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the SQUARE Healthcare bulletin

Since 1993

- Ebolavirus
- Substance Abuse Disorder
- Otosclerosis
- Autism
- Colorectal Carcinoma

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the SQUARE
healthcare bulletin

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Editorial

Dear Doctor

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

A blend of interesting topics has been incorporated in this issue. We have highlighted the "Ebolavirus", a serious viral illness that originated in Africa, where there is currently an outbreak. The 2014 Ebola outbreak in West Africa is the largest in history. About 70% of the people who have gotten Ebola in this outbreak have died. A detailed article on "Substance Abuse Disorder" has been included here. Substance abuse disorders are among the most prevalent psychiatric disorders and are frequently co-morbid with other psychiatric and health conditions and accompanied by social problems; however, they remain under-recognized and under-treated. We bring all the details on "Otosclerosis", which is the primary disease affecting the homeostasis of otic capsule and is among the most common causes of acquired hearing loss. You will find a piece of writing on "Autism", the most common condition in a group of developmental disorders known as the autism spectrum disorders. Besides, we also focused on "Colorectal Carcinoma", the most common type of gastrointestinal cancer which is a multifactorial disease process, with etiology encompassing genetic factors, environmental exposures (including diet), and inflammatory conditions of the digestive tract.

We hope that you will find this edition both interesting and informative.

On behalf of the management of *SQUARE* we wish you all healthy, prosperous, safe and blissful lives !

Thank you !

Omar Akramur Rab

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Key title: The square (Dhaka)
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Ebolavirus

Ebolaviruses were first described after outbreaks of Ebolavirus disease (EVD), a type of hemorrhagic fever having a very high case fatality rate in southern Sudan in June 1976 and in Zaire in August 1976. The name Ebolavirus is derived from the Ebola River in Zaire (now the Democratic Republic of the Congo). This genus was introduced in 1998 as the "Ebolalike viruses". In 2002 the name was changed to Ebolavirus and in 2010, the genus was emended. The genus Ebolavirus is included in the family Filoviridae, order Mononegavirales. The members of this genus are called Ebolaviruses. The five known virus species are named for the region where each was originally identified. The five characterized members of the Ebolavirus genus are:

Ebola Virus (EBOV)

Formerly known as "Zaire virus" or "Zaire ebolavirus", has the highest case fatality rate. The first outbreak took place on 26 August 1976 in Yambuku. Mabalo Lokela, a 44-years old school-teacher, became the first recorded case.

Sudan Ebolavirus (SUDV)

Like EBOV, SUDV emerged in 1976 and it was at first assumed to be identical with EBOV. SUDV is believed to have broken out first amongst cotton factory workers in Nzara, Sudan (now in South Sudan), in June 1976, with the first case reported as a worker exposed to a potential natural reservoir.

Reston Ebolavirus (RESTV)

This virus was discovered during an outbreak of simian hemorrhagic fever virus (SHFV) in crab eating macaques from Hazleton Laboratories (now Covance) in 1989. Since the initial outbreak in Reston, Virginia, it has since been found in nonhuman primates in Pennsylvania, Texas, and Siena, Italy. In each case, the affected animals had been imported from a facility in the Philippines, where the virus has also infected pigs. Despite its status as a Level-4 organism and its apparent pathogenicity in monkeys, RESTV did not cause disease in exposed human laboratory workers.

Taï Forest Ebolavirus (TAFV)

Formerly known as as "Côte d'Ivoire ebolavirus", it was first discovered among chimpanzees from the Taï Forest in Côte d'Ivoire, Africa, in 1994.

Bundibugyo Ebolavirus (BDBV)

On November 24, 2007, the Uganda Ministry of Health confirmed an outbreak of Ebola in the Bundibugyo District. After confirmation of samples tested by the United States National Reference Laboratories and the CDC, the World Health Organization confirmed the presence of the new species.

Each species of the genus Ebolavirus has one member virus, and four of these cause Ebolavirus disease (EVD) in humans; the fifth, Reston virus, has caused EVD in other primates. Zaire ebolavirus is the type species (reference or example species) for the genus Ebolavirus, which has the highest mortality rate and is also responsible for the largest number of outbreaks among the the five known members of the genus, including the recent outbreak with the most deaths (7000 death in the year 2014 according to WHO). This discussion regards mainly to this specific virus.

Structure

EBOV carries a negative-sense RNA genome in virions that are cylindrical/tubular, and contain viral envelope, matrix, and nucleocapsid components. The overall cylinders are generally approximately 80 nm in diameter, and have a virally encoded glycoprotein (GP) projecting as 7-10 nm long spikes from its lipid bilayer surface. The cylinders are of variable length, typically 800 nm, but sometimes up to 1000 nm long. The outer viral envelope of the virion is derived by budding from domains of host cell membrane into which the GP spikes have been inserted during their biosynthesis. Individual GP molecules appear with spacings of about 10 nm. Viral proteins VP40 and VP24 are located between the envelope and the nucleocapsid, in the matrix space. At the center of the virion structure is the nucleocapsid, which is composed of a series of viral proteins attached to an 18-19 kb linear, negative-sense RNA without 3-polyadenylation or 5-capping; the RNA is helically wound and complexed with the NP, VP35, VP30, and L proteins; this helix has a diameter of 80 nm and contains a central channel of 20-30 nm in diameter.

The overall shape of the virions after purification and visualization (e.g., by ultracentrifugation and electron microscopy, respectively) varies considerably; simple cylinders are far less prevalent than structures showing reversed direction, branches, and loops (e.g., U-, shepherd's crook-, 9- or eye bolt-shapes, or other or circular/coiled appearances), the origin of which may be in the laboratory techniques applied. The characteristic "threadlike" structure is, however, a more general morphologic characteristic of filoviruses (alongside their GP-decorated viral envelope, RNA nucleocapsid, etc.).

Genome

Each virion contains one molecule of linear, single-stranded, negative-sense RNA, 18,959 to 18,961 nucleotides in length. The 3- terminus is not polyadenylated and the 5- end is not capped. This viral genome codes for seven structural proteins and one non-structural protein. The gene order is 3- - leader - NP - VP35 - VP40 - GP/sGP - VP30 - VP24 - L - trailer - 5-; with the leader and trailer being non-transcribed regions, which carry important signals to control transcription, replication, and packaging of the viral genomes into new virions. Sections of the NP, VP35 and the L genes from filoviruses have been identified as endogenous in the genomes of several groups of small mammals. As is typical of RNA-coded viruses, the Ebolavirus was found to mutate rapidly, both within a person during the progression of disease and in the reservoir among the local human population.

Ecology

Ebolavirus is a zoonotic pathogen. Intermediary hosts have been reported to be "various species of fruit bats throughout central and sub-Saharan Africa". Evidence of infection in bats has been detected through molecular and serologic means. However, ebolaviruses have not been isolated in bats. End hosts are humans and great apes, infected through bat contact or through other end hosts. Pigs on the Philippine islands have been reported to be infected with Reston virus, so other interim or amplifying hosts may exist.

Transmission

Because the natural reservoir host of Ebolaviruses has not yet been identified, the way in which the virus first appears in a human at the start of an outbreak is unknown. However, scientists believe that the first patient becomes infected through contact with an infected animal, such as a fruit bat or primate (apes and monkeys), which is called a spillover event. Person-to-person transmission follows and can lead to large numbers of affected people. In some past Ebola outbreaks, primates were also affected by Ebola and multiple spillover events occurred when people touched or ate infected primates.

When an infection occurs in humans, the virus can be spread to others through direct contact (through broken skin or mucous membranes in, for example, the eyes, nose, or mouth) with blood or body fluids (including but not limited to urine, saliva, sweat, feces, vomit, breast milk, and semen).

Ebola is not spread through the air, by water, or in general, by food. However, in Africa, Ebola may be spread as a result of handling bushmeat (wild animals hunted for food) and contact with infected bats. There is no evidence that mosquitoes or other insects can transmit Ebolavirus. Only a few species of mammals (e.g., humans, bats, monkeys, and apes) have shown the ability to become infected with and spread Ebolavirus.

Healthcare providers caring for Ebola patients and family and friends in close contact with Ebola patients are at the highest risk of getting sick because they may come in contact with infected blood or body fluids.

During outbreaks of Ebola, the disease can spread quickly within healthcare settings (such as a clinic or hospital). Exposure to Ebola can occur in healthcare settings where hospital staff are not wearing appropriate personal protective equipment.

Dedicated medical equipment (preferably disposable, when possible) should be used by healthcare personnel providing patient care. Proper cleaning and disposal of instruments, such as needles and syringes, also are important. If instruments are not disposable, they must be sterilized before being used again. Without adequate sterilization of instruments, virus transmission can continue and amplify an outbreak.

Once people recover from Ebola, they can no longer spread the virus to people in the community. Although Ebolavirus has been detected in semen after patients have recovered, it is not known if the virus can be spread through sex (including oral sex). As a precaution, men who have recovered from Ebola are advised to abstain from sex (including oral sex) for three months. If abstinence is not possible, condoms may help prevent the spread of disease.

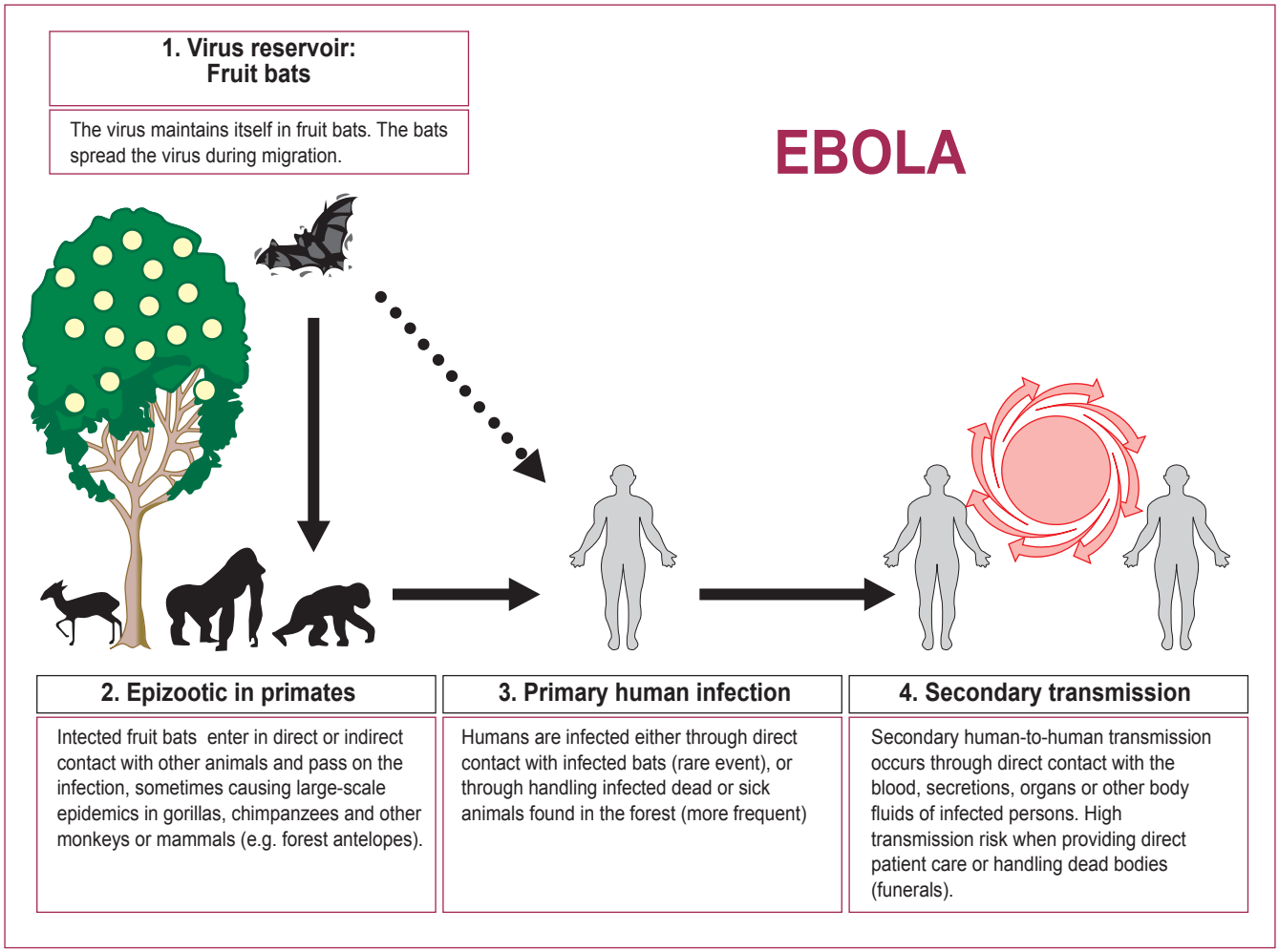

Figure: Transmission of Ebolavirus

Entry

There are two candidates for host cell entry proteins. The first is a cholesterol transporter protein, the host-encoded Niemann-Pick C1 (NPC1), which appears to be essential for entry of Ebola virions into the host cell and for its ultimate replication. When cells from Niemann-Pick Type C patients lacking this transporter were exposed to Ebola virus in the laboratory, the cells survived and appeared impervious to the virus, further indicating that Ebola relies on NPC1 to enter cells; mutations in the NPC1 gene in humans were conjectured as a possible mode to make some individuals resistant to this deadly viral disease.

