany the anxiety include fatigue, headaches, muscle tension, muscle aches, difficulty swallowing, trembling, twitching, irritability, sweating, nausea, lightheadedness, having to go to the bathroom frequently, feeling out of breath and hot flashes.

When their anxiety level is mild, people with GAD can function socially and hold down a job. Although they don't avoid certain situations as a result of their disorder, people with GAD can have difficulty carrying out the simplest daily activities if their anxiety is severe.

GAD affects about 6.8 million adult Americans and about twice as many women as men. The disorder comes on gradually and can begin across the life cycle though the risk is highest between childhood and middle age. It is diagnosed when someone spends at least 6 months worrying excessively about a number of everyday problems. There is evidence that genes play a modest role in GAD.

Other anxiety disorders, depression or substance abuse, often accompany GAD, which rarely occurs alone. GAD is commonly treated with medication or cognitive-behavioral therapy but co-occurring conditions must also be treated using the appropriate therapies.

Obsessive-Compulsive Disorder (OCD)

Obsessive-compulsive disorder (OCD) is an anxiety disorder characterized by intense, recurrent, unwanted thoughts (obsessions) and rituals (compulsions) that are beyond the person's control. Examples of these rituals can include hand washing, counting, checking, hoarding, repeating, cleaning and the endless rearranging of objects in order to ensure they are in precise alignment. To the person affected, these rituals and thoughts are recognized as senseless and distressing but extremely difficult to control. If the person does not perform these rituals, anxiety increases dramatically and the person becomes concerned that something terrible will happen because of his or her neglect.

While anxiety disorders generally affect women more often than men, OCD affects both genders equally. However, the degree to which OCD affects each person varies. For some it is mild, but for others, it can control their lives if left untreated. This disorder is typically first seen in adolescence or early childhood. OCD is sometimes accompanied not only by depression but also eating disorders, substance abuse, attention deficit hyperactivity disorder (ADHD) and other anxiety disorders. OCD affects more than 3 million Americans in any given year.

The course of the disease is quite varied. Symptoms may come and go, ease over time or get worse. If OCD becomes severe, it can keep a person from working or carrying out normal responsibilities at home. People with OCD may try to help themselves by avoiding situations that trigger their obsessions or they may use alcohol or drugs to calm themselves.

Panic Disorder

Panic disorder is an anxiety disorder and is characterized by unexpected and repeated episodes of intense fear accompanied by physical symptoms.

Panic disorder is a real illness that can be successfully treated. It is characterized by sudden attacks of terror, usually accompanied by a pounding heart, sweatiness, shortness of breath, weakness, faintness or dizziness. During these attacks, people with panic disorder may flush or feel chilled; their hands may tingle or feel numb; and they may experience nausea, chest pain or smothering sensations. Panic attacks usually produce a sense of unreality, a fear of impending doom or a fear of losing control.

A fear of one's own unexplained physical symptoms is also a symptom of panic disorder. People having panic attacks sometimes believe they are having heart attacks, losing their minds or on the verge of death. They can't predict when or where an attack will occur and between episodes many worry intensely and dread the next attack.

Panic attacks can occur at any time even during sleep. An attack usually peaks within 10 minutes but some symptoms may last much longer. Panic disorder affects about 6 million American adults and is twice as common in women as men. Panic attacks often begin in late adolescence or early adulthood but not everyone who experiences panic attacks will develop panic disorder. Many people have just one attack and never have another. The tendency to develop panic attacks appears to be inherited.

People who have full-blown, repeated panic attacks can become very disabled by their condition and should seek treatment before they start to avoid places or situations where panic attacks have occurred.

Some people's lives become so restricted that they avoid normal activities such as grocery shopping or driving. About one-third become housebound or are able to confront a feared situation only when accompanied by a spouse or other trusted person. When the condition progresses this far, it is called agoraphobia or fear of open spaces.

Early treatment can often prevent agoraphobia but people with panic disorder may sometimes go from doctor to doctor for years and visit the emergency room repeatedly before someone correctly diagnoses their condition.

Panic disorder is often accompanied by other serious problems such as depression, drug abuse or alcoholism. These conditions need to be treated separately. Symptoms of depression include feelings of sadness or hopelessness, changes in appetite or sleep patterns, low energy and difficulty concentrating. Most people with depression can be effectively treated with antidepressant medications, certain types of psychotherapy or a combination of the two.

Post-Traumatic Stress Disorder (PTSD)

Post-Traumatic Stress Disorder, PTSD is an anxiety disorder that can develop after exposure to a terrifying event or ordeal in which grave physical harm occurred or was threatened. Traumatic events that may trigger PTSD include violent personal assaults, natural or human-caused disasters, accidents or military combat.

PTSD was first brought to public attention in relation to war veterans, but it can result from a variety of traumatic incidents such as mugging, rape, torture, being kidnapped or held captive, child abuse, car accidents, train wrecks, plane crashes, bombings or natural disasters such as floods or earthquakes.

People with PTSD may startle easily, become emotionally numb (especially in relation to people with whom they used to be close), lose interest in things they used to enjoy, have trouble feeling affectionate, become irritable, become more aggressive or even become violent. They avoid situations that remind them of the original incident and anniversaries of the incident are often very difficult. PTSD symptoms seem to be worse if the event that triggered them was deliberately initiated by another person as in a mugging or a kidnapping. Most people with PTSD repeatedly relive the trauma in their thoughts during the day and in nightmares when they sleep. These are called flashbacks. Flashbacks may consist of images, sounds, smells or feelings and are often triggered by ordinary occurrences, such as a door slamming or a car backfiring on the street. A person having a flashback may lose touch with reality and believe that the traumatic incident is happening all over again.

Not every traumatized person develops full-blown or even minor PTSD. Symptoms usually begin within 3 months of the incident but occasionally emerge years afterward. They must last more than a month to be considered PTSD. The course of the illness varies. Some people recover within 6 months, while others have symptoms that last much longer. In some people, the condition becomes chronic.

PTSD affects about 7.7 million American adults but it can occur at any age including childhood. Women are more likely to develop PTSD than men and there is some evidence that susceptibility to the disorder may run in families. PTSD is often accompanied by depression, substance abuse or one or more of the other anxiety disorders.

Research on Possible Risk Factors for PTSD

Currently, many scientists are focusing on genes that play a role in creating fear memories. Understanding how fear memories are created may help to refine or find new interventions for reducing the symptoms of PTSD. For example, PTSD researchers have pinpointed genes that make:

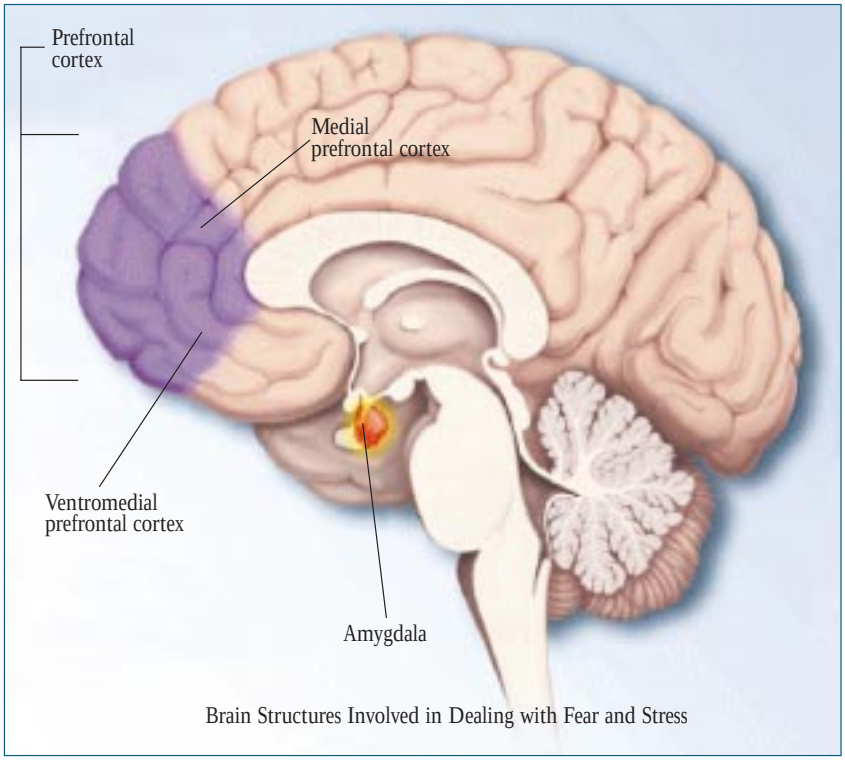
- Stathmin, a protein needed to form fear memories. In one study, mice that did not make stathmin were less likely than normal mice to "freeze," a natural, protective response to danger, after being exposed to a fearful experience. They also showed less innate fear by exploring open spaces more willingly than normal mice.
- GRP (gastrin-releasing peptide), a signaling chemical in the brain released during emotional events. In mice, GRP seems to help control the fear response and lack of GRP may lead to the creation of greater and more lasting memories of fear.

