

the SQUARE

Londonia

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Fditorial

Dear Doctor:

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

We hope you've been enjoying this publication very much!

This issue of "the *SQUARE*" features a variety of articles including "chronic cough", is the most common presenting symptom in adults who seek medical treatment in an ambulatory setting. The management of chronic cough presents a challenge for the clinician. We also bring you all the details on "viral gastroenterology", a leading cause of severe diarrhea in both adults and children. We have also focused on "breast cancer", the second most common type of cancer in women. In addition, we highlighted on "Dyslexia", a learning disability that can hinder a person's ability to read, write, spell, and sometimes speak.

Besides, our regular feature comprises "SQUARE in International Business" as well.

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

Finally, on behalf of the management of *SQUARE*, we wish you an ecstatic, healthy and prosperous life.

Thank you!

Omar Akramur Rab

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Managing Editor Omar Akramur Rab MBBS, FCGP, FIAGP PG Dip. Business Management (India)

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Associate Editor Md. Mahfuzur Rahman Sikder MBBS

Members of the Editorial Board Muhammadul Haque MBA A. H. Mahbub Alam M Pharm. PhD

Special Contribution Kazi Shamim Al Mamun MBBS Md Muhitul Matin MBBS

Acknowledgement Product Management Department International Marketing Department

Information Assistance Md. Masudul Alam

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Cough is an important physiologic mechanism that defends against respiratory pathogens and helps clear the tracheobronchial tree of mucus, foreign particles and noxious aero-sols. Excessive cough is one of the most common symptoms for which patients seek medical care and may represent up to one-third of a pulmonologist's outpatient practice referrals. Estimating the duration of cough is the first step in narrowing the list of possible diagnoses. There is controversy about how best to define chronic cough. According to the current study, chronic cough affects 10% to 20% of adults and is defined as lasting longer than 8 weeks in adults and longer than 4 weeks in children.

The Pathophysiology of Cough

The pathophysiology of cough is incompletely understood. Cough is commonly triggered by mechanical or chemical stimulation of receptors in the pharynx, larynx, trachea and bronchi. Cough receptors also exist in the nose, paranasal sinuses, external auditory ear canals, tympanic membranes, parietal pleura, esophagus, stomach, pericardium and diaphragm.

Signs and Symptoms of Chronic Cough

Although the signs of a cough are self-explanatory, what differentiates the cause of a cough are the associated signs and symptoms. The signs and symptoms of the chronic cough can be hard to assess, because many causes of the chronic cough have overlapping signs and symptoms.

A chronic cough can occur with other signs and symptoms, which may include:

- □ A runny or stuffy nose
- A sensation of liquid running down the back of the throat
- Wheezing and shortness of breath
- Heartburn or a sour taste in the mouth
- In rare cases, coughing up blood

Causes of Chronic Cough

The etiologies of chronic cough are numerous and may include pathology from the nose and nasopharynx to the distal bronchial tree. Obvious causes of chronic cough such as low--grade chronic

condition is simultaneously present.

immunocompetent, nonsmoking patients with normal chest radiograph findings. In order of frequency, they are as follows: 1. Upper airway cough syndrome (UACS), previously

Chronic Cough

- referred to as postnasal drip syndrome (PNDS)
- 2. Asthma
- 3. Gastroesophageal reflux disease (GERD)

These 3 conditions make up what is called the "pathogenic triad of chronic cough."

A fourth etiology that deserves mention is nonasthmatic eosinophilic bronchitis (NAEB), which is relatively common, easy to diagnose and treat and should be considered early on in the diagnostic evaluation.

Focusing on the diagnosing and treating these conditions is extremely successful at treating chronic cough.

Upper airway cough syndrome

Postnasal drip syndrome refers to the sensation of secretions from the nose or sinuses that drain into the pharynx in addition to nasal discharge and frequent throat clearing. Unfortunately, this is largely based on patients' subjective symptoms, which frequently do not show any significant physical examination findings. In fact, 20% of patients with PNDS-induced cough are unaware of the presence of postnasal drip or its link to their cough. Even the presence of mucus in the oropharynx or cobblestoning of the oropharyngeal mucosa only suggest this as a cause. These findings are sensitive but not specific.