The second candidate is TIM-1(T-cell immunoglobulin and mucin domain 1) also known as HAVcr-1 (Hepatitis A virus cellular receptor 1). TIM-1 was shown to bind to the receptor binding domain of the EBOV glycoprotein. TIM1 is expressed in tissues known to be seriously impacted by EBOV lysis (trachea, cornea, and conjunctiva). A monoclonal antibody against the TIM-1, ARD5, blocked EBOV binding and infection.

The studies suggest NPC1 and TIM-1 may be potential therapeutic targets for an Ebola anti-viral drug and as a basis for a rapid field diagnostic assay.

Replication

Being acellular, viruses such as Ebola do not replicate through any type of cell division; rather, they use a combination of host- and virally encoded enzymes, alongside host cell structures, to produce multiple copies of themselves. These then self-assemble into viral macromolecular structures in the host cell.

Pathogenesis

Ebolavirus infects and replicate very efficiently in namely monocytes, macrophages, dendritic cells and other cells including endothelial cells, liver cells, fibroblasts and adrenal gland cells.

Following infection with the virus, the immune cells carry the virus to nearby lymph nodes where further reproduction of the virus takes place. From there, the virus can enter the bloodstream and lymphatic system and spread throughout the body. Macrophages are the first cells infected with the virus, and this infection results in programmed cell death. Other types of white blood cells, such as lymphocytes, also undergo programmed cell death leading to an abnormally low concentration of lymphocytes in the blood.

Endothelial cells may be infected within 3 days after exposure to the virus. The breakdown of endothelial cells leading to vascular injury can be attributed to EBOV glycoproteins. The widespread hemorrhage that occurs in affected people causes edema and hypovolemic shock. The damage to human cells, caused by infection of the endothelial cells, decreases the integrity of blood vessels. This loss of vascular integrity increases with the synthesis of GP, which reduces the availability of specific integrins responsible for cell adhesion to the intercellular structure and causes damage to the liver, leading to improper clotting. The dysfunction in bleeding and clotting commonly seen in EVD has been attributed to increased activation of the extrinsic pathway of the coagulation cascade due to excessive production of tissue factor by macrophages and monocytes.

After infection, a secreted glycoprotein, small soluble glycoprotein (sGP) (or Ebola virus glycoprotein [GP]), is synthesized. EBOV replication overwhelms protein synthesis of infected cells and the host immune defenses. The GP forms a trimeric complex, which tethers the virus to the endothelial cells. The sGP forms a dimeric protein that interferes with the signaling of neutrophils, another type of white blood cell, which enables the virus to evade the immune system by inhibiting early steps of neutrophil activation. The presence of viral particles and the cell damage resulting from viruses budding out of the cell causes the release of chemical signals (such as TNF--, IL-6 and IL-8), which are molecular signals for fever and inflammation.

Immune System Evasion

EBOV proteins blunt the human immune response to viral infections by interfering with the cells' ability to produce and respond to interferon proteins such as interferon-alpha, interferon-beta, and interferon gamma. The VP24 and VP35 structural proteins of EBOV play a key role in this interference.

When a cell is infected with EBOV, receptors located in the cell's cytosol or outside of the cytosol recognize infectious molecules associated with the virus. On TLR (Toll like receptor) activation, proteins including interferon regulatory factor 3 and interferon regulatory factor 7 trigger a signaling cascade that leads to the expression of type 1 interferons. The type 1 interferons are then released and bind to the IFNAR1 (interferon receptor α 1) and IFNAR2 (interferon receptor α 2) expressed on the surface of a neighboring cell. Once interferon has bound to its receptors on the neighboring cell, the signaling proteins STAT1 and STAT2 are activated and move to the cell's nucleus.This triggers the expression of interferon-stimulated genes, which code for proteins with antiviral properties. EBOV's V24 protein blocks the production of these antiviral proteins by preventing the STAT1 signaling protein in the neighboring cell from entering the nucleus. The VP35 protein directly inhibits the production of interferon-beta. By inhibiting these immune responses, EBOV may quickly spread throughout the body.

Clinical Presentation

Symptoms may appear anywhere from 2 to 21 days after exposure to Ebola, but the average is 8 to 10 days. Symptoms of Ebola include

- Fever
- Severe headache
- Muscle pain
- Weakness
- Fatigue
- Diarrhea
- Vomiting
- Abdominal pain
- Unexplained hemorrhage (bleeding or bruising)

Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.

Diagnosis

Diagnosing Ebola in a person who has been infected for only a few days is difficult because the early symptoms, such as fever, are nonspecific to Ebola infection and often are seen in patients with more common diseases, such as malaria and typhoid fever.

However, if a person has the early symptoms of Ebola and has had contact with the blood or body fluids of a person sick with Ebola, contact with objects that have been contaminated with the blood or body fluids of a person sick with Ebola or contact with infected animals, he/she should be isolated and public health professionals notified. Samples from the patient can then be collected and tested to confirm infection.

Ebolavirus is detected in blood only after onset of symptoms, most notably fever, which accompany the rise in circulating virus within the patient's body. It may take up to three days after symptoms start for the virus to reach detectable levels. Laboratory tests used in diagnosis include :

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	• Antigen-capture enzyme-linked immunosorbent assay (ELISA) • IgM ELISA • Polymerase chain reaction (PCR) • Virus isolation
Later in disease course or after recovery	• IgM and IgG antibodies
Retrospectively in deceased patients	• Immunohistochemistry • PCR • Virus isolation

Treatment

No FDA-approved vaccine or medicine (e.g., antiviral drug) is available for Ebola.

Symptoms of Ebola and complications are treated as they appear. The following basic interventions, when used early, can significantly improve the chances of survival:

- Providing intravenous fluids (IV) and balancing electrolytes.
- Maintaining oxygen status and blood pressure.
- Treating other infections if they occur.

Intensive supportive care is required. Careful monitoring of fluid and electrolyte balance and renal function, providing supportive drug therapy like painkillers, antiemetic for vomiting, anxiolytic for agitation, +/-antibiotics and/or antimalarial drugs. Experimental vaccines and treatments for Ebola are under development, but they have not yet been fully tested for safety or effectiveness.

Several new treatment options are under development, such as ZMap, a cocktail of three monoclonal antibodies produced in plants, convalescent plasma, hyperimmune globulins made in horses or cattle, siRNA (Lipid Nanoparticle Small interfering RNAs), BCX4430 (a chemical which blocks viral replication), T705 (chemical substitution of constituent needed for viral replication).

By December 2014 two trials of an experimental Ebola vaccine appears to be safe and produces an immune response that could protect people against the deadly virus, according to early clinical trial results reported by the U.S. National Institutes of Health. Another expriment vaccine developed by Govt. of Canada is claimed promising too.

Recovery from Ebola depends on good supportive care and the patient's immune response. People who recover from Ebola infection develop antibodies that last for at least 10 years, possibly longer. It is not known if people who recover are immune for life or if they can become infected with a different species of Ebola. Some people who have recovered from Ebola have developed long-term complications, such as joint and vision problems.

History

Ebola is found in several African countries. Since 1976, Ebola outbreaks have occurred in the following countries:

Previous outbreak

- Democratic Republic of the Congo (DRC)
- Gabon
- Ivory Coast
- Republic of the Congo (ROC)
- South Sudan
- Uganda
- South Africa (imported)

Recent Outbreak

CDC classification of countries with reported Ebola cases for evaluation of persons in the United States

Widespread transmission	**Affected areas**
Guinea	Entire country
Liberia	Entire country
Sierra Leone	Entire country
Cases in urban settings with uncertain control measures	Affected areas
Mali	Bamako
Cases in urban settings with effective control measures	**Affected areas**
United States	Dallas, TX; New York City
Previously affected countries	**Affected areas**
Nigeria	Lagos, Port Harcourt
Senegal	Dakar
Spain	Madrid

Prevention and Control

a. Personal protective measures :

If a person travels to or is in an area affected by an Ebola outbreak, s/he should make sure to do the followings :

- Practice careful hygiene. For example, wash hands with soap and water or an alcohol-based hand sanitizer and avoid contact with blood and body fluids.
- Avoid handling items that may have come in contact with an infected person's blood or body fluids (such as clothes, bedding, needles, and medical equipment).
- Avoid funeral or burial rituals that require handling the body of someone who has died from Ebola.
- Avoid contact with bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals.
- Avoid facilities in West Africa where Ebola patients are being treated.
- After returning, monitor health for 21 days and seek medical care immediately if there is any development of symptoms of Ebola.

Healthcare workers who may be exposed to people with Ebola should follow these steps:

- Wear appropriate personal protective equipment (PPE).
- Practice proper infection control and sterilization measures.
- Isolate patients with Ebola from other patients.
- Avoid direct, unprotected contact with the bodies of people who have died from Ebola.
- Notify health officials if they had direct contact with the blood or body fluids, such as but not limited to, feces, saliva, urine, vomit, and semen of a person who is sick with Ebola. The virus can enter the body through broken skin or unprotected mucous membranes in, for example, the eyes, nose, or mouth.
- Reducing the risk of wildlife-to-human transmission from contact with infected fruit bats or monkeys/apes and the consumption of their raw meat. Animals should be handled with gloves and other appropriate protective clothing. Animal products (blood and meat) should be thoroughly cooked before consumption.
- Reducing the risk of human-to-human transmission from direct or close contact with people with Ebola symptoms, particularly with their bodily fluids. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.