Researchers have also found a version of the 5-HTTLPR gene, which controls levels of serotonin — a brain chemical related to mood-that appears to fuel the fear response. Like other mental disorders, it is likely that many genes with small effects are at work in PTSD.

Studying parts of the brain involved in dealing with fear and stress also helps researchers to better understand possible causes of PTSD. One such brain structure is the amygdala, known for its role in emotion, learning and memory. The amygdala appears to be active in fear acquisition or learning to fear an event (such as touching a hot stove), as well as in the early stages of fear extinction or learning not to fear.

Storing extinction memories and dampening the original fear response appears to involve the prefrontal cortex (PFC) area of the brain involved in tasks such as decision-making,

problem-solving, and judgment. Certain areas of the PFC play slightly different roles. For example, when it deems a source of stress controllable, the medial PFC suppresses the amygdala an alarm center deep in the brainstem and controls the stress response. The ventromedial PFC helps sustain long-term extinction of fearful memories and the size of this brain area may affect its ability to do so.



Brain Structures Involved in Dealing with Fear and Stress

Individual differences in these genes or brain areas may only set the stage for PTSD without actually causing symptoms. Environmental factors such as childhood trauma, head injury or a history of mental illness may further increase a person's risk by affecting the early growth of the brain. Also personality and cognitive factors, such as optimism and the tendency to view challenges in a positive or negative way, as well as social factors, such as the availability and use of social support appear to influence how people adjust to trauma. More research may show what combinations of these or perhaps other factors could be used someday to predict who will develop PTSD following a traumatic event.

Social Phobia (Social Anxiety Disorder)

Social Phobia or Social Anxiety Disorder is an anxiety disorder characterized by overwhelming anxiety and excessive self-consciousness in everyday social situations. Social phobia can be limited to only one type of situation- such as a fear of speaking in formal or informal situations or eating or drinking in front of others or in its most severe form, may be so broad that a person experiences symptoms almost anytime they are around other people.

Social phobia also called social anxiety disorder is diagnosed when people become overwhelmingly anxious and excessively self-conscious in everyday social situations. People with social phobia have an intense, persistent and chronic fear of being watched and judged by others and of doing things that will embarrass them. They can worry for days or weeks before a dreaded situation. This fear may become so severe that it interferes with work, school and other ordinary activities and can make it hard to make and keep friends.

While many people with social phobia realize that their fears about being with people are excessive or unreasonable, they are unable to overcome them. Even if they manage to confront their fears and be around others, they are usually very anxious beforehand, are intensely uncomfortable throughout the encounter and worry about how they were judged for hours afterward.

Social phobia can be limited to one situation (such as talking to people, eating or drinking or writing on a blackboard in front of others) or may be so broad (such as in generalized social phobia) that the person experiences anxiety around almost anyone other than the family.

Physical symptoms that often accompany social phobia include blushing, profuse sweating, trembling, nausea, dry mouth and difficulty talking. When these symptoms occur, people with PTSD feel as though all eyes are focused on them.

Social phobia is a common disorder affecting over 5 million people in a given year. It often begins in childhood and rarely develops after age 25. People with social phobia are often aware that their fears are irrational but are unable to lessen or erase these fears. Women and men are equally likely to develop the disorder which usually begins in childhood or early adolescence. There is some evidence that genetic factors are involved. Social phobia is often accompanied by other anxiety disorders or depression and substance abuse may develop if people try to self-medicate their anxiety.

DIFFERENTIALS of Anxiety Disorders

Anxiety disorders have one of the longest differential diagnosis lists of all psychiatric disorders. Anxiety is a nonspecific syndrome and can be due to a variety of medical or psychiatric syndromes.

Acute Respiratory Distress Syndrome	Digitalis Toxicity	Inhalant-Related Psychiatric Disorders
Addison Disease	Dissociative Disorders	Injecting Drug Use
Adrenal Crisis	Dysthymic Disorder	Insomnia
Alcohol-Related Psychosis	Encephalopathy, Dialysis	Irritable Bowel Syndrome
Alcoholism	Encephalopathy, Hepatic	Lyme Disease
Amphetamine-Related Psychiatric Disorders	Encephalopathy, Hypertensive	Malingering
Anaphylaxis	Encephalopathy, Uremic	Meningitis
Androgen Excess	Epilepsy Surgery	Multifocal Atrial Tachycardia
Anorexia Nervosa	Esophageal Motility Disorders	Personality Disorders
Apnea, Sleep	Esophageal Spasm	Phobic Disorders
Asthma	Euthyroid Hyperthyroxinemia	Premenstrual Dysphoric Disorder
Atrial Fibrillation	Factitious Disorder	Primary Hypersomnia
Atrial Tachycardia	Fibromyalgia	Primary Insomnia
Body Dysmorphic Disorder	Folic Acid Deficiency	Schizoaffective Disorder
Brief Psychotic Disorder	Food Poisoning	Schizophrenia
Bulimia	Gastritis, Acute	Shared Psychotic Disorder
Caffeine-Related Psychiatric Disorders	Gastritis, Chronic	Sleep Disorder, Geriatric
Cannabis Compound Abuse	Goiter	Sleep Disorders
Cardiogenic Shock	Goiter, Diffuse Toxic	Somatoform Disorders
Conversion Disorders	Hallucinogens	Stimulants
Delirium	Hyperaldosteronism, Primary	Syndrome of Inappropriate Secretion of
Delirium Tremens	Hypercalcemia	Antidiuretic Hormone
Delusional Disorder	Hyperparathyroidism	Thyroiditis, Subacute
Depression	Hyperprolactinemia	Tourette Syndrome
Diabetes Mellitus, Type 1	Hypersensitivity Reactions, Delayed	Undifferentiated Connective-Tissue Disease
Diabetic Ketoacidosis	Hypersensitivity Reactions, Immediate	Unstable Angina

Other Problems to be Considered

Adult respiratory distress syndrome (ARDS)
AIDS
Thyrotoxicosis

A variety of anxiety symptoms such as panic, worry, rumination and obsessions can present in a variety of psychiatric illnesses including mood disorders, psychotic disorders, personality disorders, somatoform disorders and cognitive impairment disorders (eg. delirium). Anxiety also can be observed as part of a drug withdrawal or drug intoxication effect.

Other important causes in the differential include medication-induced anxiety (eg. due to epinephrine or other sympathomimetics, theophylline or other neurostimulant bronchodilators, analgesics containing caffeine, corticosteroids, antivirals, others); migraine, seizure disorders or other CNS-based disorders; and sleep disorders such as restless legs syndrome, sleep apnea and periodic limb movement. Heroin abuse also should be considered in the differentials.

WORKUP

Lab Studies

- When the index of suspicion for anxiety being produced by a medical disorder is low (lack of physical findings, younger age, typical anxiety disorder presentation), initial lab studies might be limited to the following:
  - CBC count
  - Chemistry profile
  - Thyroid function tests
  - Urinalysis
  - Urine drug screen
- For presentations with a higher index of suspicion for other medical causes of anxiety (eg. atypical anxiety disorder presentation, older age, specific physical examination abnormalities), more detailed evaluations may be indicated as follows:
  - To rule out CNS disorder using electroencephalogram, lumbar puncture or brain CT scan as indicated by history and associated clinical findings.

- To rule out cardiac disorder using ECG or treadmill ECG.
- To rule out infectious causes using rapid plasma reagent test, lumbar puncture (CNS infections) or HIV testing.

Imaging Studies

- ❏ Diagnostic imaging studies are not indicated in the diagnosis of primary anxiety disorders unless specific general medical conditions need to be ruled out.
- ❏ Imaging studies may be helpful, however, to rule out anxiety due to a general medical condition eg. cephalic CT scan or MRI to evaluate for pathological intracranial processes.

Procedures

- ❏ Psychosurgery is used in rare cases of severe treatment-refractory OCD.
- ❏ Electroconvulsive therapy is not effective for anxiety disorders but may successfully treat comorbid conditions such as severe major depression and is especially indicated when the patient is at high risk for suicide.

Treatment of Anxiety Disorders

In general, anxiety disorders are treated with medication, specific types of psychotherapy or both. Treatment choices depend on the problem and the person's preference. Before starting the treatment, a careful diagnostic evaluation should be done to determine whether a person's symptoms are caused by an anxiety disorder or a physical problem. If an anxiety disorder is diagnosed, the type of disorder or the combination of disorders that are present must be identified as well as any coexisting conditions such as depression or substance abuse. Sometimes alcoholism, depression or other coexisting conditions have such a strong effect on the individual that treating the anxiety disorder must wait until the coexisting conditions are brought under control.

A. Medications

Medication will not cure anxiety disorders but it can keep them under control while the person receives psychotherapy. The principal medications used for anxiety disorders are antidepressants, anti-anxiety drugs and beta-blockers to control some of the physical symptoms. With proper treatment, many people with anxiety disorders can lead normal, fulfilling lives.