PNDS has been broadened to UACS, referring to a myriad of rhinosinus conditions that are related to cough. A nasal discharge, frequent need to clear the throat and mucoid or mucopurulent secretions in the posterior pharynx suggest an upper airway cough syndrome. Sinus imaging may be diagnostic of acute or chronic sinusitis.

UACS includes the following:

- □ PNDS
- Allergic rhinitis
- Vasomotor rhinitis Nonallergic rhinitis with
- eosinophilia (NARES) Postinfectious rhinitis
- Bacterial sinusitis
- Allergic fungal sinusitis
- **□** Rhinitis due to anatomic abnormalities **□** Rhinitis due to physical
- or chemical irritants
- Occupational rhinitis Rhinitis medicamentosa
- □ Rhinitis of pregnancy

UACS is considered the most common cause of chronic cough and has been implicated as the cause in up to 87% of patients.

Although oftentimes a causative etiology for the rhinitis might be suggested from the patient's history and symptomatology, the hallmark of UACS is that this syndrome has no pathognomonic findings and the diagnosis



the clinician lies in how to efficiently and systematically evaluate

the patient without an overly exhaustive workup. Further

compounding this is the fact that oftentimes more than one

Prospective studies have shown that 3 conditions account for

the etiologic cause of chronic cough in 92-100% of



Chronic Cough

is made on the basis of response to specific therapy, which includes antihistamines and decongestants.

Asthma

The hallmarks of asthma are variable airflow obstruction and airway hyperresponsiveness, which manifest as shortness of breath, wheezing, dyspnea and cough. Cough occurs in all asthmatics and in a subset of patients with cough-variant asthma (CVA), it is the only presenting symptom.

Gastroesophageal reflux disease

The following 2 mechanisms have been postulated for GERD-associated cough:

- Distal esophageal acid exposure that stimulates an esophageal-tracheobronchial cough reflex via the vagus nerve
- Decomposition of esophageal contents into the laryngopharynx and tracheobronchial tree

The second cause is called laryngopharyngeal reflux (LPR) or extraesophageal or silent GERD, and it differs from traditional GERD in that it does not manifest as heartburn and tends to occur when the patient is upright as opposed to lying flat. This silent GERD can be present in as many as 75% of patients with chronic cough. Symptoms of LPR include throat clearing, hoarseness and globus sensation.

Nonasthmatic eosinophilic bronchitis

Nonasthmatic eosinophilic bronchitis has been implicated as an etiology of chronic cough in 13-33% of patients. It is characterized by eosinophilic infiltration of the bronchial tree as well as the absence of variable airflow obstruction and airway hyperresponsiveness.

Other causes

A myriad of other causes account for the remaining 5-10%. They include the following:

- □ Bronchiectasis
- □ Bronchiolitis
- Bronchogenic carcinoma Pertussis
- □ Chronic aspiration
- obstructive 🗅 Sarcoidosis Chronic pulmonary
 - (COPD)
- (CHF)
- □ Foreign body

Evaluation of Children

In children, upper and lower respiratory tract infections, asthma and GERD are the most common causes of chronic cough. In older children, cough-variant asthma, sinusitis and psychogenic cough increase in frequency.

The evaluation of chronic cough in children is similar to the evaluation in immunocompetent adults. However, in younger children, the adenosine 5'-monophosphate bronchial challenge has been shown to be more specific than the methacholine challenge (87 percent versus 57 percent) in differentiating asthma from other chronic pulmonary diseases of childhood.

In children, asthmatic symptoms may be caused by GERD (prevalence ranging from 34 percent to 89 percent). Some evidence suggests that treatment of GERD with antireflux medications may reduce the symptoms of asthma, leading to a reduction in asthma medication requirements.

Sinusitis, tuberculosis, pertussis and cystic fibrosis are other causes of chronic cough that should be considered in children. Foreign body aspiration is a possibility in young children who have chronic cough. Recurrent infections may indicate an immunologic disorder as the cause of cough.

Finally, chronic cough in children can be caused by several congenital abnormalities and disorders, including vascular rings, tracheoesophageal fistulas and primary ciliary dyskinesia. However, these conditions are rare.

Workup and Management

An anatomic and diagnostic approach has been recommended as a framework for workup of chronic cough with demonstrated success in treatment in up to 98% of patients.

Every patient with chronic cough needs a thorough history taken and physical examination performed as part of their evaluation. The history and physical examination should attempt to identify anatomic locations of the afferent limb of the cough reflex in light of the common causes.