Outbreak containment measures include:

- Prompt and safe burial of the dead
- Identifying people who may have been in contact with someone infected with Ebola
- Monitoring the health of contacts for 21 days
- Separating the healthy from the sick to prevent further spread, maintaining good hygiene and a clean environment

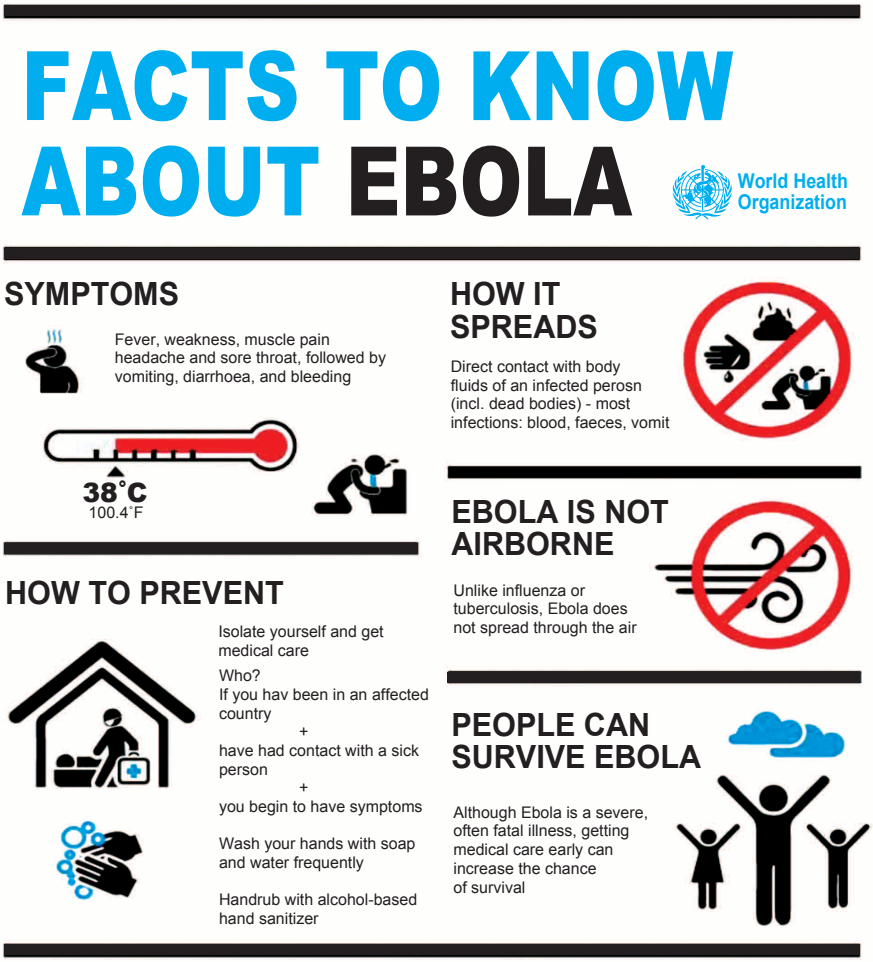

Figure: Facts to know about Ebola

b. Public health measures

Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilisation. Community engagement is key to successfully controlling outbreaks.

Raising awareness of risk factors for Ebola infection and protective measures that individuals can take is an effective way to reduce human transmission. Risk reduction messaging should focus on several factors:

Ebola & Bangladesh

A 2013 study named "Ebola Virus Antibodies in Fruit Bats, Bangladesh" found 3.5% bats positive for antibodies against Ebola Zaire and Reston viruses though no virus was detected by PCR. These bats might be a reservoir for Ebola or Ebola-like viruses in the region.

Ministry of Health and Family Welfare held a meeting and formed an 11 member "Monitoring Committee". A technical committee is also working at Directorate level. A 20 bed Ebola ward opened in Kurmitola General Hospital, Dhaka. Medical team formed in 25 point of entries. People coming from infected countries are being followed for 21 days on arrival to Bangladesh. Personal protective equipments (PPE) have been donated in all Medical teams including UN Missions in the infected countries. Drafting of Standard Oprerating Procedures is in progress with WHO support. Institute of Epidemiology, Disease Control and Research (IEDCR)/Directorate General of Health Services (DGHS) is conducting training for the Rapid Response Team members at National, District and Upazila levels.

References :

- www.cdc.org
- www.who.int
- www.ncbi.nlm.nih.gov

World Health Organization defines substance abuse as the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs. Use of these substances poses a significant threat to the health, social and economic fabric of families, communities and nations. Moreover, substance abuse is very costly exacting over many billion dollars annually worldwide. This is also usually responsible for serious crime, loss of work productivity and healthcare cost for rehabilitation.

Use of psychoactive substance may lead to dependence syndrome. This syndrome may include a cluster of behavioral, cognitive and physiological phenomena that develop after repeated use of the substances. This also leads to a strong desire to take the drug, difficulties in controlling its use and persisting in its use despite known harmful consequences, increased tolerance and sometimes a physical withdrawal state. Substance abusers give a higher priority to drug use than to other activities and obligations.

The Global Burden

The extent of worldwide psychoactive substance use is estimated at 2 billion alcohol users, 1.3 billion smokers and 185 million drug users. In an initial estimate of factors responsible for the global burden of disease, tobacco, alcohol and illicit drugs contributed together 12.4% of all deaths worldwide in the year 2000. It has also been estimated that they account for 8.9% of total years of life lost. The burden from psychoactive substance use is higher in the developed countries than developing countries.

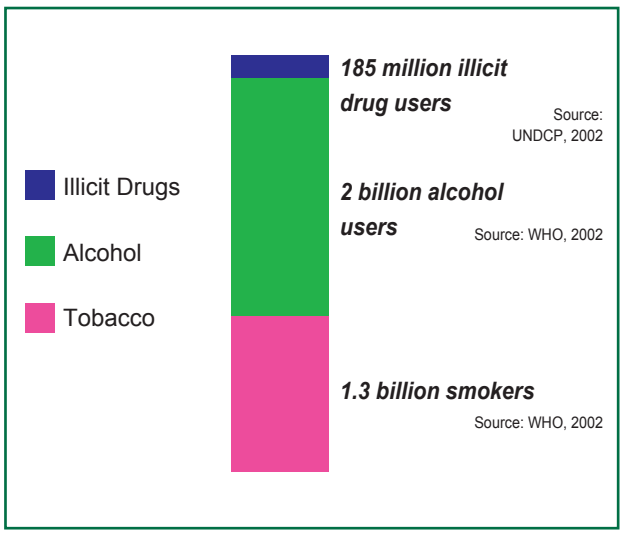

Figure: Worldwide extent of psychoactive substance use

There is variation of abuse of the tree psychoactive substances across the WHO regions. The disease burden in Disability Adjusted Life Years (DALY) is significantly higher in Europe and the Western Pacific than in Africa and the Eastern Mediterranean. Tobacco is the largest burden in Europe and South-East Asia while alcohol poses the largest burden in Africa, the Americas and Western Pacific. There is also variation among these three categories of psychoactive substances in different age groups. Illicit drug use inflicts its mortality burden earliest in life, alcohol mainly (65%) before the age of 60 years while 70% of the tobacco deaths occur after the age of 60 years.

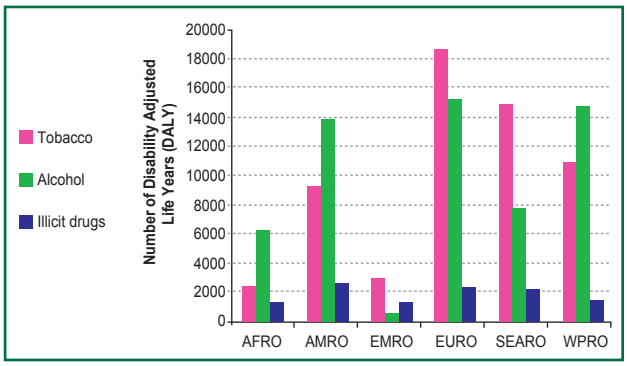

Figure: WHO Regions disease burden in 2000 attributable to selected risk factors

General Principles of Management

Individuals with substance use disorders may have diverse clinically important features and domains of functioning. A multimodal approach to treatment is typically required. The goals of treatment include the achievement of abstinence or reduction in the use and effects of substances, reduction in the frequency and severity of relapse to substance use and improvement in psychological and social functioning.

a. Assessment :

A comprehensive psychiatric evaluation is essential to guide the treatment of a patient with a substance use disorder. The assessment includes:

- A detailed history of the patient's past and present substance use
- The effects of substance use on the patient's cognitive, psychological, behavioral and physiological functioning
- A general medical and psychiatric history and examination
- A history of psychiatric treatments and outcomes
- A family and social history
- Screening of blood, breath, or urine for substance used
- Other laboratory tests to help confirm the presence or absence of conditions that frequently co-occur with substance use disorders

b. Psychiatric management :

Psychiatric management is the foundation of treatment for patients with substance use disorders. Many patients benefit from involvement in self-help group meetings, and such involvement can be encouraged as part of psychiatric management. Psychiatric management has the following specific objectives:

- Motivating the patient to change
- Establishing and maintaining a therapeutic alliance with the patient
- Assessing the patient's safety and clinical status
- Managing the patient's intoxication and withdrawal states
- Developing and facilitating the patient's adherence to a treatment plan
- Preventing the patient's relapse
- Educating the patient about substance use disorders and
- Reducing the morbidity and complications of substance use disorders.

c. Specific treatments :

Psychiatric management is generally combined with specific treatments carried out in a collaborative manner with professionals of various disciplines at a variety of sites, including community-based agencies, clinics, hospitals, detoxification programs and residential treatment facilities.

Pharmacological treatments are beneficial for selected patients with specific substance use disorders. The goals of treatment and the specific therapies chosen to achieve these goals may vary among patients and even for the same patient at different phases of an illness. The categories of pharmacological treatments are:

- Medications to treat intoxication and withdrawal states
- Medications to decrease the reinforcing effects of abused substances
- Agonist maintenance therapies
- Antagonist therapies
- Abstinence-promoting and relapse prevention therapies and
- Medications to treat co-morbid psychiatric conditions

Psychosocial treatments are also essential components of a comprehensive treatment program. Evidence-based psychosocial treatments include cognitive behavioral therapies (CBT), motivational enhancement therapy (MET), behavioral therapies, psychodynamic therapy/interpersonal therapy (IPT), self-help manuals, behavioral self-control, brief interventions, case management, group and family therapies etc.

d. Formulation and implementation of a treatment plan:

Because many substance use disorders are chronic, patients usually require long-term treatment, although the intensity and specific components of treatment may vary over time. The duration of treatment should be tailored to the individual patient's needs and may vary from a few months to several years. It is important to intensify the monitoring for substance use during periods when the patient is at a high risk of relapsing, including during the early stages of treatment, times of transition to less intensive levels of care, and the first year after active treatment has ceased.

e. Treatment settings :

Treatment settings vary with regard to the availability of specific treatment modalities, the availability of general, medical and psychiatric care and the overall milieu and treatment philosophy. Patients should be treated in the least restrictive setting that is likely to be safe and effective. Commonly available treatment settings include hospitals, residential treatment facilities, partial hospitalization programs and outpatient programs. Decisions regarding the site of care should be based on the patient's ability to cooperate with and benefit from the treatment offered, refrain from illicit use of substances, and avoid high-risk behaviors.

Hospitalization is appropriate in certain cases :

- Patients who have a substance abuse but cannot be safely treated in an outpatient or emergency department setting
- Patients with risk for severe or complicated withdrawal syndromes (e.g., delirium tremens)
- Patients with concurrent general medical conditions that make ambulatory detoxification unsafe
- Patients with a documented history of not benefitting from treatment in a less intensive setting (e.g., residential, outpatient)
- Patients with a level of psychiatric co-morbidity(depression with suicidal thoughts, acute psychosis) that would markedly impair their ability to participate in, adhere to or benefit from treatment
- Patients who manifest substance use or other behaviors that constitutes an acute danger to themselves or others.

Residential treatment is indicated for patients who do not meet the clinical criteria for hospitalization but whose lives and social interactions have come to focus predominantly on substance use, who lack sufficient social and vocational skills, and who lack substance-free social supports to maintain abstinence in an outpatient setting. Residential treatment of 3 months is associated with better long-term outcomes in such patients.

Partial hospitalization should be considered for patients who require intensive care but have a reasonable probability of refraining from illicit use of substances outside a restricted setting. Partial hospitalization settings are frequently used for patients leaving hospitals or residential settings who remain at high risk for relapse. These include patients who are thought to lack sufficient motivation to continue in treatment, have psychiatric co-morbidity and/or a history of relapse to substance use in the immediate post-hospitalization or post-residential period and are returning to a high-risk environment and have limited psychosocial supports for abstaining from substance use. Partial hospitalization programs are also indicated for patients who are doing poorly despite intensive outpatient treatment.