Antidepressants

Antidepressants were developed to treat depression but are also effective for anxiety disorders. Although these medications begin to alter brain chemistry after the very first dose, their full effect requires a series of changes to occur; it is usually about 4 to 6 weeks before symptoms start to fade. It is important to continue taking these medications long enough to let them work.

SSRIs

Some of the newest antidepressants are called selective serotonin reuptake inhibitors or SSRIs. SSRIs alter the levels of the neurotransmitter serotonin in the brain which like other neurotransmitters, helps brain cells communicate with one another.

Fluoxetine, sertraline, escitalopram, paroxetine and citalopram are some of the SSRIs commonly prescribed for panic disorder, OCD, PTSD and social phobia. SSRIs are also used to treat panic disorder when it occurs in combination with OCD, social phobia or depression. Venlafaxine, a drug closely related to the SSRIs is used to treat GAD. These medications are started at low doses and gradually increased until they have a beneficial effect.

SSRIs have fewer side effects than older antidepressants but they sometimes produce slight nausea or jitters when people first start to take them. These symptoms fade with time. Some people also experience sexual dysfunction with SSRIs which may be helped by adjusting the dosage or switching to another SSRI.

Tricyclics

Tricyclics are older than SSRIs and work as well as SSRIs for anxiety disorders other than OCD. They are also started at low doses that are gradually increased. They sometimes cause dizziness, drowsiness, dry mouth and weight gain which can usually be corrected by changing the dosage or switching to another tricyclic medication.

Tricyclics include imipramine which is prescribed for panic disorder and GAD, and clomipramine which is the only tricyclic antidepressant useful for treating OCD. Clomipramine (Anafranil, a tricyclic agent) has a US Food and Drug Administration (FDA) indication in the treatment of OCD and is the only tricyclic agent effective in the treatment of this condition. Indeed, it can be effective in cases refractory to treatment with SSRI agents.

MAOIs

Monoamine oxidase inhibitors (MAOIs) are the oldest class of antidepressant medications. The MAOIs most commonly prescribed for anxiety disorders are phenelzine followed by tranylcypromine and isocarboxazid which are useful in treating panic disorder and social phobia. People who take MAOIs cannot eat a variety of foods and beverages (including cheese and red wine) that contain tyramine or take certain medications, including some types of birth control pills, pain relievers (such as Ibuprofen or Acetaminophen), cold and allergy medications and herbal supplements; these substances can interact with MAOIs to cause dangerous increases in blood pressure. The development of a new MAOI skin patch may help lessen

these risks. MAOIs can also react with SSRIs to produce a serious condition called "serotonin syndrome" which can cause confusion, hallucinations, increased sweating, muscle stiffness, seizures, changes in blood pressure or heart rhythm and other potentially life-threatening conditions.

Anti-Anxiety Drugs

High-potency benzodiazepines combat anxiety and have few side effects other than drowsiness. Because people can get used to them and may need higher and higher doses to get the same effect. Benzodiazepines are generally prescribed for short periods of time especially for people who have abused drugs or alcohol and who become dependent on medication easily. One exception to this rule is people with panic disorder who can take benzodiazepines for up to a year without harm.

Clonazepam is used for social phobia and GAD, lorazepam is helpful for panic disorder and alprazolam is useful for both panic disorder and GAD.

Some people experience withdrawal symptoms if they stop taking benzodiazepines abruptly instead of tapering off and anxiety can return once the medication is stopped.

Buspirone, an azapirone is a newer anti-anxiety medication used to treat GAD. Possible side effects include dizziness, headaches and nausea. Unlike benzodiazepines, buspirone must be taken consistently for at least 2 weeks to achieve an anti-anxiety effect.

Beta-Blockers

Beta-blockers such as propranolol which is used to treat heart conditions can prevent the physical symptoms that accompany certain anxiety disorders, particularly social phobia. When a feared situation can be predicted (such as giving a speech), a beta-blocker can be used to keep physical symptoms of anxiety under control.

The FDA has granted specific indications to the following disorders and agents: generalized anxiety disorder (venlafaxine, buspirone, escitalopram, paroxetine, duloxetine), social phobia (paroxetine, sertraline, venlafaxine), OCD (fluoxetine, sertraline, paroxetine, fluvoxamine) and PTSD (sertraline, paroxetine).

Patients with panic disorder frequently present to the emergency department with chest pain or dyspnea, fearing that they are dying of myocardial infarction. Anxiety symptoms often accompany or can exacerbate respiratory conditions such as asthma and chronic obstructive pulmonary disease.

- ❏ If clinically indicated, obtain necessary studies to rule out myocardial infarction and pulmonary embolism (ECG, chest x-ray).
- ❏ Intravenous or oral acute sedation with benzodiazepines may be used. Untreated panic attacks can subside spontaneously within 20-30 minutes, especially with reassurance and a calming environment.
- ❏ If possible, avoid long-term benzodiazepines for chronic anxiety disorders, because chronic benzodiazepine use may be associated with tolerance, withdrawal and treatment-emergent anxiety.

B. Psychotherapy

Psychotherapy helps people with a mental disorder:

- ❏ Understand the behaviors, emotions and ideas that contribute to his or her illness.
- ❏ Understand and identify the life problems or events -- like a major illness, a death in the family, a loss of a job or a divorce -- that contribute to their illness and help them understand which aspects of those problems they may be able to solve or improve.
- ❏ Regain a sense of control and pleasure in life.
- ❏ Learn coping techniques and problem-solving skills.

Types of Therapy

Therapy can be given in a variety of formats, including:

- ❏ Individual: This therapy involves only the patient and the therapist.
- ❏ Group: Two or more patients may participate in therapy at the same time. Patients are able to share experiences and learn that others feel the same way and have had the same experiences.
- ❏ Marital/couples: This type of therapy helps spouses and partners understand why their loved one has a mental disorder, what changes in communication and behaviors can help and what they can do to cope.
- ❏ Family: Because family is a key part of the team that helps people with mental illness get better, it is sometimes helpful for family members to understand what their loved one is going through, how they themselves can cope and what they can do to help.

C. Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (CBT) is very useful in treating anxiety disorders. The cognitive part helps people change the thinking patterns that support their fears and the behavioral part helps people change the way they react to anxiety-provoking situations.

For example, CBT can help people with panic disorder learn that their panic attacks are not really heart attacks and help people with social phobia learn how to overcome the belief that others are always watching and judging them. When people are ready to confront their fears, they are shown how to use exposure techniques to desensitize themselves to situations that trigger their anxieties.

People with OCD who fear dirt and germs are encouraged to get their hands dirty and wait increasing amounts of time before washing them. The therapist helps the person cope with the anxiety that waiting produces; after the exercise has been repeated a number of times, the anxiety diminishes. People with social phobia may be encouraged to spend time in feared social situations without giving in to the temptation to flee and to make small social blunders and observe how people respond to them. Since the response is usually far less harsh than the person fears, these anxieties are lessened. People with PTSD may be supported through recalling their traumatic event in a safe situation, which helps reduce the fear it produces. CBT therapists also teach deep breathing and other types of exercises to relieve anxiety and encourage relaxation.

Exposure-based behavioral therapy has been used for many years to treat specific phobias. The person gradually encounters the object or situation that is feared, perhaps at first only through pictures or tapes then later face-to-face. Often the therapist will accompany the person to a feared situation to provide support and guidance.

CBT is undertaken when people decide they are ready for it and with their permission and co-operation. To be effective, the therapy must be directed at the person's specific anxieties and must be tailored to his or her needs. There are no side effects other than the discomfort of temporarily increased anxiety.

CBT or behavioral therapy often lasts about 12 weeks. It may be conducted individually or with a group of people who have similar problems. Group therapy is particularly effective for social phobia. Often "homework" is assigned for participants to complete between sessions. There is some evidence that the benefits of CBT last longer than those of medication for people with panic disorder and the same may be true for OCD, PTSD and social phobia. If a disorder recurs at a later date, the same therapy can be used to treat it successfully a second time.

Medication can be combined with psychotherapy for specific anxiety disorders and this is the best treatment approach for many people

D. Diet

- ❏ Discontinue (or decrease to a low reasonable level) caffeine-containing products such as coffee, tea, colas.
- ❏ Over-the-counter preparations and herbal remedies should be reviewed with special caution because ephedrine and other herbal compounds may precipitate or exacerbate anxiety symptoms.

E. Activity

- ❏ If no medical contraindication exists, at least a mild-to-moderate daily exercise program is recommended.

Complications

- ❏ Agoraphobia
- ❏ Major depression
- ❏ Suicide
- ❏ Homicide (especially in patients with PTSD)
- ❏ Alcohol abuse and dependence
- ❏ Sedative abuse and dependence
- ❏ Social dysfunction and withdrawal
- ❏ Occupational impairment
- ❏ Marital and familiar dysfunction, divorce

Prognosis

- ❏ Anxiety disorders can range from mild and transient to severe and chronic.
- ❏ Early treatment improves prognosis and limits social and occupational impairment.