The character and timing of chronic cough and the presence or absence of sputum production do not permit an etiologic diagnosis and should not be used as the sole basis for empiric therapy. What is of value from the medical history is whether or not the patient is or has been a smoker; is taking an ACE inhibitor; is living in a geographic area where tuberculosis or certain fungal diseases are endemic; has any systemic symptoms, a history of cancer, tuberculosis or AIDS; or has a large pulmonary mass visible on chest radiograph.

Chest imaging is best reserved for evaluation of cough in smokers; in patients with hemoptysis or constitutional symptoms, such as fever and weight loss; and in persons with chronic cough that does not respond to initial therapy.

If the chest radiograph findings are abnormal, further workup depends on the specific finding. Chest CT scan, bronchoscopy, needle biopsy and sputum studies are all potentially warranted studies if a pulmonary lesion is found.

The management of chronic cough presents a challenge for the clinician. Management should begin with elimination of

□ Psychogenic cough

□ Interstitial lung disease

Neuromuscular disorders

- disease 🗅 Tracheoesophageal fistula
 - □ Tuberculosis
- □ Congestive heart failure □ Zenker diverticulum

irritant exposures such as tobacco smoke (primary or secondary) and occupational agents or ACE inhibitor use in those patients whose history indicates such action. Most patients have a resolution of their cough within 4 weeks of smoking cessation. Cough related to ACE inhibitor use usually subsides within 2 weeks, but the median time has been reported to be 26 days.

For the immunocompetent nonsmoker who does not use ACE inhibitors and has normal chest radiograph findings, a systematic approach to the most common causes of chronic cough is warranted, keeping in mind that more than one cause may be present. The body of literature regarding specific treatments and the expected time frame of response is extensive and the accuracy of the diagnosis is confirmed by the patient's response to these treatments. From both theoretical and cost effectiveness standpoints, empiric treatment of the 3 most common causes of cough is favored over extensive testing at the outset. Further, sequential and additive therapy may be needed because more than one cause of cough is often present.

Upper airway cough syndrome

Because upper airway cough syndrome (UACS) is the most common cause of chronic cough, it should be treated first. In patients in whom the cause of the UACS-induced cough is apparent, specific therapy directed at this condition should be instituted. This includes avoiding environmental irritants and offending antigens, treating sinusitis with antibiotics and weaning patients of nasal decongestants for rhinitis medicamentosa. Further workup may include allergy testing for allergic rhinitis or sinus CT scan for sinusitis, as indicated.

For patients in whom the cause is not apparent, empiric therapy should be instituted with a combination of an antihistamine and decongestant. First-generation antihistamines such as azatadine and dexbrompheniramine plus pseudoephedrine have shown more effectiveness than newer, less-sedating antihistamines. Patients typically respond within 2 weeks of initiating therapy but may sometimes take several months. Upper airway cough syndrome due to allergic rhinitis that does not respond to antihistamines should be treated with intranasal corticosteroids. Chronic sinusitis may require prolonged antibiotics directed against Haemophilus influenzae.

Asthma

Asthma should be considered only after the UACS evaluation and empirical treatment trial are complete. Wheezing on chest auscultation or airflow obstruction on pulmonary function tests suggests asthma. Ideally, patients should undergo spirometry and bronchoprovocation challenge with methacholine, which reveals reversible airflow obstruction.

The initial treatment of asthma consists of beta-2 agonists and inhaled corticosteroids (ICS) and response is usually seen

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within 1 week, with complete resolution taking up to 8 weeks. Some patients may require a trial of oral corticosteroids before a response is seen. However, because leukotriene inhibitors have been shown to be effective in patients with asthma-induced cough, they should be tried prior to oral corticosteroid therapy. Cough caused by asthma that does not respond after 2 weeks of bronchodilators and corticosteroids suggests another contributing condition.

Gastroesophageal reflux disease

Prospective studies have shown that in a patient who has undergone empiric therapy for UACS, asthma, and NAEB and has had no response or only a partial response, a 92% probability exists that their chronic cough is due to GERD. The criterion standard for diagnosis of GERD is dual-channel 24-hour pH probe monitoring. Alternatively, flexible nasopharyngoscopy can reveal glottic changes associated with reflux. These include laryngeal edema and erythema, laryngeal pseudosulcus, and posterior commissure hypertrophy or pachydermia.