Outpatient treatment of substance use disorders is appropriate for patients whose clinical condition or environmental circumstances do not require a more intensive level of care. As in other treatment settings, a comprehensive approach is optimal, using, where indicated, a variety of psychotherapeutic and pharmacological interventions along with behavioral monitoring. Most treatment for patients with alcohol dependence or abuse can be successfully conducted outside the hospital, although patients with alcohol withdrawal must be detoxified in a hospital setting that provides frequent clinical assessment and any necessary treatments. For many patients with cocaine use disorder, clinical and research experience suggests the effectiveness of intensive outpatient treatment. The treatment of patients with nicotine dependence or a marijuana use disorder occurs on an outpatient basis unless patients are hospitalized for other reasons.

f. Clinical features influencing treatment:

In planning and implementing treatment, a clinician should consider several variables with regard to patients: co-morbid psychiatric and general medical conditions, gender-related factors, age, social milieu and living environment, cultural factors, gay/lesbian/bisexual/transgender issues, and family characteristics. A patient's cessation of substance use may also be associated with changes in his or her psychiatric symptoms or the metabolism of medications that will necessitate adjustment of psychotropic medication doses.

In women of childbearing age, the possibility of pregnancy needs to be considered. Many substances have the potential to affect the fetus and psychosocial treatment to encourage substance abstinence during pregnancy is recommended. In pregnant smokers, treatment with nicotine replacement therapy may be helpful. For pregnant women with an opioid use disorder, treatment with methadone or buprenorphine can be a useful adjunct to psychosocial treatment.

Management of Specific Substance Abuse

A. Nicotine use disorder :

Pharmacological treatment is recommended for individuals who wish to stop smoking but have not achieved cessation and prefer to use medications. There are six medications approved by the US FDA for nicotine dependence, including five nicotine replacement therapies (patch, gum, spray, lozenge, and inhaler) and bupropion. These are all first-line agents that are equally effective in alleviating withdrawal symptoms and reducing smoking. Significant adverse events, including dependence, are rare. Nortriptyline and clonidine have utility as second-line agents but appear to have more side effects.

Psychosocial treatments are also effective for the treatment of nicotine dependence and include CBT, behavioral therapies, brief interventions and MET provided in individual, group or telephone formats or via self-help materials and internet-based formats. The efficacy of treatment is related to the amount of psychosocial treatment received. The 12-step programs, hypnosis, and in-patient therapy have not been proven effective.

B. Benzodiazepine use disorder :

Dependence and withdrawal syndrome have been well described in chronic benzodiazepine users over a range of therapeutic and supra-therapeutic doses. There is less information on dependence and withdrawal in benzodiazepine abusers, who sometimes use the drugs intermittently or in binges. The severity of withdrawal symptoms is significantly related to the size of previous dosage in the abusers. Regular daily benzodiazepine users are more likely than intermittent users to develop symptoms. Clinical observations suggest that some poly-drug users, like some prescribed dose patients, can withdraw benzodiazepines without difficulty, especially poly-drug users maintained on methadone. The duration of withdrawal symptoms is not clear. Acute symptoms in the first few weeks may merge into prolonged anxiety and insomnia which may continue for weeks or months.

Withdrawal methods for long-term prescribed therapeutic dose benzodiazepine users are well established and consist mainly of slow dosage tapering over weeks or months in an outpatient setting, combined with psychological support. But, a long period of outpatient dosage tapering is unlikely to be adhered to since additional benzodiazepines may be obtained illicitly. Benzodiazepine abusers commonly use high doses and are at particular risk of severe withdrawal symptoms including epileptic fits if the drugs are stopped abruptly. Therefore, a moderately rapid, controlled schedule of detoxification in an inpatient unit is preferable. Several methods have been described. The most common technique is substitution of a slowly eliminated benzodiazepine (usually diazepam) for the abused shorter acting drugs which is followed by dosage tapering over 2 or more weeks.

C. Alcohol use disorder :

The acutely intoxicated patient should be monitored and maintained in a safe environment. Symptoms of alcohol withdrawal typically begin within 4-12 hours after cessation or reduction of alcohol use, peak in intensity during the second day of abstinence, and generally resolve within 4-5 days. Serious complications include seizures, hallucinations, and delirium. The treatment of patients in moderate to severe withdrawal includes efforts to reduce central nervous system irritability and restore physiological homeostasis and generally requires the use of thiamine and fluids, benzodiazepines and in some patients, other medications such as anticonvulsants, clonidine or antipsychotic agents. Once clinical stability is achieved, the tapering of benzodiazepines and other medications should be carried out as necessary, and the patient should be observed for the re-emergence of withdrawal symptoms and the emergence of signs and symptoms suggestive of co-occurring psychiatric disorders.

Specific pharmacological therapies for alcohol-dependent patients have well-established efficacy. Naltrexone may attenuate some of the reinforcing effects of alcohol, although data on its long-term efficacy are limited. The use of long-acting, injectable naltrexone may promote adherence, but published research is limited and FDA approval is pending. Acamprosate, a γ-aminobutyric acid (GABA) analog that may decrease alcohol craving in abstinent individuals, may also be an effective adjunctive medication in motivated patients who are concomitantly receiving psychosocial treatment. Disulfiram is an effective adjunct to a comprehensive treatment program for reliable, motivated patients whose drinking may be triggered by events that suddenly increase alcohol craving.

Psychosocial treatments found effective for some patients with an alcohol use disorder include MET, CBT, behavioral therapies, marital and family therapies, group therapies and psychodynamic therapy/IPT. Recommending that patients participate in self-help groups is often helpful.

D. Marijuana use disorder :

Studies of the treatment for marijuana use disorders are limited. No specific pharmacological therapies for marijuana withdrawal or dependence can be recommended. Motivational interventions may be effective for the treatment of marijuana dependence, but further study of these approaches is necessary

E. Opioid use disorder :

Acute opioid intoxication of a mild to moderate degree usually does not require specific treatment. However, severe opioid overdose marked by respiratory depression, may be fatal and requires treatment in an emergency department or in-patient setting. Naloxone will reverse respiratory depression and other manifestations of opioid overdose.

The treatment of opioid withdrawal is directed at safely ameliorating acute symptoms and facilitating the patient's entry into a long-term treatment program. Strategies found to be effective include:

- Substitution of methadone or buprenorphine for the opioid followed by gradual tapering
- Abrupt discontinuation of opioids, with the use of clonidine to suppress withdrawal symptoms and
- Clonidine-naltrexone detoxification

It is essential that the treating physician assess the patient for the presence of other substances, particularly alcohol, benzodiazepines or other anxiolytic or sedative agents, because the concurrent use of or withdrawal from other substances can complicate the treatment of opioid withdrawal.

Maintenance treatment with methadone or buprenorphine is appropriate for patients with a prolonged history (>1 year) of opioid dependence. The goals of treatment are to achieve a stable maintenance dose of opioid agonist and facilitate engagement in a comprehensive program of rehabilitation. Maintenance treatment with naltrexone is an alternative strategy, although the utility of this strategy is often limited by lack of patient adherence and low treatment retention.

Psychosocial treatments are effective components of a comprehensive treatment plan for patients with an opioid use disorder. Behavioral therapies, CBT, psychodynamic psychotherapy and group and family therapies have been found to be effective for some patients with an opioid use disorder. Recommending regular participation in self-help groups may also be useful.

F. Cocaine use disorder :

Cocaine intoxication is usually self-limited and typically requires only supportive care. However, hypertension, tachycardia, seizures, and persecutory delusions can occur with cocaine intoxication and may require specific treatment. Acutely agitated patients may benefit from sedation with benzodiazepines.

Pharmacological treatment is not ordinarily indicated as an initial treatment for patients with cocaine dependence. In addition, no pharmacological therapies have FDA indications for the treatment of cocaine dependence. However, for individuals who fail to respond to psychosocial treatment alone, some medications (topiramate, disulfiram, or modafinil) may be promising when integrated into psychosocial treatments.

For many patients with a cocaine use disorder, psychosocial treatments focusing on abstinence are effective. In particular, CBT, behavioral therapies, and 12-step-oriented individual drug counseling can be useful, although efficacy of these therapies varies across subgroups of patients. Recommending regular participation in a self-help group may improve the outcome for selected patients with a cocaine use disorder.

G. Methamphetamine use disorder :

Methamphetamine increases the amount of the neurotransmitter dopamine, leading to high levels of that chemical in the brain. Dopamine is involved in reward, motivation, the experience of pleasure, and motor function. Methamphetamine's ability to release dopamine rapidly in reward regions of the brain produces the euphoric "rush" or "flash" that many users experience. Repeated methamphetamine use can easily lead to addiction-a chronic, relapsing disease characterized by compulsive drug seeking and use. Long-term users of methamphetamine may experience anxiety, confusion, insomnia, and mood disturbances and display violent behavior. They may also show symptoms of psychosis, such as paranoia, visual and auditory hallucinations and delusions. Long-term methamphetamine use has many negative consequences for physical health, including extreme weight loss, severe dental problems ("meth mouth") and skin sores caused by scratching.

Methamphetamine dependence is a serious public health problem worldwide for which there are no approved pharmacological treatments. Psychotherapy is still the mainstay of treatment; however, relapse rates are high. The search for effective pharmacological treatment has intensified in the last decade. Early pilot data are encouraging for administering D-amphetamine and methylphenidate as treatment for heavy metamphetamine users but they will need to be confirmed by larger trials. Acute overdose may be treated with beta-blockers.

H. Inhalant use disorder :

Inhalant abuse has now-a-days become popular in a certain group of population, especially among the young. This involves breathing in a substance directly from its container (sniffing or snorting), placing a rag over the nose and mouth soaked in the substance and inhaling (huffing), or pouring the substance into a plastic bag and breathing the fumes (bagging).

Abused substances include fuels, solvents, propellants, glues, adhesives, and paint thinners. Inhaled solvents likely share cellular actions with γ-aminobutyric acid-receptor drugs (e.g., benzodiazepines, barbiturates, alcohol), resulting in a depressant effect. Use of inhalants can produce a euphoric feeling similar to that experienced with other illicit drugs. When a person using inhalants becomes hypercapnic and hypoxic by rebreathing from a closed bag, the effects of the inhalant are intensified.

Patients who have been abusing inhalants may report dizziness, irritability, tiredness, loss of appetite, headache, photophobia, or cough. Most symptoms are nonspecific and can be mistaken for those of other illnesses or syndromes. Signs of recent inhalant abuse include paint or oil stains on clothing or skin, spots or sores around the mouth, red eyes, rhinorrhea, chemical odor on the breath and a dazed appearance. Tolerance to inhalants can develop with frequent use. A withdrawal syndrome has been described, although it occurs infrequently.

The treatment of acute inhalation-related injury and illness is generally supportive. Acute dysrhythmias should be treated according to established protocols. Beta blockers should be administered early to protect the catecholamine-sensitized heart. Acid-base and metabolic disturbances should be corrected. Cardiopulmonary monitoring is recommended because of the risk of apnea and cardiac arrest after acute exposure. Treatment also involves counseling and strict abstinence.

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Otosclerosis is a common cause of progressive deafness in young adults. It is a disease of the middle ear affecting mainly the stapes, one of the three tiny bony ossicles of the ear. About 1 or 2 in 100 people are affected by the disease where women aged between 15 and 30 years are most commonly affected than men. In otosclerosis, both the ears are usually affected but sometimes, only one ear is affected. Untreated otosclerosis can cause profound hearing loss.

Etiology

The exact cause of otosclerosis is not entirely known. Some factors are thought to be related with the conditions. These are :

- ***Family history :*** Otosclerosis tends to run in families as an autosomal dominant pattern with variable penetrance; in about half of all patients, there is a family history of similar problem.
- ***Gender :*** Women are more likely to develop otosclerosis than men but the cause is not clear.
- ***Pregnancy :*** Susceptible women may develop otosclerosis during pregnancy; pre-existing condition may become worse during pregnancy.
- ***Race :*** Caucasians tend to be most commonly affected
- ***Viral infections :*** Viral infection, in particular, measles virus infection has been suggested as a causative factor in otosclerosis in genetically susceptible population.
- ***Osteogenesis imperfecta :*** People with osteogenesis imperfecta are at increased risk of developing otosclerosis.
- ***Non-fluoridated water :*** Some evidences suggest that drinking non-fluoridated water may increase the risk of otosclerosis in susceptible people.
- ***Autoimmunity*** may also plays role in the causation of otosclerosis.