Prevention

Prevention of anxiety essentially involves an awareness of life's stresses and the ability to cope with them. This can often be a difficult task in our busy and hectic 21st century.

- ❏ In essence, someone might develop coping mechanisms for all of life's stresses. Strategies might include these:
  - Physical well-being through exercise, healthy eating habits, and adequate rest
  - Avoiding the use of caffeine, illicit drugs, or the inappropriate use of stimulants or other prescription medications
  - Meditation
  - Relaxation exercises including deep breathing
  - Visualization
  - Interpersonal skills in dealing with difficult people and situations or parenting skills training in dealing with the children

Home Care

Family members should receive information about the effect of anxiety disorders on mood, behavior and relationships. Family members can assist in care by reinforcing the need for medical treatment and supervision. They may also assist by providing a collaborative resource for monitoring the severity of the patient's anxiety symptoms and response to treatment interventions.

References

eMedicine
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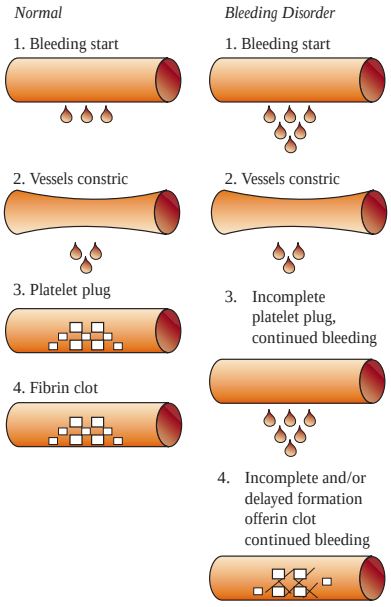
MedlinePlus
The National Institute of Mental Health (NIMH), USA

Bleeding Disorder

Bleeding disorder is a general term for a wide range of medical problems that lead to poor blood clotting and continuous bleeding. They are also known as coagulopathy, abnormal bleeding and clotting disorders. When someone has a bleeding disorder they have a tendency to bleed longer. The disorders can result from defects in the blood vessels or from abnormalities in the blood itself. The abnormalities may be in blood clotting factors or in platelets.

Blood clotting or coagulation, is the process that controls bleeding. It changes blood from a liquid to a solid. It's a complex process involving as many as 20 different plasma proteins, or blood clotting factors. Normally, a complex chemical process occurs using these clotting factors to form a substance called fibrin that stops bleeding. When certain coagulation factors are deficient or missing, the process doesn't occur normally.

CLOTTING **ILLUSTRATION**



Within seconds of an injury, the blood platelets, bunch together around the wound. Blood proteins, platelets, calcium and other tissue factors react together and form a clot, which acts like a net over the wound. Over the next several days to weeks, the clot strengthens, then dissolves when the wound is healed.

In people with bleeding disorders, clotting factors are missing or don't work as they should. This causes them to bleed for a longer time than those whose blood factor levels are normal. It's a myth that persons with bleeding disorders bleed to death from minor injuries or their blood flows faster. Bleeding problems can range from mild to severe.

SYMPTOMS INCLUDE:

- ❏ Excessive bleeding
- ❏ Excessive bruising
- ❏ Bleeding into joints
- ❏ Easy bleeding
- ❏ Nose bleeds
- ❏ Abnormal menstrual bleeding

BLEEDING DISORDER RISKS INCLUDE:

- ❏ Scarring of the joints or joint disease
- ❏ Vision loss from bleeding into the eye
- ❏ Chronic anemia from blood loss
- ❏ Neurologic or psychiatric problems
- ❏ Death, which may occur with large amounts of blood loss or bleeding in critical areas, such as the brain.

CAUSES

Some bleeding disorders are present at birth and are caused by rare inherited disorders. Others are developed during certain illnesses (such as vitamin K deficiency, severe liver disease), or treatments (such as use of anticoagulant drugs or prolonged use of antibiotics). They can include hemophilia and other very rare blood disorders. There are many causes of bleeding disorders, including:

- ❏ von Willebrand's disease , which is an inherited blood disorder thought to affect between 1% and 2% of the population
- ❏ Immune system-related diseases, such as allergic reactions to medications or reactions to an infection
- ❏ Cancer, such as leukemia
- ❏ Liver disease
- ❏ Bone marrow problems
- ❏ Disseminated intravascular coagulation, which is a condition often associated with child bearing, cancer or infection in which the body's clotting system functions abnormally
- ❏ Pregnancy-associated eclampsia.
- ❏ Antibodies, a type of immune system protein that destroy blood clotting factors
- ❏ Medicines such as aspirin, heparin, warfarin and drugs used to break up blood clots

History of Bleeding Disorders

EARLY HISTORY

References to excessive and unexplained bleeding have been made since antiquity. In the Talmud, a collection of Jewish Rabbinical writings from the 2nd century AD, it was written that male babies did not have to be circumcised if two brothers had already died from the procedure. In the 12th century AD, an Arabian physician from Cordoba named Albucasis wrote of males in a particular village, who had died of uncontrollable bleeding. Occasional references to bleeding can be found in the scientific literature of following centuries.

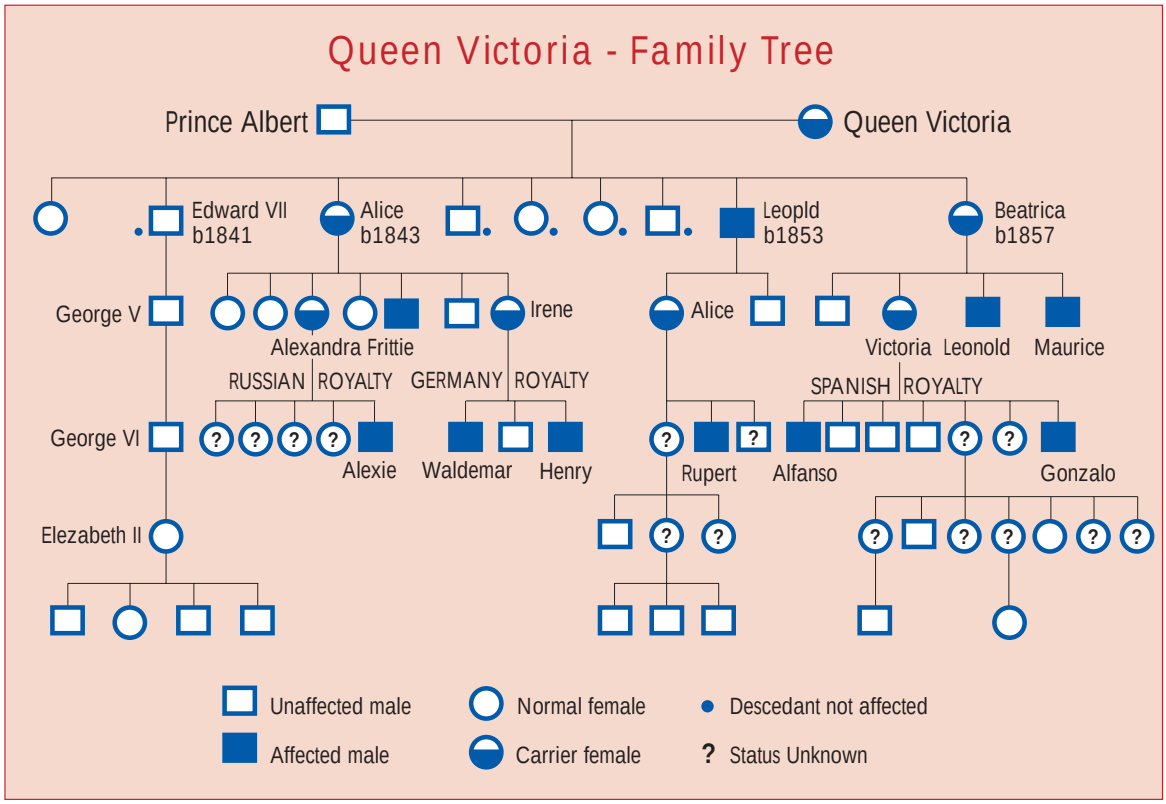
In the U.S., the transmission of hemophilia from mothers to sons was first described in the early 19th century. In 1803, the Philadelphia physician Dr. John Conrad Otto wrote an account of "a hemorrhagic disposition existing in certain families." He recognized that a particular bleeding condition was hereditary and predominately affected males. He traced the disease back through three generations to a woman who had settled near Plymouth, New Hampshire in 1720. The word "hemophilia" first appeared in a description of a bleeding disorder condition at the University of Zurich in 1828.