Simply because of the percentages, empiric therapy with acid suppression and lifestyle and dietary modification has been advocated as initial management instead of testing, which is reserved for refractory cases. Lifestyle modifications include limiting fat intake; avoiding caffeine, chocolate, mints, citrus products, alcohol, and smoking; and limiting vigorous exercise that increases intraabdominal pressure.

The choice of acid suppressive medication can include histamine 2 (H2) blockers, proton pump inhibitors (PPIs), and prokinetic agents. However, note that maximal medical therapy refers to twice daily PPI (since H2 blockers may be inadequate) in addition to a prokinetic agent with concurrent lifestyle and dietary modifications. Although response can be seen in as little as 2 weeks, at least a 6-8 week trial is needed to fully evaluate a response to treatment, with some patients requiring as long as 6 months.

Nonallergic eosinophilic bronchitis

Because its diagnosis is made easily, nonallergic eosinophilic bronchitis (NAEB) is the next etiology to consider, even though GERD is more common. An induced sputum test that reveals increased eosinophils is the diagnostic procedure of choice. Treatment includes inhaled corticosteroid (ICS), with oral corticosteroids reserved for refractory cases. Response is usually seen within 4 weeks.

References : eMedicine Mayo Clinic American Family Physician The New England Journal of Medicine Current Medical Diagnosis and Treatment 2008 National Lung Health Education Program

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Breast cancer is the second leading cause of cancer deaths in women today (after lung cancer) and is the most common cancer among women, excluding nonmelanoma skin cancers. Breast cancer death rates have been dropping steadily since 1990, because of earlier detection and better treatments.

In general, breast cancer rates have risen about 30% in the past 25 years in western countries, due in part to increased screening which detects the cancer in earlier stages. In the United States, though, breast cancer rates decreased by 10% between 2000-2004, due in part to a reduction in the use of hormone replacement therapy. Although breast cancer rates are rising in many western countries, deaths from the disease have decreased in some countries as a result of improved screening and treatment.

Breast cancer is mostly, though not exclusively, a disease of women. The incidence of the disease increases with age, with an inflection around menopause, which is not evident for other forms of cancer. It is generally more common among urban rather than rural residents as well as among women of higher socioeconomic status. In comparison to Asian women in China or Japan, Cauca-sian women in the western world have a considerably higher breast cancer risk.

Family history has long been known to be a risk factor for breast cancer. Both maternal and paternal relatives are important. The risk is highest if the affected relative developed breast cancer at a young age, had cancer in both breasts, or if she is a close relative. First-degree relatives, (mother, sister, daughter) are most important in estimating risk. Several second-degree relatives (grandmother, aunt) with breast cancer may also increase risk. Having relatives with both breast and ovarian cancer also increases a woman's risk of developing breast cancer.

About 5-10% of breast cancers are believed to be hereditary, as a result of mutations, or changes, in certain genes that are passed along in families. BRCA1 (breast cancer 1) and BRCA2 (breast cancer 2) are abnormal genes that, when inherited, markedly increase the risk of breast cancer to a lifetime risk estimated between 40 and 85%. Women with these abnormal genes also have an increased likelihood of developing ovarian cancer. Women who have the BRCA1 gene tend to develop breast cancer at an early age.

The lifetime probability of developing breast cancer in developed countries is about 4.8%, according to the American Cancer Society (the probability is about 13% for any type of cancer). In developing countries, the lifetime probability of developing breast cancer is about 1.8%.

Types of breast cancers :

There are several types of breast cancer, although some of them are quite rare. In some cases a single breast tumor can

FACTORS EVALUATED IN RELATION TO BREAST **CANCER RISK**

Risk factor	Category/change	Strength
Gender	Women vs. men	++++
Age	Increase	+ + + +
Ethnic group	Caucasian vs. Asian	+ + +
Family history	Yes vs. no	+ + +
Specific genes	Yes vs. no	++++
Cancer in other breast	Yes vs. no	+ + +
Height	Increase	+ +
Postmenopausal obesity	Increase	+ +
Birth weight	Increase	+
Having been breastfed	No vs. yes	0
Growth in early life	Increase	+
Atypical hyperplasia	Present vs. absent	+ + +
Mammographic density	High vs. low density	+ + +
(mammary gland mass)	(increasing mass)	
Age at menarche	Earlier	+ +
Age at menopause	Later	+ +
Type of menopause	Natural vs. artificial	+ +
Age at 1st full term pregnancy	Later	+ + +
Age at other pregnancies	Later	+
Parity overall	Lower	+ +
Pregnancy timing	Proximal vs. distant	+
Lactation	No vs. yes	+
Abortion	No vs. yes	0
Oral contraceptive use (recent)	Increase	+
Hormone replacement	Increase	+ +
Plant foods and olive oil	Reduced intake	+
Saturated fat	Increased intake	+
Physical activity	Reduced	+
Ethanol intake	Increase	+
Ionizing radiation	Increased	+
Magnetic fields	Increased	0
Organochlorines	Increased	0