Pathogenesis

In normal hearing, the sound wave passes from the tympanic membrane to the three small bony ossicles (malleus, incus and stapes) of the middle air that amplify sound waves. The stapes is the innermost of these ossicles. It is the smallest bone in the body and sits in the oval window into the cochlea. It is free to vibrate within the window, allowing transmission of sound waves to the cochlea of the inner ear.

In otosclerosis, abnormal bone material grows around the stapes. The growth is very gradual. Eventually, the stapes becomes thickened and fused with the bone of the cochlea. This reduces normal sound transmission resulting in a conductive deafness. In most cases, the stapes is the only bone to be affected. Over time, it can sometimes also affect the bony shell of the cochlea and the nerve cells within it. Damage to the nerve cells can interrupt transmission of nerve signal to the brain. In that case, sensorineural hearing loss as well as loss of balance may be evident. Otosclerosis tends to target one ear at first, but both ears are eventually affected. Dizziness may occur but the mechanism is unknown, although there is speculation that it derives from the release of enzymes from metabolically active bone into the inner ear.

Clinical Features

- Hearing loss is the main symptom of otosclerosis that generally begins between the ages of 10 and 30 years. A person with otosclerosis usually has speech which is quiet, while people with cochlear (or nerve) deafness usually speak loudly.
- Dizziness or imbalance is a feature of otosclerosis in roughly 25% of cases.
- Between 40% and 65% of patients have tinnitus
- Pain is not usually a symptom of otosclerosis

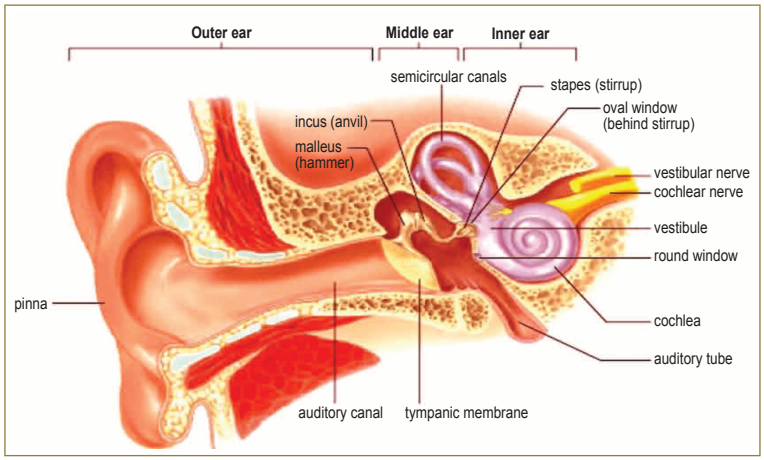

Figure : Normal human ear

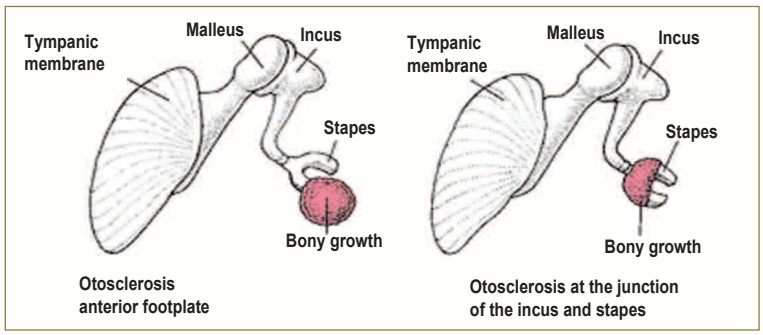

Figure : Abnormal bony growth in otosclerosis

Diagnosis

Diagnosis of otosclerosis is usually made by a combination of family history, progressive conductive hearing loss pattern, and exclusion of alternatives. Some tests are also used, such as,

- Hearing test: Hearing tests may show the typical conductive loss pattern.
- Acoustic reflexes may eventually be absent, but early on may show the "on-off" effect.
- Tympanometry often shows stiffening of the ossicular chain.
- CT scan of the temporal bone is specific but insensitive. It may be the only way to document otosclerosis early in the disease and also to check for damage to the cochlear nerve and labyrinth.

Treatment

Treatment may not be needed until the degree of hearing loss is significant. There are four treatment options.

A. Conservative approach : Otosclerosis does not have to be treated in all the times. It is usually advisable to have a hearing test repeated once a year or earlier if hearing worsens.

B. Medical treatment : Some studies have suggested that taking fluoride, calcium and vitamin D supplements may help to slow the progression of otosclerosis. However, this treatment needs further research before it can be confirmed. A recent study found that patients treated with fluoride had smaller otosclerotic foci on CT scanning. Side effects of fluoride include occasional gastric upset, itching and arthritis. If aggravation of arthritis occurs, the fluoride is stopped and the joints return to their previous state in a few weeks. Once the otospongiosis phase of otosclerosis is over and there is a clear-cut otosclerosis documented by conductive hearing loss, fluoride may be stopped.

C. Hearing Aids : Hearing aids are helpful with all kinds of conductive deafness, including otosclerosis.

D. Surgical Treatment : Surgical treatment of otosclerosis includes surgical removal of the stapes (stapedectomy) followed by replacement with a prosthesis. Teflon, polyethylene and stainless steel are among those commonly used as prosthesis. Surgery may also be performed with laser dissection, and studies have shown similar outcomes and few side effects with laser surgery.

Figure : Stapes prosthesis

Stapedectomy is indicated in patients with good bilateral inner-ear function, and conductive hearing loss ranging from 25 to 30 dB in elected frequencies. A successful operation can correct conductive hearing loss of otosclerosis. It also improves tinnitus. It does not help the sensory component of the hearing loss. It also does not affect the vertigo that is sometimes associated with otosclerosis.

Stapedectomy may fail for a number of reasons. There may be displacement of the prosthesis, reclosure of the fenestra or erosion of the incus. The disease may progress so that correction of the conductive component is inadequate. In some cases, repeat stapedectomy may be performed following failure of the initial repair, but revision surgery is less successful than initial surgery at improving hearing loss.

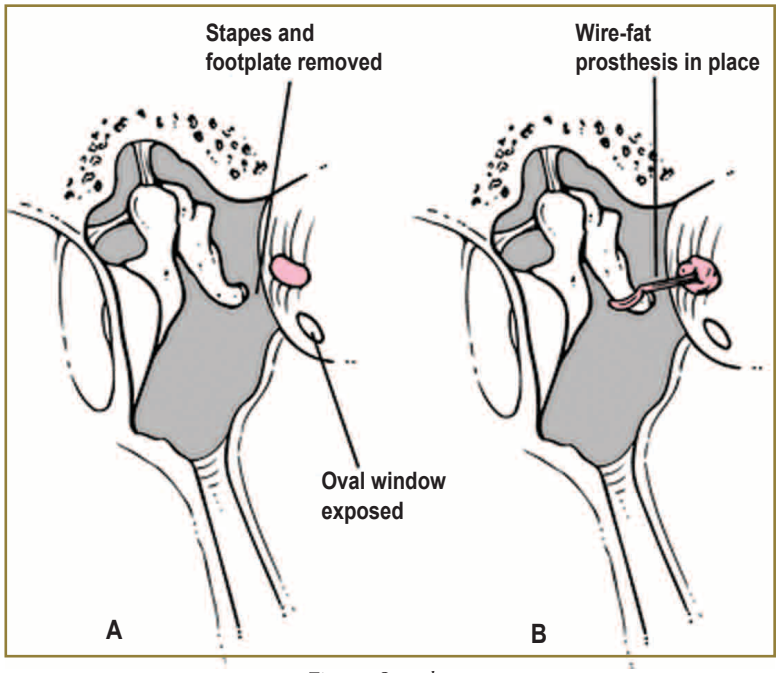

Figure : Stapedectomy

Some adverse events may occur after stapedectomy. About 2% patients had severe hearing loss due to damage to the cochlea but modern techniques have improved this figure. Giddiness or unsteadiness is common immediately after the operation but usually clears within a few days. Sometimes injury to the nerve concerned with taste may result in metallic taste on the side of the tongue for a month or two after the operation.

After stapedectomy, it is important to protect the structures within the ear from infection, pressure and noise to reduce the risk of complications. So blowing the nose, cold exposure, changes in air pressure (air travel or scuba diving), loud noise should be avoided.

Cochlear implants are used successfully in patients with otosclerosis. Patients with the best preoperative hearing levels are most likely to benefit. Cochlear implants are more difficult to position in otosclerosis due to sclerosis of the inner ear. Patients may also experience facial nerve stimulation by the cochlear implant, more common in patients with severe disease. Facial nerve stimulation requires revision surgery or calibration of the implant in order to relieve this side effect. Cochlear implantation has been performed as initial treatment and following stapedectomy with good results.

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Autism is a condition that was identified in 1943. Autism (sometimes called "classical autism") is the most common condition in a group of developmental disorders known as the autism spectrum disorders (ASDs). Autism is characterized by impaired social interaction, problems with verbal and nonverbal communication and unusual, repetitive or severely limited activities and interests.

Prevalence

Male to female ratio is 4: 1. Studies have shown that the number of individuals with autism is on the rise.

About 1 percent of the world population has autism spectrum disorder.

Prevalence in the United States is estimated at 1 in 68 births.

More than 3.5 million Americans live with an autism spectrum disorder.

Prevalence of autism in U.S. children increased by 119.4 percent from 2000 (1 in 150) to 2010 (1 in 68).

Prevalence has increased by 6-15 percent each year from 2002 to 2010.

1 percent of the adult population of the United Kingdom has autism spectrum disorder.

In Bangladesh, no research has been carried out but a recent 2013 pilot study in Bangladesh, utilizing community health workers, has found prevalence of all kinds of neurodevelopmental disability is 7.1%. Whereas, for ASD, the study indicates a prevalence of 0.15% (3% in Dhaka city and 0.07% in rural area).

Causes

There is no known single cause for autism spectrum disorder, but it is generally accepted that it is caused by abnormalities in brain structure or function. Brain scans show differences in the shape and structure of the brain in children with autism compared to the neurotypical children. Researchers are investigating a number of theories, including the links among heredity, genetics and medical problems.

In many families, there appears to be a pattern of autism or related disabilities, further supporting the theory that the disorder has a genetic basis. While no one gene has been identified as causing autism, researchers are searching for irregular segments of genetic code that children with autism may have inherited. It also appears that some children are born with a susceptibility to autism, but researchers have not yet identified a single "trigger" that causes autism to develop.

Other researchers are investigating the possibility that under certain conditions, a cluster of unstable genes may interfere with brain development, resulting in autism. Still other researchers are investigating problems during pregnancy or delivery as well as environmental factors such as viral infections, metabolic imbalances and exposure to chemicals.

Autism tends to occur more frequently than expected among individuals who have certain medical conditions, including fragile X syndrome, tuberous sclerosis, congenital rubella syndrome and untreated phenylketonuria (PKU). Some harmful substances ingested during pregnancy also have been associated with an increased risk of autism.

Research indicates other factors besides the genetic component are contributing to the rise in increasing occurrence of autism - for example, environmental toxins (e.g., heavy metals such as lead mercury), which are more prevalent than in the past. Those with autism (or those at risk) may be especially vulnerable to such toxins, as their ability to metabolize and detoxify these exposures might be compromised.