A ROYAL DISEASE

Hemophilia has often been called the "Royal Disease." Queen Victoria of England (1837-1901) was a carrier of the hemophilia gene and subsequently passed the disease on to several royal families. Victoria's eighth child Leopold had hemophilia and suffered from frequent hemorrhages, which were reported in the British Medical Journal in 1868. Leopold died at the age of 31 of a brain hemorrhage. Leopold's daughter Alice was a carrier and her son, Viscount Trematon was born with hemophilia. Viscount died in 1928, of a brain hemorrhage similar to the one that killed his grandfather.

FINDING THE CAUSE

In the 20th century researchers looked for the cause of excessive bleeding. Until then, they had believed that the blood vessels of people with hemophilia were simply more fragile.



1920s

Von Willebrand disease, the most common hereditary bleeding disorder was first recognized by the Finnish physician Erik von Willebrand in 1925. He published his first paper on the disease in 1926. In it, he presented the pedigree of a Scandinavian family from the island of Aland, reporting bleeding symptoms in 23 of 66 family members.

1930s

Previously it was thought that defective platelets were the likely cause of bleeding disorders. But in 1937, doctors at Harvard University found they could correct the clotting problem by adding platelet-free plasma. They called the substance "anti-hemophilic globulin."

1940s

In 1944 Dr. Pavlosky from Buenos Aires, Argentina, did a lab test which showed that blood from a person with hemophilia could correct the clotting problem in a second person with hemophilia and vice-versa. He had stumbled upon two

patients, each with a deficiency in different proteins - Factor VIII and Factor IX. This led to the eventual recognition of hemophilia A and hemophilia B as two distinct diseases. By the end of the decade people with hemophilia had a life expectancy of less than 30 years. Treatment was limited to icing joints where internal bleeding occurred and painful transfusions of whole blood.

1950s & 1960s

In the 1950s and early 1960s, hemophilia and other bleeding problems were still being treated with whole blood or fresh plasma. Unfortunately, there were not enough factor VIII or IX proteins in these treatments to stop serious internal bleeding. Many people with severe hemophilia and some people with mild or moderate forms, died in childhood or early adulthood. The most common causes of death were bleeding in vital organs especially the brain and excessive bleeding after minor surgery or trauma. By the mid-1960s the clotting factors were identified and named. An article in Nature in 1964 described the clotting process in detail. The interaction of the different factors in blood clotting was termed the "coagulation cascade." By the 1970s, freeze-dried powdered concentrates containing factor VIII and IX became available.

1990s TO PRESENT

Treatment for hemophilia and other bleeding disorders advanced in the 1990s. The safety and efficacy of factor concentrates improved. Factor products became safer as tighter screening methods were implemented and advanced modes of viral inactivation were utilized. In addition, synthetic (not derived from plasma) factor products were manufactured using recombinant technologies. In 1992, the first recombinant factor VIII product was approved by the Food and Drug Administration (FDA). In 1997, the first factor IX product was granted FDA approval. Additional synthetic drugs such as desmopressin acetate (DDAVP) were also introduced to treat mild-to-moderate hemophilia A and von Willebrand disease. By the mid 1990s prophylactic (a preventative treatment regimen) therapy in children with hemophilia became more common.

Hemophilia A (Factor VIII Deficiency)

Hemophilia A

Hemophilia A is the most common type of hemophilia. It is also known as factor VIII deficiency or classic hemophilia. It is largely an inherited disorder in which one of the proteins needed to form blood clots is missing or reduced. In about 30% of cases, there is no family history of the disorder and the condition is the result of a spontaneous gene mutation. Approximately one in 5000 males born in the United States has hemophilia. All races and economic groups are affected equally.

Genetics

The factor VIII gene is located on the X chromosome and consists of 26 exons; many different defects in the gene have been identified, ranging from single-base changes to deletions and inversions. Major disruption of the gene, e.g' a large deletion, results in severe haemophilia whereas a single base change will only cause a partial loss of function, with moderate or mild disease. As the factor VIII gene is on the X chromosome, haemophilia A is a sex-linked disorder. Thus all daughters of haemophiliacs are obligate carriers and sisters have a 50% chance of being a carrier. If a carrier has a son, he has a 50% chance of having haemophilia, and a daughter has a 50% chance of being a carrier. Haemophilia `breeds true' within a family. All members will have the same abnormality of the factor VIII gene; thus if one individual has severe haemophilia, so will all others affected. Female carriers of haemophilia may have reduced factor VIII levels because of random inactivation of the X chromosome in the developing fetus (lyonisation). A reduced factor VIII level in a carrier will result in a mild bleeding disorder; thus all known or suspected carriers of haemophilia should have their factor VIII level measured. The use of molecular genetic techniques has revolutionised the ability to identify carriers and make an antenatal diagnosis of haemophilia. If the factor VIII mutation causing the haemophilia in a particular family is known, antenatal diagnosis can be undertaken in a female who has a high probability of being a carrier. This is accomplished by chorionic villous sampling, usually around 11 weeks' gestation, sexing the fetus and using informative factor VIII probes.

When a person with hemophilia is injured, he does not bleed harder or faster than a person without hemophilia, he bleeds longer. Small cuts or surface bruises are usually not a problem, but more traumatic injuries may result in serious problems and potential disability (called "bleeding episodes").

There are different levels of hemophilia: mild, moderate, and severe :

- People with mild hemophilia (6% to 49% factor level) usually have problems with bleeding only after serious injury, trauma, or surgery. In many cases, mild hemophilia is not discovered until an injury or surgery or tooth extraction results in unusual bleeding. The first episode may not occur until adulthood.
- People with moderate hemophilia, about 15% of the hemophilia population, tend to have bleeding episodes after injuries. They may also experience occasional bleeding episodes without obvious cause. These are called "spontaneous bleeding episodes."
- People with severe hemophilia, about 60% of the hemophilia population, have bleeding following an

injury and may have frequent spontaneous bleeding episodes, often into the joints and muscles.

Everyone inherits two sex chromosomes, X and Y, from his or her parents. A female inherits one X chromosome from her mother and one X chromosome from her father (XX). A male inherits one X chromosome from his mother and one Y chromosome from his father (XY). The gene that causes hemophilia is located on the X chromosome.

A woman who gives birth to a child with hemophilia often has other male relatives who also have hemophilia. Sometimes, a baby will be born with hemophilia when there is no known family history. This means either that the gene has been "hidden" (that is, passed down through several generations of female carriers without affecting any male members of the family) or the change in the X chromosome is new (a "spontaneous mutation").

There are four possible outcomes for the baby of a woman who is a carrier. These four possibilities are repeated for each and every pregnancy :

1. A girl who is not a carrier
2. A girl who is a carrier
3. A boy without hemophilia
4. A boy with hemophilia

With each pregnancy, a woman who is a carrier has a 25% chance of having a son with hemophilia. Since the father's X chromosome determines the baby will be a girl, all the daughters of a man with hemophilia will be carriers. None of his sons, which is determined by the father through his Y chromosome, will have hemophilia.

Hemophilia B (Factor IX Deficiency)

Hemophilia B

Hemophilia B is the second most common type of hemophilia. It can also be known as factor IX deficiency, or Christmas disease. It was originally named "Christmas disease" for the first person diagnosed with the disorder back in 1952. It is largely an inherited disorder in which one of the proteins needed to form blood clots is missing or reduced. In about 30% of cases, there is no family history of the disorder and the condition is the result of a spontaneous gene mutation.

Hemophilia B is far less common than Hemophilia A. Occurring in about one in 25000 male births, hemophilia B affects about 3300 individuals in the United States. All races and economic groups are affected equally.

Diagnosis of Hemophilia

Accurate diagnosis is important and essential for effective management. Hemophilia should be suspected in patients presenting with a history of :

- Easy bruising in early childhood
- Spontaneous bleeding (particularly into the joints and soft tissue) and
- Excessive bleeding following trauma or surgery.

While the history of bleeding is usually lifelong, some severe hemophilic children may not have bleeding symptoms until after the age of one or later when they begin walking and exploring their world. Patients with mild hemophilia may not have excessive bleeding unless they experience trauma or surgery.

- A family history of bleeding is commonly obtained. Hemophilia generally affects males on the maternal side. However, both FVIII and FIX genes are prone to new mutations and as many as 1/3 of all patients may not have a family history of these disorders.
- Screening tests will show a prolonged activated partial thromboplastin time (aPTT) in severe and moderate cases but may not show prolongation in mild hemophilia. A definitive diagnosis depends on factor assay to demonstrate deficiency of FVIII or FIX.
- The severity of bleeding manifestations in hemophilia is generally correlated with the clotting factor level as shown in the following table.