Association : ++++ very strong, +++ strong, ++ modest, + weak, 0 nil have a combination of these types or have a mixture of invasive and in situ cancer.

Ductal carcinoma in situ

Ductal carcinoma in situ (DCIS; also known as intraductal carcinoma) is the most common type of non-invasive breast cancer. DCIS means that the cancer cells are inside the ducts but have not spread through the walls of the ducts into the surrounding breast tissue. DCIS sometimes becomes invasive cancer although it is not known how to tredict which lesions will become invasive.

About 1 in 5 new breast cancer cases will be DCIS. Nearly all women diagnosed at this early stage of breast cancer can be cured. A mammogram is often the best way to find DCIS

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early. DCIS with tumor necrosis is likely to be more aggressive. The term comedocarcinoma is often used to describe DCIS with necrosis.

Lobular carcinoma in situ

Although not a true cancer, lobular carcinoma in situ (LCIS; also called lobular neoplasia) is sometimes classified as a type of non-invasive breast cancer. It begins in the milk-producing glands but does not grow through the wall of the lobules.

LCIS itself does not become an invasive cancer very often, but women with this condition do have a higher risk of developing an invasive breast cancer in the same breast or in the opposite breast. For this reason, women with LCIS should make sure they have regular mammograms.

Invasive (or infiltrating) ductal carcinoma (IDC)

This is the most common type of invasive breast cancer. Invasive (or infiltrating) ductal carcinoma (IDC) starts in a milk passage (duct) of the breast, breaks through the wall of the duct, and grows into the fatty tissue of the breast. At this point, it may be able to spread (metastasize) to other parts of the body through the lymphatic system and bloodstream. About 8 of 10 invasive breast cancers are infiltrating ductal carcinomas.

Invasive (or infiltrating) lobular carcinoma

Invasive lobular carcinoma (ILC) starts in the milkproducing glands (lobules). Like IDC, it can spread (metastasize) to other parts of the body. About 1 out of 10 invasive breast cancers are ILCs. Invasive lobular carcinoma may be harder to detect by a mammogram than invasive ductal carcinoma.

Inflammatory breast cancer : This uncommon type of invasive breast cancer accounts for about 1% to 3% of all breast cancers. Usually there is no single lump or tumor. Instead, inflammatory breast cancer (IBC) makes the skin of the breast look red and feel warm and gives the skin a thick, pitted appearance that looks a lot like an orange peel. The affected breast may become larger or firmer, tender, or itchy. In its early stages, inflammatory breast cancer is often mistaken for infection (mastitis). Because there is no defined lump, it may not show up on a mammogram, which may make it even harder to find it early. It tends to have a higher chance of spreading and a worse outlook than typical invasive ductal or lobular cancer.

Medullary carcinoma : This special type of infiltrating breast cancer has a rather well-defined boundary between tumor tissue and normal tissue. It also has some other special features, including the large size of the cancer cells and the presence of immune system cells at the edges of the tumor. Medullary carcinoma accounts for about 3% to 5% of breast cancers. The outlook (prognosis) for this kind of breast

Breast Cancer

cancer is generally better than for the more common types of invasive breast cancer. True medullary cancer is very rare, and that cancers that are called medullary cancer should be treated as the usual invasive ductal breast cancer.

Breast Cancer Worldwide			
Breast (All ages)	Incidence	Deaths	
China	18.7	5.5	
Zimbabwe	19	14.1	
India	19.1	10.4	
Japan	32.7	8.3	
Brazil	46	14.1	
Singapore	48.7	15.8	
Italy	74.4	18.9	
Switzerland	81.7	19.8	
Australia	83.2	18.4	
Canada	84.3	21.1	
Netherlands	86.7	27.5	
UK	87.3	24.3	
Sweden	87.8	17.3	
Denmark	88.7	27.8	
France	91.9	21.5	
United States	101.1	19	

Note: numbers are per 100,000.Source: J. Ferlay, F. Bray, P. Pisani and D.M. Parkin. GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No. 5, version 2.0. IARCPress, Lyon, 2004.