Characteristics of Autism

The degrees of severity in people with an Autism Spectrum Disorder can be wide ranging. But all those affected have impairment in social interaction, communication and behavior (Figure-1). According to 'American Psychiatric Association' 1994, the core defining features of autism are :

- Impairments in socialization
- Impairments in verbal and non-verbal communication
- Restrictive and repetitive patterns of behavior or interest

They may also exhibit

- Lack of imaginative play
- Attention problems
- Repeated body movement (hand flapping, rocking, etc.)
- Unusual attachment to objects
- Resistance in any change in routine
- Apparent insensitivity to physical dangers and pain
- Disruptive, aggressive or self-injurious behavior
- Lack of eye contact
- Echolalia
- Lack of interest in peers
- Failure to point at objects

Appropriate social behavior does not come naturally to children with autism. They cannot interpret facial expressions or emotions. They do not know how to share or make friends. Individuals with autism may also experience sensitivities in the five senses of -sight, hearing, touch, smell and taste, although, some autistic children show exceptional skill in areas such as art, music, calculation, calendars, computers or memory.

Early Identification

The characteristic behaviors of autism spectrum disorder may be apparent in infancy (18 to 24 months), but they usually become clearer during early childhood (24 months to 6 years).

The National Institute of Child Health and Human Development (NICHD) list five behaviors that warrant further evaluation:

- Does not babble or coo by 12 months
- Does not gesture (point, wave, grasp) by 12 months
- Does not say single words by 16 months
- Does not say two-word phrases on his or her own by 24 months
- Has any loss of any language or social skill at any age

Any of these five "red flags" does not mean any child has autism. But because the disorder's symptoms vary so widely, a child showing these behaviors should be evaluated by a multidisciplinary team.

Diagnosis

When parents become concerned that their child is not following a typical developmental course, they turn to experts, including psychologists, educators and medical professionals, for a diagnosis.

At first glance, some people with autism may appear to have an intellectual disability, sensory processing issues, or problems with hearing or vision. To complicate matters further, these conditions can co-occur with autism. However, it is important to distinguish autism from other conditions, as an accurate and early diagnosis can provide the basis for an appropriate educational and treatment program.

Other medical conditions or syndromes, such as sensory processing disorder, can present symptoms that are confusingly similar to autism.

There are many differences between a medical diagnosis and an educational determination, or school evaluation, of a disability. A medical diagnosis is made by a physician based on an assessment of symptoms and diagnostic tests. A medical diagnosis of autism spectrum disorder, for instance, is most frequently made by a physician according to the *Diagnostic and Statistical Manual* (*DSM-5*, released 2013) of the American Psychological Association. This manual guides physicians in diagnosing autism spectrum disorder according to a specific number of symptoms.

A brief observation in a single setting cannot present a true picture of someone's abilities and behaviors. The person's developmental history and input from parents, caregivers and/or teachers are important components of an accurate diagnosis.

An educational determination is made by a multidisciplinary evaluation team of various school professionals. The evaluation results are reviewed by a team of qualified professionals and the parents to determine whether a student qualifies for special education and related services under the Individuals with Disabilities Education Act (IDEA).

School Evaluation

The first step in obtaining special education services is for the child to be evaluated. The evaluation can be done when child is first suspected of having a disability (pre-placement evaluation) or when child's level of functioning changes in one or more areas (re-evaluation).

Medical Diagnosis

There are no medical tests for diagnosing autism. An accurate diagnosis must be based on observation of the individual's communication, behavior and development levels. However many of the behaviors associated with autism are shared by other disorders, various medical tests may be ordered to rule out or identify other possible causes of the symptoms being exhibited.

Differential Diagnosis

Following is a list of related syndromes/disorders that manifest behaviors similar to those of autism and/or are more prevalent in individuals with autism :

Congenital Rubella Syndrome	Untreated Phenylketonuria (PKU)
Cornelia deLange Sydrome	Prader-Willi Syndrome
Down syndrome	Rett Syndrome
Fragile X Syndrome	Tourette syndrome
Klüver-Bucy Syndrome	Tuberous Sclerosis
Landau-Kleffner Syndrome	Williams Syndrome
Lesch-Nyhan Syndrome	

Related Conditions

Seizures : It is estimated that around 30 percent of people with autism develop epilepsy, some in early childhood and others as they go through hormone level changes in puberty.

Chronic Constipation and/or Diarrhea : Medical literature states that about 45 percent of children with autism and 47 percent of adults on the spectrum have gastrointestinal symptoms. Diarrhea is most common, abdominal pain is cited next most frequently, and constipation is reported slightly less. Constipation in autism is usually not hard, impacted stools, but the slow passage of stools with long gaps in between, and loose stools when they do come.

Sleep Problems : Many individuals with autism have sleep problems. Night waking may be due to gastrointestinal issues, allergies, environmental intolerances, seizures or the effects of medications. Other potential causes are sleep apnea (pauses in breathing when the airway becomes obstructed during sleep), sleep terrors or confusional arousals. Children with sensory processing difficulties may have more problems falling asleep and increased periods of night waking.

Pica : About 30 percent of children with autism have moderate to severe pica, which means they eat non-food items such as paint, sand, dirt, paper, etc. Pica can be dangerous as ingesting these inedible substances can cause choking, digestive problems, parasitic infections and other illnesses.

Low Muscle Tone : About 30 percent of children with autism have moderate to severe loss of muscle tone, which can limit their gross and fine motor skills.

Sensory Processing Disorder : Many people with autism have sensory processing disorder (formerly known as sensory integration disorder), which involves unusual sensitivities to sounds, sights, touch, taste and smells. High-pitched intermittent sounds, such as fire alarms or school bells, may be painful to these children. Scratchy fabrics and clothing tags may also be intolerable, and some children have visual sensitivities, such as to the flickering of fluorescent lights.

Allergies/ Immune System : Many children with autism also suffer immune system deficiencies or immune dysregulation. Within the autism spectrum population, there are groups that will experience rashes, allergic sensitivities, gastrointestinal, ear and other infections as a result. Immune deficiencies and/or immune dysregulation make a person with autism more vulnerable to infection, chronic inflammation and autoimmune reactions, most frequently in the brain and gastrointestinal tract.

Pain : Some people with autism have very high pain thresholds while others have very low pain thresholds. There are interventions, such as sensory integration therapy, designed to help normalize their senses.

Screening Instruments

Early identification is associated with dramatically better outcomes for people with autism. The earlier a child is diagnosed, the earlier he or she can begin benefiting from early intervention treatment and education.

The Centers for Disease Control and Prevention's National Center on Birth Defects and Developmental Disabilities (NCBDDD) recommends that all children be screened for autism by their family pediatrician three times by the age of three - at nine, 18, and 24 or 30 months. Treatment should start when an autism diagnosis is suspected, rather than when a formal diagnosis is made.

The advantages of early intervention cannot be overemphasized. Children who receive intensive therapy can make tremendous strides in their overall functioning.

The NCBDDD provides a wealth of information on the early signs of autism through its "Learn the Signs. Act Early"initiative.

While there is no one behavioral or communications test that can detect autism, several screening instruments have been developed for use in diagnosing it.

Treatment

There is no cure for autism. Therapies and behavioral interventions are designed to remedy specific symptoms and can bring about substantial improvement. The ideal treatment plan coordinates therapies and interventions that target the core symptoms of autism: impaired social interaction, problems with verbal and nonverbal communication, and obsessive or repetitive routines and interests. Most professionals agree that the earlier the intervention, the better.

Educational/behavioral interventions :

Therapists use highly structured and intensive skill-oriented training sessions to help children develop social and language skills. Family counseling for the parents and siblings of children with autism often helps families cope with the particular challenges of living with an autistic child.

Medications :

An antidepressant medication to handle symptoms of anxiety, depression, or obsessive-compulsive disorder. Anti-psychotic medications are used to treat severe behavioral problems. Seizures can be treated with one or more of the anticonvulsant drugs. Stimulant drugs, such as those used for children with attention deficit disorder (ADD), are sometimes used effectively to help decrease impulsivity and hyperactivity.

Other therapies :

There are a number of controversial therapies or interventions available for autistic children, but few, if any, are supported by scientific studies. Parents should use caution before adopting any of these treatments.

Prognosis

There is no magical cure for autism. Early diagnosis and intensive behavioral intervention in optimal educational settings can have a significant, positive and lasting impact on children with autism. They can benefit from placement in a good educational program.

With intensive intervention, many children diagnosed with the disorder before the age of 5 go on to attend mainstream school.

Proper evaluation of each child's strengths and limitations, appropriate training and an autism friendly environment can help them to perform to their maximum potential

Living with Autism : Scenario in Bangladesh

In Bangladesh, like in many other developing countries, neurodevelopmental disabilities such as autism are basically seen through the lens of misinformation and stigma. Dissemination within a community of a modern protocol of autism is a highly complex, multifactorial challenge. Bangladesh, despite these complexities and challenges, has successfully taken the base steps to deal autism. Distinguishing the issue as a national policy priority, Bangladesh is now trying to develop a rights-based paradigm for individuals with autism.

Rights Ensured in Bangladesh :

The National Parliament of the Government of Bangladesh has promulgated two important acts to protect the rights and ensure safety of the differently able persons. One act is (i) The Disability Rights Law, 2013 and the other is (ii) Neuro-Developmental Disability Protection Trust Act, 2013.

The Disability Rights Law, 2013

- Ensures rights & dignity of the persons with disabilities by stipulating 21 rights
- Rights to educational, physical and psychological improvement
- Rights to participation in social and state activities
- Rights to get the national identity cards and be listed in the voters roll
- Mandates enrolment in regular schools, reservation of seats on all forms of public transportation, accessibility provisions in all public places (including retrofitting), equal opportunities in employment, and protection of inherited property rights

Neuro-Developmental Disability Protection Trust Act, 2013

- Highlights the issues related to providing physical, psychological, and economic assistance to all persons with disabilities
- Their nurture, security and rehabilitation
- ensures their social empowerment
- Focuses to develop pertinent education system and knowledge paradigm

Role Played by Bangladesh in Global Setting

Both within country as well as in the global context, Bangladesh is playing a commendable role in undertaking appropriate policies, and social awareness and intervention programs to mitigate the emerging and increasing problem of autism. Some of the pro-active roles of the Government of Bangladesh include the formation of South Asian Autism Network (SAAN) and preparation of its Charter.

In July 2012, Bangladesh hosted the largest regional conference on autism during which the Dhaka Declaration on Autism Spectrum Disorders was ratified by 7 regional countries. Bangladesh tabled "Resolution 67/82" addressing the socioeconomic needs of individuals, families and societies affected by autism spectrum disorders, developmental disorders and associated disabilities at the United General Assembly in 2013 which was unanimously adopted. Bangladesh was also the one to initiate the WHO resolution titled "Comprehensive and coordinated efforts for the management of autism spectrum disorders" proposed by the state of Qatar to the WHO Executive Board meeting held in May 2013, which was adopted unanimously.