Severity	Clotting factor level % activity (IU/ml)	Bleeding episodes
Severe	1% (< 0.01)	Spontaneous bleeding, predominantly in joints and muscles
Moderate	1% - 5% (0.01 – 0.05)	Occasional spontaneous bleeding. Severe bleeding with trauma, surgery
Mild	5% - 40% (0.05 – 0.40)	Severe bleeding with major trauma or surgery

Bleeding Manifestations in Hemophilia

Sites of bleeding

Serious	**Life - threatening**
Joints (Hemarthrosis)	Central nervous system (CNS)
Muscle/soft tissue	Gastrointestinal (GI)
Mouth/gums/nose	Neck/throat
Hematuria	Severe trauma

Incidence of different sites of bleeding

Hemarthrosis : 70%-80%
Muscle/soft tissue : 10%-20%
Other major bleeds : 5%-10%
Central nervous syatem (CNS) bleeds : < 5%

Incidence of bleeding into different joints

Knee: 45%
Elbow: 30%
Ankle: 15%

Shoulder: 3%
Wrist: 3%
Hip: 2%
Other: 2%

Management of Hemophilia

Principles of care

The general principles of care for hemophilia management include the following:

- ❏ Prevention of bleeding should be the goal.
- ❏ Acute bleeds should be treated early (within two hours, if possible).
- ❏ Home therapy should be used to manage only uncomplicated mild/moderate bleeding episodes.
- ❏ All severe bleeds should be managed in the clinic or hospital setting.
- ❏ Clotting factor concentrate replacement or DDAVP should be given to achieve appropriate factor levels prior to any invasive procedures.
- ❏ As much as possible, patients should avoid trauma by adjusting their lifestyle.
- ❏ Patients should be advised to avoid use of drugs that affect platelet function, particularly acetylsalicyclic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs) except certain COX-2 inhibitors. The use of paracetamol/acetaminophen is a safe alternative for analgesia.
- ❏ Intramuscular injections, difficult phlebotomy and arterial punctures must be avoided.
- ❏ Regular exercise should be encouraged to promote strong muscles, protect joints and improve fitness.
- ❏ Contact sports should be avoided but swimming and cycling with appropriate gear should be encouraged.

Management of bleeding

- ❏ During an episode of acute bleeding an assessment should be performed to identify the site of bleeding and treatment should be given early.
- ❏ Patients usually recognize early signs of bleeding even before manifestation of physical signs – they often experience a tingling sensation or "aura". Treatment at this stage will stop bleeding early, resulting in less tissue damage and the use of less clotting factor concentrates.
- ❏ All patients should carry easily accessible identification indicating the diagnosis, severity, inhibitor status, type of product used and contact information of the treating physician/clinic. This will facilitate management in an emergency and prevent unnecessary investigations before treatment.
- ❏ In severe bleeding episodes especially in the head, neck, chest and gastrointestinal and abdominal regions that are potentially life-threatening, treatment should be initiated immediately, even before assessment is completed.
- ❏ If bleeding does not resolve despite adequate treatment, clotting factor level should be monitored and inhibitors should be checked if the level is unexpectedly low.
- ❏ Administration of desmopressin (DDAVP) can raise FVIII level sufficiently high (2-8 times baseline levels) in patients with mild to moderate hemophilia A.

Adjunctive management

The following treatment strategies are important, particularly where clotting factor concentrates are limited or not available and may lessen the amount of treatment products required.

- ❏ RICE (rest, ice, compression, and elevation) is an important adjunctive management for bleeding in muscles and joints in addition to increasing factor level with clotting factor concentrates or desmopressin in mild hemophilia A. Bleeding muscles and joints can be kept at rest by splinting, casting or using crutches or a wheelchair. Application of cold/ice packs is useful to decrease inflammation but ice should be wrapped in a towel and not be applied directly to the skin. It is recommended that ice be applied for 20 minutes, every four to six hours until swelling and pain decrease.
- ❏ Antifibrinolytic drugs (e.g., tranexamic acid, epsilon amino caproic acid) for 5-10 days is effective as adjunctive treatment for mucosal bleeds (e.g., epistaxis, mouth bleed) and is used to decrease the use of coagulation products in dental extractions. These drugs should be avoided in renal bleeding as unlysed clots in the renal pelvis and ureter can behave like stones resulting in ureteric colic and obstructive nephropathy. Antifibrinolytic drugs should not be given concurrently with non-activated or activated prothrombin complex concentrates because of potential thrombotic complications.
- ❏ Certain COX-2 inhibitors may be used judiciously for joint inflammation after an acute bleed and in chronic arthritis.

Home therapy

Home therapy allows immediate access to treatment and hence optimal early treatment. This is ideally achieved with clotting factor concentrates or other lyophilized products that are safe and can be stored in a domestic fridge and reconstituted easily. However, home therapy is possible (though may be difficult) even with cryoprecipitate, provided the patients have a simple but reliable storage freezer at home – but concentrates should not be frozen.

- ❏ Home treatment must be supervised closely by the comprehensive care centre and be started after adequate education and preparative teaching. A certification program can be instituted and the technique monitored at comprehensive visits.

- Teaching should include recognizing a bleed and its common complications, dosage calculation, preparation, storage and administration of clotting factor, aseptic techniques, performing venipuncture (or access of central venous catheter), record keeping as well as proper storage and disposal of needles and handling of blood spills.
- Encouragement, support and supervision are key to successful home therapy and periodic reassessment of educational needs, techniques and compliance must be performed. A periodic re-certification program can be instituted.
- Patients or parents should keep bleeding records that include date and site of bleeding, dosage and lot numbers of product used as well as any adverse effects.
- Home care can be started on young children with adequate venous access and motivated family members who have undergone adequate training. Older children and teenagers can learn self-infusion with family support.

Prophylaxis

Prophylaxis is the administration of clotting factors at regular intervals to prevent bleeding and must be the goal of all hemophilia care programs until a cure is available.

- The practice of primary prophylaxis was conceived from the observation that moderate hemophilia patients with clotting factor level > 1% seldom have spontaneous bleeding and have much better preservation of joint function. Prophylactic replacement of clotting factor has been shown to be useful even when factor levels are not maintained above 1% at all times.
- In patients with repeated bleeding particularly into specific joints (target joints), short-term secondary prophylaxis for 4-8 weeks can be used to interrupt the bleeding cycle. This may be combined with intensive physiotherapy or synoviorthesis.
- Prophylactic administration of clotting factor concentrates is advisable prior to engaging in activities with higher risk of injury to prevent bleeding.
- Currently the most commonly suggested protocol for prophylaxis is the infusion of 25-40 IU/kg of clotting factor concentrates three times a week for those with hemophilia A and twice a week for those with hemophilia B. However, it should be recognized that many different protocols are followed for prophylaxis even within the same country and the optimal regimen remains to be defined. Different clotting factor replacement protocols for prophylaxis are currently being evaluated.
- Such a regimen in younger children often (but not always) requires the insertion of a venous access device that must be kept scrupulously clean to avoid infectious complications and be adequately flushed after each administration to prevent clots developing in the line. The risks and morbidity associated with such devices should be weighed against the advantages of starting prophylaxis early.

Surgery

The following issues are of prime importance when performing elective surgery on persons with hemophilia:

- Surgical procedures should be performed in co-ordination with a team experienced in the management of hemophilia.
- Procedures should take place in a centre with adequate laboratory support for reliable monitoring of clotting factor level.
- Pre-operative assessment should include inhibitor screening.a
- Availability of sufficient quantities of clotting factor concentrates should be ensured before undertaking major surgery for hemophilia.
- The dosage and duration of clotting factor concentrate coverage depends on the type of surgery performed.

Future Therapies

Experimental methods are currently being investigated as possible breakthroughs for curing bleeding disorders.

Researchers are working on a method to insert better functioning factor VIII or factor IX genes into the cells of people with hemophilia so their blood will clot more effectively. It is hoped that gene therapy will lead to patients having fewer bleeding episodes. Gene therapy might eventually help people with hemophilia begin producing their own clotting factor thereby removing or at least lessening their dependence on weekly infusions. With this advance, there exists the potential for someone born with severe hemophilia to eventually have significantly milder symptoms.

Several new technologies are also being implemented to advance hemophilia treatment. These new technologies, once used to destroy viruses in blood have been successful in virtually eliminating the risk of contracting HIV or hepatitis C from clotting factor today. New products have consistently been developed which have an even higher purity than have ever been available before.

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National Hemophilla Foundation USA

Guideline for the Management of Hemophilla

MedlinePlus

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Lactose Intolerance

Minorities who have experienced gastrointestinal problems consuming milk are learning new strategies to enjoy milk and other dairy foods. This means that minorities (and non-minorities) with lactose intolerance no longer need to miss out on essential nutrients provided by dairy foods.

Lactose intolerance is the inability to metabolize lactose, a sugar found in milk and other dairy products, because the required enzyme lactase is absent or its availability is lowered. It is estimated that 70% of adult humans are lactose intolerant.