Metaplastic carcinoma : Metaplastic carcinoma (also known as carcinoma with metaplasia) is a very rare type of invasive ductal cancer. These tumors include cells that are normally not found in the breast, such as cells that look like skin cells (squamous cells) or cells that make bone. These tumors are treated like invasive ductal cancer.

Mucinous carcinoma : Also known as colloid carcinoma, this rare type of invasive breast cancer is formed by mucus-producing cancer cells. The prognosis for mucinous carcinoma is usually better than for the more common types of invasive breast cancer.

Paget disease of the nipple : This type of breast cancer starts in the breast ducts and spreads to the skin of the nipple and then to the areola, the dark circle around the nipple. It is rare, accounting for only about 1% of all cases of breast cancer. The skin of the nipple and areola often appears crusted, scaly, and red, with areas of bleeding or oozing. The woman may notice burning or itching.

Paget disease is almost always associated with either ductal carcinoma in situ (DCIS) or, more often, with infiltrating ductal carcinoma. If no lump can be felt in the breast tissue and the biopsy shows DCIS but no invasive cancer, the prognosis is excellent.

Tubular carcinoma : Tubular carcinomas are another special type of invasive ductal breast carcinoma. They are called tubular because of the way the cells are arranged when seen under the microscope. Tubular carcinomas account for about 2% of all breast cancers and tend to have a better prognosis than most other infiltrating ductal or lobular carcinomas.

Papillary carcinoma : The cells of these cancers tend to be arranged in small, finger-like projections when viewed under the microscope. These cancers are most often considered to be a subtype of ductal carcinoma in situ (DCIS), and are treated as such. In rare cases they are invasive, in which case they are treated like invasive ductal carcinoma, although the outlook is likely to be better. These cancers tend to be diagnosed in older women, and they make up no more than 1% or 2% of all breast cancers.

Stages of breast cancer

Stage 0 (carcinoma in situ)

There are 2 types of breast carcinoma in situ:

Ductal carcinoma in situ (DCIS) is a noninvasive condition in which abnormal cells are found in the lining of a breast duct. The abnormal cells have not spread outside the duct to other tissues in the breast. In some cases, DCIS may become invasive cancer and spread to other tissues, although it is not known at this time how to predict which lesions will become invasive.

Lobular carcinoma in situ (LCIS) is a condition in which abnormal cells are found in the lobules of the breast. This condition seldom becomes invasive cancer; however, having lobular carcinoma in situ in one breast increases the risk of developing breast cancer in either breast.

Stage I

In stage I, cancer has formed. The tumor is 2 centimeters or smaller and has not spread outside the breast.

Stage IIA

In stage I I A:

- □ no tumor is found in the breast, but cancer is found in the axillary lymph nodes; or
- **u** the tumor is 2 centimeters or smaller and has spread to the axillary lymph nodes; or
- the tumor is larger than 2 centimeters but not larger than 5 centimeters and has not spread to the axillary lymph nodes. Pea, peanut, walnut, and lime show tumor sizes.



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Stage IIB

In stage IIB: the tumor is either :

- □ larger than 2 centimeters but not larger than 5 centimeters and has spread to the axillary lymph nodes; or
- □ larger than 5 centimeters but has not spread to the axillary lymph nodes.

Stage IIIA

- In stage IIIA:
- □ no tumor is found in the breast. Cancer is found in axillary lymph nodes that are attached to each other or to other structures, or cancer may be found in lymph nodes near the breastbone; or
- the tumor is 2 centimeters or smaller. Cancer has spread to axillary lymph nodes that are attached to each other or to other structures, or cancer may have spread to lymph nodes near the breastbone; or
- the tumor is larger than 2 centimeters but not larger than 5 centimeters. Cancer has spread to axillary lymph nodes that are attached to each other or to other structures, or cancer may have spread to lymph nodes near the breastbone; or
- the tumor is larger than 5 centimeters. Cancer has spread to axillary lymph nodes that may be attached to each other or to other structures, or cancer may have spread to lymph nodes near the breastbone.