Institutional Development Accomplished

- In 1999, Jatiyo Protibondhi Unnayan Foundation (JPUF) was founded to ensure that the persons with disabilities have adequate support to participate in the mainstream society
- In June of 2010 The Center for Neurodevelopment and Autism in Children (CNAC) was inaugurated. It is the first government initiative that is linked to a medical university
- 10 Shishu Bikash Kendra (Child Development Centers) in medical college hospitals has been established
- 73 Disability Service Centre is functioning in district & upazila level having an special Autism Corner. Another 60 is under process.
- The JPUF has been running a special school for the autistic children since 2011. 30 children with disabilities from 30 poor families are studying in this special school without any tuition fee

Approaches to Educate Children with Neuro Developmental Disorders (NDDs)

- Autism has been incorporated in the primary education curriculum
- Development of strategic action plan for children with special needs under umbrella of inclusive education
- Development of a module on autism sensitization by the National Academy for Education Management (NAEM)
- Inclusion of autism in national curriculum of Text Book Board "autism" as a subject in the "Physical Teaching, Health Science and Sports" book of Class IX and X and in "Economics" book of Class VIII
- Allowance of 20 minutes additional time in public examinations for all children with autism
- Allocation of 2% reserved seats for autistic children for admission in academic institutions not run by the public sector

Research and Skill Development Initiated

Two national level survey projects have been conducted:

- First was a door to door survey for all form of disabilities conducted by Ministry of Social Welfare
- Second, a pilot screening project for developmental disorders in children through the community health clinics

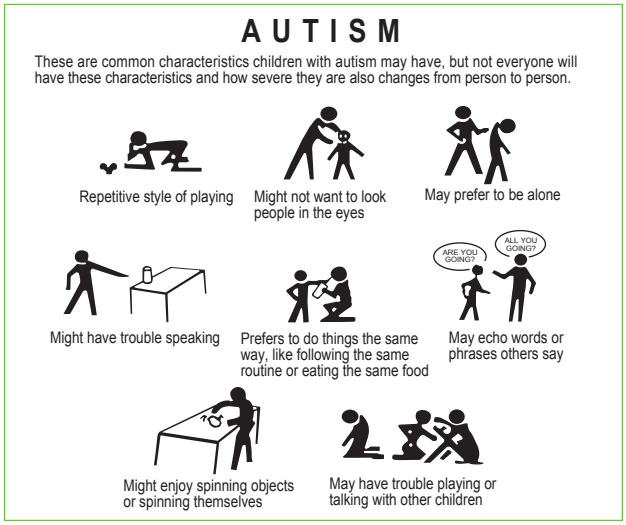

Figure-1 : Autism characteristics

Arranged training of 3676 doctors, 480 nurses, 270 physiotherapists, and 186 special educators in Center for Neurodevelopment & Autism in Children, Bangabandhu Sheikh Mujib Medical University (BSMMU) and in National Institute of Mental Health

Arranged training of 2,575 health workers and social activists through 103 batches on autism and neuro-developmental disabilities in 70 sub-districts of 64 districts of Bangladesh

JPUF (Jatiyo Protibondhi Unnayan Foundation) has developed the capacity to conduct following training programs :

- Training for the mothers of mentally challenged children
- Behavior modification and picture exchange communication system and
- Autism and development disorder management training of parents' role in managing children with ASD

Public Awareness in Bangladesh

Every year, on 2nd April, the Ministry of Health and Family Welfare (MoHFW) observes the World Autism Awareness Day. The Ministry of Primary and Mass Education (MoPME) has developed a short episode of 'Meena' cartoon to raise awareness of autism. The MoPME staged an interactive popular theater in 158 sub-district level on autism. Today, Bangladesh is a leading country championing the cause of autism at national, regional and global levels

References :

- http://www.autism-society.org/
- http://www.nlm.nih.gov/medlineplus/autismspectrumdisorder.html
- Autistic Children's Welfare Foundation, Bangladesh.
- Society for the Welfare of Autistic Children

Colorectal carcinoma is a common condition. It is the third most common cancer worldwide and the fourth most common cause of death. Worldwide, colorectal cancer represents 9.4% of all incident cancer in men and 10.1% in women. It affects men and women almost equally. It is more common in urban people. About two thirds of all colorectal neoplasm develops in the colon and the remainder in the rectum. Most are adenocarcinomas which evolve from polyps.

Geographical Variations

Colorectal cancer is not uniformly common throughout the world. There is a large geographic difference in the global distribution of colorectal cancer. It is mainly a disease of developed countries with a Western culture. In fact, the developed world accounts for over 63% of all cases. The incidence rate varies up to 10-fold between countries with the highest rates and those with the lowest rates. It ranges from more than 40 per 100,000 people in the United States, Australia, New Zealand, and Western Europe to less than 5 per 100,000 in Africa and some parts of Asia. 108,100 and 40,800 individuals were diagnosed with cancer of the colon and rectum, respectively in 2005 in United States. For 2008, it was estimated that ~148,900 new cases would be diagnosed and ~49,900 people would die of the disease.

Different populations worldwide experience different incidence rates of colorectal cancer, and these rates change with time. In parts of Northern and Western Europe, the incidence of colorectal cancer may be stabilizing, and possibly declining gradually in the United States. Elsewhere, the incidence is increasing rapidly, particularly in countries with a high-income economy that have recently made the transition from a relatively low-income economy, such as Japan, Singapore, and Eastern European countries. Incidence rates have at least doubled in many of these countries since the mid-1970s.

Risk Factors

Several risk factors are associated with the incidence of colorectal cancer. Those that an individual cannot control include age and hereditary factors. In addition, colorectal cancer is widely considered to be an environmental disease, with a substantial number of environmental and lifestyle risk factors may play an important role in the development of colorectal cancer. Environmental role has been identified from studies in migrants and their offspring. Among migrants from low-risk to high-risk countries, incidence rates of colorectal cancer tend to increase toward those typical of the population of the host country. For example, colorectal cancer incidence in the offspring of Japanese migrants to the United States now approaches or surpasses that in the white population, and is three or four times higher than among the Japanese in Japan.

❑ ***Age :***

Incidence of colorectal cancer increases after the age of 40, rising sharply after the age 50. More than 90% of colorectal cancer cases occur in people aged 50 or older. However, colorectal cancer appears to be increasing among younger persons. In fact, in the United States, colorectal cancer is now one of the 10 most commonly diagnosed cancers among men and women aged 20 to 49 years.

❑ ***Personal history of adenomatous polyps :***

Neoplastic tubular and villous polyps/adenomas of the colon and rectum are precursor lesions of colorectal cancer. Nearly 95% of sporadic colorectal cancers develop from these adenomas. A long latency period, estimated at 5 to 10 years, is usually required for the development of malignancy from adenomas. Detection and removal of an adenoma prior to malignant transformation may reduce the risk of colorectal cancer.

❑ ***Personal history of inflammatory bowel disease :***

Inflammatory bowel disease (Ulcerative colitis and Crohn's disease) increase an individual's overall risk of developing colorectal cancer. The relative risk of colorectal cancer in patients with IBD is estimated between 4- to 20-fold. Therefore, regardless of age individuals with IBD are highly encouraged to be screened for colorectal cancer on a more frequent basis.

❑ ***Family history of colorectal cancer or adenomatous polyps :***

Though the majority of colorectal cancer cases occur in persons without a family history, up to 20% of people with colorectal cancer have other family members affected by this disease. It is higher in people with a stronger family history, such as a history of colorectal cancer or adenomatous polyps in any first-degree relative younger than age 60 or a history of colorectal cancer or adenomatous polyps in two or more first-degree relatives at any age.

❑ ***Inherited genetic risk :***

Approximately 5 to 10% of colorectal cancers are a consequence of recognized hereditary conditions. The most common inherited conditions are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC), also called Lynch syndrome. FAP is caused by mutations in the tumor suppressor gene APC. HNPCC is associated with mutations in genes involved in the DNA repair pathway, namely the MLH1 and MSH2 genes.

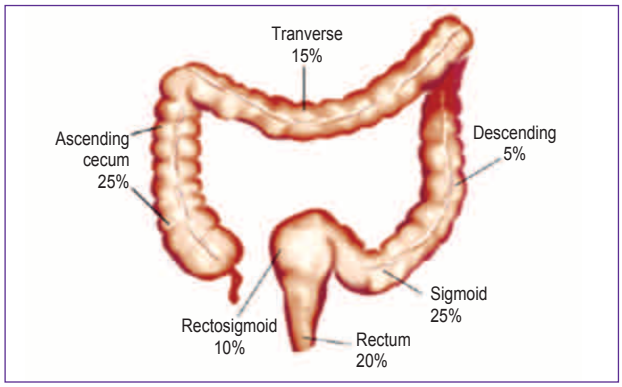

Figure : Large intestine

HNPCC may account for ~2 to 6% of colorectal cancers. The lifetime risk of colorectal cancer in people with the recognized HNPCC-related mutations may be as high as 70 to 80% and the average age at diagnosis in their mid-40s. FAP accounts for less than 1% of all colorectal cancer cases. Unlike individuals with HNPCC, who develop only a few adenomas, people with FAP characteristically develop hundreds of polyps, usually at a relatively young age, and one or more of these adenomas typically undergoes malignant transformation as early as age 20. By age 40, almost all people with this disorder will have developed cancer if the colon is not removed. Prenatal testing and pre-implantation genetic diagnosis are possible if a disease-causing mutation is identified in an affected family member.

- ***Nutritional practices :***

Diet strongly influences the risk of colorectal cancer, and changes in food habits might reduce up to 70% of this cancer burden. Diets high in animal fat and red meat are a major risk factor for colorectal cancer.

The implication of fat, as a possible etiologic factor, is linked to the concept of the typical Western diet, which favors the development of a bacterial flora capable of degrading bile salts to potentially carcinogenic N-nitroso compounds. Potential underlying mechanisms for a positive association of red meat consumption with colorectal cancer include the presence of heme iron in red meat. In addition, some meats are cooked at high temperatures, resulting in the production of heterocyclic amines and polycyclic aromatic hydrocarbons, both of which are believed to have carcinogenic properties.

In addition, some studies suggest that people who eat a diet low in fruits and vegetables may have a higher risk of colorectal cancer. Differences in dietary fiber intake might have been responsible for the geographic differences in the colorectal incidence rates. For example, dietary fiber has been proposed as accounting for the differences in the rates of colorectal cancer between Africa and Westernized countrieson the basis that increased intake of dietary fiber may dilute fecal content, increase fecal bulk and reduce transit time.

- ***Physical activity and obesity :***

Several lifestyle-related factors have been linked to colorectal cancer. Two modifiable and interrelated risk factors, physical inactivity and excess body weight, are reported to account for about a fourth to a third of colorectal cancers. There is abundant evidence that higher overall levels of physical activity are associated with a lower risk of colorectal cancer, including evidence of a dose-response effect, with frequency and intensity of physical activity inversely associated with risk.

- ***Cigarette smoking :***

The association between cigarette smoking and lung cancer is well established, but smoking also is extremely harmful to the colon and rectum. Evidence shows that 12% of colorectal cancer deaths are attributed to smoking. The carcinogens found in tobacco increase cancer growth in the colon and rectum, and increase the risk of being diagnosed with this cancer. Cigarette smoking is important for both formation and growth of adenomatous polyps, the recognized precursor lesions of colorectal cancer. Larger polyps in the colon and rectum had been associated with long-term smoking. Evidence also demonstrates an earlier average age of onset of colorectal cancer among who smoke cigarettes.

- ***Heavy alcohol consumption :***

As with smoking, the regular consumption of alcohol may be associated with increased risk of developing colorectal cancer. Alcohol consumption is a factor in the onset of colorectal cancer at a younger age as well as a disproportionate increase of tumors in the distal colon. Reactive metabolites of alcohol such as acetaldehyde can be carcinogenic. There is also an interaction with smoking. Tobacco may induce specific mutations in DNA that are less efficiently repaired in the presence of alcohol. Alcohol may also function as a solvent, enhancing penetration of other carcinogenic molecules into mucosal cells. Additionally, the effects of alcohol may be mediated through the production of prostaglandins, lipid peroxidation and the generation of free radical oxygen species. Lastly, high consumers of alcohol may have diets low in essential nutrients, making tissues susceptible to carcinogenesis.

Clinical Presentation

The clinical presentation of colorectal cancer depends on the affected sites. Some others features may also be present linking the presence of colorectal cancer.

- Some patients remain asymptomatic until the cancer is far advanced
- The most common presenting features of colorectal cancer or large polyps are per rectal bleeding, persisting alteration in bowel habit and anemia
- If right colon is affected, there may be weight loss, anemia, occult bleeding, mass in right iliac fossa
- If left colon is affected, there may be often colicky pain, rectal bleeding, bowel obstruction, tenesmus, mass in left iliac fossa, early change in bowel habit
- During presentation, the disease more likely to be advanced in right colon cancer then left colon and rectal cancer
- Approximately 55% of patients present with advanced colorectal cancer with spread to the local lymph nodes and distant metastasis to other organs
- Jaundice and hepatomegaly indicate advanced disease with extensive liver metastases (20-25% of patients have clinically detectable liver metastases at the time of the initial diagnosis and a further 40-50% of patients develop liver metastases within three years of primary surgery)
- Peritoneal metastases with ascites are often also present
- Metastasis in sites without liver and peritoneum e.g., lungs, brain and bone are unusual
- Rarer clinical features include: pneumaturia, gastrocolic fistula, ischiorectal or perineal abscesses, deep vein thrombosis etc.