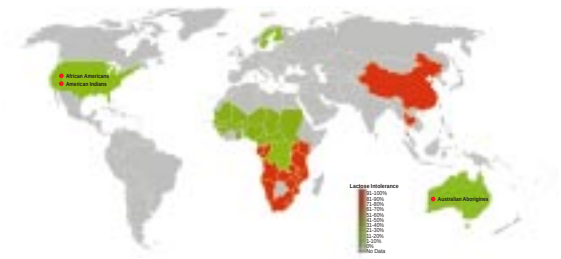
Classification

There are three major types of lactose intolerance :

1. **Primary lactose intolerance**. Environmentally induced when weaning a child in non dairy consuming societies. This is found in many Asian and African cultures, where industrialized and commercial dairy products are uncommon.
2. **Secondary lactose intolerance.** Environmentally induced, resulting from certain gastrointestinal diseases including exposure to intestinal parasites such as giardia. In such cases the production of lactase may be permanently disrupted. A very common cause of **temporary** lactose intolerance is gastroenteritis, particularly when the gastroenteritis is caused by rotavirus. Another form of temporary lactose intolerance is lactose overload in infants.
3. **Congenital lactase deficiency.** A genetic disorder which prevents enzymatic production of lactase. Present at birth and diagnosed in early infancy.

Prevalence

Between 30 and 50 million Americans are lactose intolerant and certain ethnic and racial populations are more affected than others. Up to 80 percent of African Americans, 80 to 100 percent of American Indians and 90 to 100 percent of Asian Americans are lactose intolerant. The condition is least common among people of northern European descent. Babies that are born prematurely are also more likely to be lactose intolerant because lactase levels do not increase until the third trimester of a woman's pregnancy.



Lactose Intolerance by Region (African countries are only a rough guess)

Lactose intolerance levels also increase with age. At ages 2-3 yrs., 6 yrs. and 9 - 10 yrs., the amount of lactose intolerance is, respectively :

- 6% to 15% in white Americans and northern Europeans
- 18%, 30% and 47% in Mexican Americans
- 25%, 45% and 60% in black South Africans
- approximately 30%, 80% and 85% in Chinese and Japanese
- 30–55%, 90% and >90% in Mestizos of Peru

Chinese and Japanese populations typically lose between 80 and 90 percent of their ability to digest lactose within three to four years of weaning. Most Japanese can consume 200 ml (8 fl oz) of milk without severe symptoms.

Symptoms

Symptoms begin about 30 minutes to 2 hours after eating or drinking foods containing lactose. The severity of symptoms depends on many factors including the amount of lactose a person can tolerate and a person's age, ethnicity and digestion rate.

Common symptoms include-

Stomach cramps, Nausea,
Bloating, Flatulence
Diarrhea etc.

As with other unabsorbed sugars (mannitol) the lactose raises the osmotic pressure of the colon contents, preventing the colon from reabsorbing water, thereby adding a laxative effect to the excessive gas production.

Diagnosis

When considering the need for confirmation, it is important to distinguish lactose intolerance from milk allergy, which is an abnormal immune response (usually) to milk proteins. However, if confirmation is necessary, three tests are available :

1. Hydrogen breath test

In a hydrogen breath test, after an overnight fast, 50 grams of lactose (in a solution with water) are swallowed. If the lactose cannot be digested, enteric bacteria metabolize it and produce hydrogen. This can be detected in the air the patient exhales. The test takes about 2 to 3 hours. A medical condition with similar symptoms is fructose malabsorption.

In conjunction, measuring the blood glucose level every 10 - 15 minutes after ingestion will show a "flat curve" in individuals with lactose malabsorption, while the lactase persistent will have a significant "top", with an elevation of typically 50 to 100% within 1 - 2 hours.

2. Stool acidity

Required for a clinical diagnosis.

3. Intestinal biopsy

An intestinal biopsy can confirm lactose intolerance following discovery of elevated hydrogen in the hydrogen breath test.

Treatment

No treatment can improve the body's ability to produce lactase, but symptoms can be controlled through diet.

Lactose Intolerance

There are 4 general principles for control of lactose intolerance : 1) Avoidance of dietary lactose, 2) Substitution to maintain nutrient intake, 3) Regulation of calcium intake, 4) Use of enzyme substitute.

1. Avoiding lactose-containing products

Since each individual's tolerance to lactose varies, according to the US National Institute of Health, "Dietary" control of lactose intolerance depends on people learning through trial and error how much lactose they can handle.

Lactose is present in 2 large food categories : Conventional dairy products and as a food additive (in dairy and non dairy products).

Dairy products-

Dairy products which are "fat reduced" or "fat free" generally have a slightly higher lactose percentage.

Milk **:** Human milk has the highest lactose percentage at around 9%. Unprocessed cow milk has 4.7% lactose. Unprocessed milk from other mammals contains similar lactose percentages (goat milk 4.1%, buffalo 4.86%, yak 4.93%, sheep milk 4.6%)

Butter **:** The butter making process by definition separates milk's water components from the fat components. Lactose, being a water soluble molecule, will not be present in the butter unless milk solids are added to the ingredients.

Yogurt : People can be more tolerant of traditionally made yogurt than milk.

Cheeses **:** Traditionally made hard cheese (such as Swiss cheese) and soft ripened cheeses may create less reaction than the equivalent amount of milk.

Buttermilk, sour cream and **icecream,** like yogurt, if made the traditional way, will generally be quite tolerable, but most modern brands add milk solids.

Examples of lactose levels in foods. Lactose labeling varies on practices, geography and manufacturing processes, lactose numbers may not be very reliable. The following are examples of lactose levels in foods which commonly set off symptoms. These quantities are to be treated as guidelines only.

Dairy product	Lactose Content
Yogurt, plain, low-fat, 240 mL	5 g
Milk, reduced fat, 240 mL	11 g
Swiss cheese, 28 g	1 g
Icecream, 120 mL	6 g
Cottage cheese, 120 mL	2–3 g

Lactose in non-dairy products

Lactose is a commercial food additive used for its texture, flavor and adhesive qualities and is found in foods such as processed meats (sausages/hot dogs, sliced meats), margarines, sliced breads, breakfast cereals, dried fruit, processed foods, medications, preprepared meals, meal replacement (powders and bars), protein supplements (powders and bars).

Alternative products

Lactose-free milk can be produced by passing milk over lactase enzyme bound to an inert carrier: once the molecule is cleaved, there are no lactose ill-effects. Finland has had Icecream, butter, and buttermilk that contain no lactose at all.

Plant based milks and derivatives are the only ones to be 100% lactose free (soy milk, almond milk, oat milk, rice milk, peanut milk).

2. Nutritional concerns

Primary lactose intolerance

where lactase enzyme activity can fall gradually after weaning in normal, otherwise healthy people. It is by far the most common form of lactose intolerance. It is unlikely to be a problem until after 5 to 7 years of age.

Treatment of Primary lactose intolerance :

Approximately 70% of patients with primary lactose intolerance will respond to a lactose-restricted diet. The remaining 30% are believed to have an underlying irritable bowel syndrome. Primary lactose intolerance can be controlled with strict adherence to a lactose-free or lactose-reduced diet.

Secondary lactose intolerance

Dairy products are relatively good and accessible sources of calcium and potassium and many countries mandate that milk be fortified with vitamin A and vitamin D. Plant based milk substitutes are not naturally rich in calcium, potassium or vitamins A or D (and, like

Lactose Intolerance

all non-animal products, contain no vitamin B12). However, prominent brands are often voluntarily fortified with many of these nutrients, although one should read the label to be certain.

An increasing number of calcium-fortified breakfast foods, such as orange juice, bread and dry cereal, have been appearing on supermarket shelves. Many fruits and vegetables are rich in potassium and vitamin A, animal products like meat and eggs are rich in vitamin B12 and the human body itself produces some vitamin D from exposure to direct sunlight. Finally, a dietitian or physician may recommend a vitamin or mineral supplement to make up for any remaining nutritional shortfall.

Treatment of Secondary lactose intolerance :

Secondary lactose intolerance is generally a self-limiting condition that resolves with treatment of the primary disorder. Patients should be advised to limit consumption of dairy products until the primary disorder is resolved. By eliminating milk products, many

patients require calcium supplementation to prevent the effects of osteoporosis. This supplementation can be accomplished using calcium carbonate.

Congenital lactase deficiency

Congenital lactase deficiency or CLD, is an autosomal recessive disorder which prevents the expression of lactase. Before the 20th century, infants with this disease rarely survived. As substitute and lactose-free infant formulas later became available, nursing infants affected with CLD could now have their normal nutritional needs met. Beyond infancy, individuals with CLD usually have the same nutritional concerns as those affected by secondary lactose intolerance.

3. Regulation of calcium intake :

How much calcium a person needs to maintain good health varies by age group. Recommendations from the report are shown in the following table.

Calcium and Lactose in Common Foods

Vegetables	Calcium Content	Lactose Content
Soymilk, fortified, 1 cup	200-300 mg	0
Sardine, with edible bones, 3 oz.	270 mg	0
Salmon, canned, with edible bones, 3 oz.	205 mg	0
Broccoli, raw, 1 cup	90 mg	0
Orange, 1 medium	50 mg	0
Pinto beans, 1/2 cup	40 mg	0
Tuna, canned, 3 oz.	10 mg	0
Lettuce greens, 1/2 cup	10 mg	0
Dairy Products	**Calcium Content**	**Lactose Content**
Yogurt, plain, low-fat, 1 cup	415 mg	5 g
Milk, reduced fat, 1 cup	295 mg	11g
Swiss cheese, 1 oz.	270 mg	1 g
Icecream, 1/2 cup	85 mg	6 g
Cottage chesse, 1/2 cup	75 mg	2-3 g

Adapted from *Manuel of chemical Dieurics* 6th ed. American Dietetic Association, 2000; and Soy Dairy Alternatives. Available at *www.soyfoods.org*.

4. Use of enzyme substitute :

When lactose avoidance is not possible or on occasions when a person chooses to consume such items, then enzymatic lactase supplements may be used.

Lactase enzymes similar to the those produced in the small intestines of humans are produced industrially by fungi of the genus aspergillus. The enzyme, galactosidase, is available in tablet form in a variety of doses, in many countries without a prescription. It functions well only in high-acid environments such as that found in the human gut due to the addition of gastric juices from the stomach. Unfortunately, too much acid can denature it, and it therefore should not be taken on an empty stomach.

Tips to Improve Tolerance to Dairy Foods

- **To adjust the amount of lactose consumed.** Individuals differ according to how much lactose they can tolerate at any one time. To determine how much lactose is well tolerated, individuals should consume a small amount of milk (less than 1 cup) with food and gradually increase the serving size until symptoms just begin to develop.
- **To drink milk with a meal or snack.** This slows gastric emptying and/or delivery of lactose to the colon, allowing more time for any remaining lactase enzyme to digest lactose. Also, when lactose is consumed with food, relatively little undigested lactose reaches the colon at any one time.
- **To choose wisely.** Some dairy foods are better tolerated than others.
- **To try lactose-free or lactose–reduced products.**

Training for tolerance. Gradually increasing intake of lactose-containing foods improves tolerance to lactose. Continued exposure to lactose may enhance the efficiency of colonic bacteria to metabolize lactose, thereby producing fewer intolerance symptoms.

Summary

Even though lactose intolerance is common, it is not a threat to good health. People who have trouble digesting lactose can learn which dairy products and other foods they can eat without discomfort and which ones they should avoid. Many people can enjoy milk, Icecream and other such products if they eat them in small amounts or eat other food at the same time. Others can use lactase liquid or tablets to help digest the lactose. Even older women at risk for osteoporosis and growing children who must avoid milk and foods made with milk can meet most of their dietary needs by eating greens, fish and other calcium-rich foods that are free of lactose. A carefully chosen diet, with calcium supplements if the doctor or dietitian recommends them, is the key to reducing symptoms.

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Test Yourself - 24

Correct Answers :

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

CONGRATULATIONS!

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Test Yourself - 25

1. **All the following are the major types of "anxiety disorders" except :**
   a. Panic disorder.
   b. Social phobia.
   c. Separation anxiety.
   d. Generalized anxiety disorder

2. **All the following are the causes of "bleeding disorder" except :**
   a. Leukemia.
   b. Medicines such as paracetamol, antibiotics.
   c. Liver disease.
   d. Pregnancy associated eclampsia.

3. **The below mentioned points are true for "lactose intolerance" except :**
   a. There are four major types of lactose intolerance.
   b. Lactose intolerance levels increase with age.
   c. Primary lactose intolerance is found in only African cultures.
   d. The symptoms begin about 30 minutes to 2 hours after eating or drinking food containing lactose.

4. **All the following points are true for "Fexo®"(Fexofenadine Hydrochloride) except :**
   a. It is rapidly absorbed after oral doses.
   b. It is indicated for seasonal allergic rhinitis, chronic idiopathic urticaria.
   c. In adult the recommended dose of "Fexo®" is 60 mg thrice daily or 120 mg once daily or 180mg once daily.
   d. Plasma concentration of "Fexo®" has been increased when given with erythromycin or ketoconazole, antacid containing aluminium.

5. **The following are correct regarding "anxiety disorders" except :**
   a. SSRIs commonly prescribed for panic disorders, OCD, PTSD and social phobias.
   b. MAOIs are the oldest class of antidepressant medications.
   c. Alprazolam is useful for both panic disorder and GAD.
   d. People taking MAOIs can eat all varieties of food.

6. **Hemophilia should be suspected in patient with a following history except:**
   a. Spontaneous bleeding particularly into the joints and soft tissues.
   b. Hematuria.
   c. Excessive bleeding following trauma and surgery.
   d. Easy bruising in early childhood.

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SQUARE Pharmaceuticals Ltd. the market leader of the Bangladesh Pharmaceutical Industry has recently gone into a strategic partnership with PC Pharma of Sri Lanka, a subsidiary of PCH Holding, the renowned corporate group having an integrated chain of well diversified businesses in Sri Lanka. Under this strategic partnership, PC Pharma which is the first of its kind in attaining the ISO 9001:2000 certification for pharmaceutical importation in Sri Lanka, would market a large range of Square's products.

Presently PC Pharma is marketing eleven products of Square and has registered another 35 for the Sri Lankan Market in its quest to having a wide range of Square products available for the best of quality-healthcare of the country in a reasonably short period of time.

The partnership ceremony was launched amid much enthusiasm and media attraction at the Hilton with having the Minister of Healthcare and Nutrition and current Chairman of the WHO Executive Board, Mr. Nimal Siripala

Officials of SQUARE Pharmaceuticals Ltd. Bangladesh and PC Pharma of Sri Lanka in the "partnership ceremony" at 'the Hilton', Sri Lanka.

Apart from the regularly demanded pharmaceutical products, this partnership would also see the launch of molecules in such therapeutic categories as antidiabetic, neuropsychiatry, antibiotics, cardiac, respiratory, dermatology and ear and eye preparations coupled with forming a partnership with Square Cephalosporins Ltd. enabling to serve with the latest generations of cephalosporin products including injectables for the Sri Lankan Market.

De Silva watching over as Chief Guest. The ceremony was then followed through by a spectacular musical entertainment program. Most of the leading doctors of the major cities of Sri Lanka along with the Director Medical Technology and Supply Dr. Dammika Jayalath, and Managing Director of the State Pharmaceutical Corporation (SPC) Professor K.U. Kamalgoda graced the occasion.

Product Profile-Fexo®

Fexo®

Composition

Fexo® 60 : Each film coated tablet contains Fexofenadine Hydrochloride INN 60 mg.

Fexo® 120 : Each film coated tablet contains Fexofenadine Hydrochloride INN 120 mg.

Fexo® 180 : Each film coated tablet contains Fexofenadine Hydrochloride INN 180 mg.

Pharmacology

Fexofenadine Hydrochloride is an antihistamine with selective peripheral H1-receptor antagonist activity. Fexofenadine is rapidly absorbed after oral doses with peak plasma concentrations being reached with in 2-3 hours post dose. It is about 60 % to 70 % bound to plasma proteins, primarily albumin and ?1-acid glycoprotein. About 5% of the total doses is metabolised, mostly by the intestinal mucosa, with only 0.5 to 1.5% of the dose undergoing hepatic biotransformation by the cyto-chrome P450 system. Elimination half-life of about 14 hours has been reported although this may be prolonged in patients with renal impairment. Excretion is mainly in the feces with only 10% being present in the urine. Fexofenadine does not appear to cross the blood-brain barrier.

Indications

Seasonal Allergic Rhinitis : **Fexo®** tablets are indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older.

Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

Chronic Idiopathic Urticaria : **Fexo®** tablets are indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older.

Fexofenadine Hydrochloride significantly reduces pruritus and the number of wheals.

Dosage & Administration

Seasonal Allergic Rhinitis and Chronic Idiopathic Urticaria:

Adults and Children 12 years and older : The recommended dose of **Fexo®** is 60 mg twice daily or 120 mg once daily or 180 mg once daily with water. A dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function.

Children 6 to 11 years : The recommended dose of **Fexo®** is 30 mg twice daily or 60 mg once daily with water. A dose of 30 mg once daily is recommended as the starting dose in pediatric patients with decreased renal function.

Doses in renal impairment

This drug is known to be substantially excreted by the kidney and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be useful to monitor renal function.

Initial doses of Fexofenadine Hydrochloride in patients with renal impairment should be reduced to 60 mg once daily.

Use in pregnancy & lactation

There are no adequate and well controlled studies in pregnant women. Fexofenadine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

It is not known if Fexofenadine is excreted in human milk. There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when Fexofenadine is administered to a nursing woman.

Drug Interaction

Plasma concentrations of Fexofenadine have been increased when given with Erythromycin or Ketoconazole. Antacid containing Aluminium

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