Differential Diagnosis

- Diverticular disease
- Irritable bowel syndrome
- Inflammatory bowel disease
- Local rectal pathology, eg haemorrhoids
- Anal cancer
- Ischaemic colitis
- Pneumatosis coli

Investigations

- **Colonoscopy :** Colonoscopy is the gold standard for diagnosis of colorectal cancer. It should be offered to all patients suspected to have colorectal carcinoma unless major co-morbidity. This usually confirms the presence of neoplasm in the colon and rectum. It also allows taking biopsy sample from a suspicious lesion.
- **Flexible sigmoidoscope :** It can reach deep enough into the bowel to detect about 60% of growth;

- **Barium enema :** It can be used as an alternative to colonoscopy for patients with major co-morbidity and when colonoscopy fails to visualize the caecum.
- **Computed tomographic (CT) colonography :** It can also an effective and safe as an alternative to colonoscopy; if a lesion suspicious of cancer is detected on CT colonography, a colonoscopy with biopsy to confirm the diagnosis should be performed.
- **Imaging :** Ultrasonography of the liver (occasionally intra-rectal ultrasound) and CT/MRI are useful in staging; MRI is more specific than CT in showing liver metastases.
- **Positron Emission Tomography (PET) :** It is valuable for detection of recurrent colorectal cancer, but has little effect on staging of primary cancer
- **Carcinoembryonic Antigen(CEA) :** Elevated pre-treatment serum levels of CEA have a negative prognostic significance
- **Others :** Full blood count, renal function tests and liver function tests

Staging

Contrast-enhanced CT of the chest, abdomen and pelvis should be used to estimate the stage of disease for patients with colon cancer.

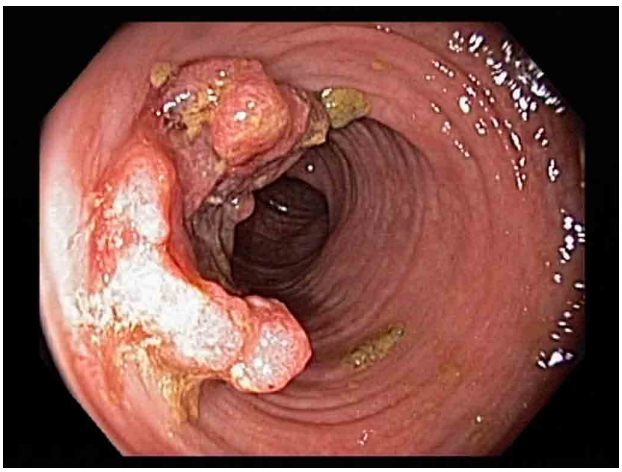

Figure : Colon Cancer

MRI should be used to assess the risk of local recurrence, as determined by anticipated resection margin, tumor and lymph node staging, to all patients with rectal cancer. If intracranial disease is suspected clinically then a contrast-enhanced MRI of the brain should be performed.

The well-known Dukes' staging classification is now gradually being replaced by the tumor/node/ metastases (TNM) classification :

- TX: primary cannot be assessed
- T0: no evidence of primary carcinoma in situ (Tis) - intraepithelial or lamina propria only.
- T1: invades submucosa.
- T2: invades muscularis propria.
- T3: invades subserosa or non-peritonealised pericolic tissues.
- T4: directly invades other tissues and/or penetrates visceral peritoneum.
- NX: regional nodes cannot be assessed.
- N0: no regional nodes involved.
- N1: 1-3 regional nodes involved.
- N2: 4 or more regional nodes involved.
- MX: distant metastasis cannot be assessed.
- M0: no distant metastasis.
- M1: distant metastasis present (may be transcoelomic spread).

Management

Surgery remains the definitive treatment for apparently localized colorectal cancer. Both radiotherapy and chemotherapy can improve survival rates after potentially curative surgery, and chemotherapy prolongs overall survival in patients with advanced disease.

If colonic stents are considered for patients presenting with acute large bowel obstruction, CT of the chest, abdomen and pelvis should be offered to confirm the diagnosis of mechanical obstruction, and to determine whether the patient has metastatic disease or colonic perforation.

A. Surgery :

Surgery may be performed either to attempt cure (removing the draining lymphatic field) or to relieve symptoms: various types of resections are practiced:

- One of the most important advances for surgery of rectal cancer has been the concept of total mesorectal excision, which reduces local recurrences and perioperative morbidity.
- Right hemicolectomy: for tumors in the caecum, ascending and proximal transverse colon.
- Left hemicolectomy: for tumors in the distal transverse colon or descending colon.
- Sigmoid colectomy: for tumors in the sigmoid colon.
- Anterior resection: if in the low sigmoid or high rectum; anastomosis is achieved at the first operation.
- Abdomino-perineal (AP) resection: for tumors low in the rectum (less than approximately 8 cm from the anal canal); permanent colostomy and removal of rectum and anus is required.
- Laparoscopic surgery (including laparoscopically assisted surgery) may be considered as an alternative to open surgery for some people with colorectal cancer.

Preoperative high-dose rate brachytherapy can be used before surgery, in patients with cancer in the middle or lower third of the rectum, to shrink the tumor. There is evidence for short-term safety and efficacy in reducing tumor bulk but evidence about the advantages of the procedure as an adjunct to surgery and its effect on long-term survival is currently inadequate.

B. Radiotherapy :

- For cancer of the rectum, radiotherapy decreases local recurrence (50% of recurrences of rectal cancer occur in the pelvis) and it improves quality of life and increases survival by 6-12 months for patients with advanced disease.

- The National Institute for Health and Clinical Excellence (NICE) recommends that radiofrequency ablation should be considered for colorectal liver metastases in patients unfit or otherwise unsuitable for hepatic resection, or in those who have previously had hepatic resection
- For patients who have previously been treated with chemotherapy, there is evidence that selective internal radiation therapy (SIRT) can prolong time to progression of non-resectable colorectal metastases in the liver.

C. Chemotherapy :

NICE recommends that when offering multiple chemotherapy drugs to patients with advanced and metastatic colorectal cancer, one of the following sequences of chemotherapy should be considered unless contra-indicated:

- FOLFOX (folinic acid plus 5-fluorouracil plus oxaliplatin) as first-line treatment, then single agent irinotecan as second-line treatment; or
- FOLFOX as first-line treatment, then FOLFIRI (folinic acid plus fluorouracil plus irinotecan) as second-line treatment; or
- XELOX (capecitabine plus oxaliplatin) as first-line treatment then FOLFIRI as second-line treatment.
- Raltitrexed should only be considered for patients with advanced colorectal cancer who are intolerant to 5-fluorouracil and folinic acid, or if these drugs are not suitable.
- Capecitabine and oxaliplatin(given together with 5-fluorouracil and folinic acid) are recommended as possible adjuvant treatments after surgery for stage III (Dukes C) colon cancer
- Irinotecan and oxaliplatin are recommended as possible treatments for people with advanced colorectal cancer
- Cetuximab in combination with FOLFOX or FOLFIRI is recommended for the first-line treatment of metastatic colorectal cancer only when all of the next criteria are met: the primary colorectal tumor has been resected or is potentially operable, the metastatic disease is confined to the liver and is unresectable, the patient is fit enough to undergo surgery to resect the primary colorectal tumor and to undergo liver surgery if the metastases become resectable after treatment with cetuximab.
- Bevacizumab in combination with oxaliplatin and either 5-fluorouracil plus folinic acid or capecitabine is not recommended for the treatment of metastatic colorectal cancer.

D. Palliative therapy:

- Resection of metastatic disease (hepatic or pulmonary metastases) can lead to 5-year survival rates of 35-58%
- Patients with solitary, multiple, and bi-lobar disease who have had radical treatment of the primary colorectal cancer, are candidates for liver resection.
- For patients with metastatic colorectal cancer, chemotherapy aims to improve survival and quality of life.
- About 15% of patients with liver metastases initially judged to be unresectable will become resectable after systemic chemotherapy, with excellent long-term survival.

Follow-up

After apparently curative resection NICE recommends :

- A minimum of two CT scans of the chest, abdomen, and pelvis in the first three years; and
- Regular serum carcinoembryonic antigen (CEA) tests (at least every six months in the first three years).

Prognosis

Around half of people diagnosed with colorectal cancer survive for at least five years after diagnosis.

- 60% are amenable to radical surgery and 75% of these will be alive at seven years (or will have died from non-tumor-related causes).
- Survival rates relative to age-matched groups without colorectal cancer, are now about 45% at five years after diagnosis. Beyond five years, relative survival rates decline only slightly (most of those who live this long are cured).
- Survival rates in the UK have been rising steadily over a period of three decades.
- Overall 5-year survival rates:
  - ✔ Stage I (T1,T2, N0, M0) 80-95%.
  - ✔ Stage IIA (T3, N0, M0) 72-75%.
  - ✔ Stage IIB (T4, N0, M0) 65-66%.
  - ✔ Stage IIIA (T1,T2, N1, M0) 55-60%.
  - ✔ Stage IIIB (T3,T4, N1, M0) 35-42%.
  - ✔ Stage IIIC (any T, any N, M1) 0-7%.

Prevention

Lower risk has been linked with:

- Decreased consumption of red meat and dietary fat
- Increased physical activity
- Cessation of smoking
- Frequent consumption of fresh vegetables and fruit
- Good nutrition
- Once daily aspirin reduces the risk of developing colorectal cancer

References :

- www.patient.co.uk/doctor/colorectal-cancer
- Clinics in Colon and Rectal Surgery

Test Yourself - 35

Correct Answers :

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

CONGRATULATIONS!

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Test Yourself - 36

1. The followings are true for "Otosclerosis" except :

a. Women aged between 15 & 30 years are most commonly affected than men.
b. The exact cause is not entirely known.
c. This condition tends to run in families.
d. In this condition only one ear is affected.

2. All the followings are correct for "Colorectal Carcinoma" except :

a. It is 3rd most common cancer worldwide and the 4th most common cause of death.
b. This cancer is uniformly common throughout the world.
c. Inflammatory bowel disease increases an individual's risk of developing this cancer.
d. Diets high in animal fat and red meat are major risk factors.

3. All the below are true for "Autism" except :

a. About one percent of the world population has ASD.
b. Sensory processing disorder can present symptoms similar to Autism.
c. It is caused only by the abnormalities in the brain structure.
d. The characteristic behaviors of ASD become clearer during 24 months to 06 years.

4. All the followings are correct for "Ebolavirus" except :

a. The name Ebolavirus is derived from the Ebola river in Zaire.
b. Symptoms may appear anywhere from 2 - 21 days after exposure to Ebolavirus.
c. An experimental Ebola vaccine appears on November 2014.
d. The virus can be spread from person to person through direct contact with blood or body fluids.

5. The followings are right for "Colorectal Cancer" except :

a. Jaundice and hepatomegaly indicate advanced disease with extensive liver metastasis.
b. The most common presenting features are per rectal bleeding, persisting alteration in bowel habit and anemia.
c. TNM classification is usually followed until now during staging of this cancer.
d. About half of people diagnosed with this condition survive for at least five years after diagnosis.

6. All the followings are correct for "Substance Abuse Disorder" except :

a. 70 percent of the tobacco deaths occur before the age of 60 years.
b. CBT and MET are the evidence-based psychosocial treatments.
c. There are six medications approved by USFDA for nicotine dependence.
d. For methamphetamine dependence there are no approved pharmacological treatments.

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