Stage IIIB

In stage IIIB: the tumor may be any size and cancer:

- □ has spread to the chest wall and/or the skin of the breast and
- may have spread to axillary lymph nodes that may be attached to each other or to other structures, or cancer may have spread to lymph nodes near the breastbone.

Stage IIIC

In stage IIIC: there may be no sign of cancer in the breast or the tumor may be any size and may have spread to the chest wall and/or the skin of the breast. Also, cancer:

- □ has spread to lymph nodes above or below the collarbone; and
- □ may have spread to axillary lymph nodes or to lymph nodes near the breastbone.

Stage IIIC breast cancer is divided into operable and inoperable stage IIIC.

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- In operable stage IIIC, the cancer : • is found in ten or more axillary lymph nodes ; or
 - is found in lymph nodes below the collarbone; or
 - is found in axillary lymph nodes and in lymph nodes near the breastbone.

In inoperable stage IIIC breast cancer, the cancer has spread to the lymph nodes above the collarbone.

Stage IV

In stage IV, the cancer has spread to other organs of the body, most often the bones, lungs, liver, or brain.

Staging and survival rates

The five-year survival rate for breast cancer is calculated based on averages. Each patient's individual tumor characteristics, state of health, genetic background, etc. will impact on survival. In addition, levels of stress, immune function, will to live and other unmeasurable factors also play a significant role in a patient's survival.

Stage	5-year Relative Survival Rate
0	100%
Ι	100%
IIA	92%
IIB	81%
IIIA	67%
IIIB	54%
IV	20%

Source: American Cancer Society

Breast cancer survival also continues to decline after five years. Survival after ten years depends on the stage; early stage breast cancers are associated with high survival rates than late stages cancers.

Overall Survival Rate		
After 5 years	88%	
After 10 years	80%	
After 15 years	71%	
After 20 years	63%	

Source: American Cancer Society

Signs and symptoms

Early breast cancer has no symptoms. It is usually not painful. The most common sign of breast cancer is a new lump or mass. A painless, hard mass that has irregular edges is more likely to be cancerous, but breast cancers can be tender, soft, or rounded.

Other possible signs of breast cancer include:

 swelling of all or part of a breast (even if no distinct lump is felt)

- □ skin irritation or dimpling
- □ breast or nipple pain
- □ nipple retraction
- □ redness, scaliness, or thickening of the nipple or breast skin

Breast Cancer

□ a discharge other than breast milk

Sometimes a breast cancer can spread to underarm lymph nodes and cause a lump or swelling there, even before the original tumor in the breast tissue is large enough to be felt.

Diagnosis of breast cancer

Diagnosis of breast cancer usually is comprised of several steps, including examination of the breast, mammography, possibly ultrasonography or MRI, and, finally, biopsy. Biopsy is the only definitive way to diagnose breast cancer.

Examination of the Breast

A complete breast examination includes visual inspection and careful palpation of the breasts, the armpits and the areas around clavicle. During that exam, doctor may palpate a lump or just feel a thickening.

Self examination of breasts

One should lie down and place her right arm behind head. The exam is done while lying down, not standing up. This is because when lying down the breast tissue spreads evenly over the chest wall and is as thin as



possible, making it much easier to feel all the breast tissue.

- □ To use the finger pads of the 3 middle fingers on left hand to feel for lumps in the right breast. Use overlapping dimesized circular motions of the finger pads to feel the breast tissue.
- To use 3 different levels of pressure to feel all the breast tissue. Light pressure is needed to feel the tissue closest to the skin; medium pressure to feel a little deeper; and firm pressure to feel the tissue closest to the chest and ribs. A firm ridge in the lower curve of each breast is normal.
- To move around the breast in an up and down pattern starting at an imaginary line drawn straight down from the axilla and moving across the breast to the middle of the sternum. Be sure to check the entire breast area going down until feel only ribs and up to the neck or clavicle.
- □ There is some evidence to suggest that the up-and-down pattern is the most effective pattern for covering the entire breast, without missing any breast tissue.
- □ And repeat the exam on left breast, using the finger pads of the right hand.
- □ While standing in front of a mirror with hands pressing

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firmly down on hips, look at the breasts for any changes of size, shape, contour or dimpling or redness or scaliness of the nipple or breast skin. (The pressing down on the hips position contracts the chest wall muscles and enhances any breast changes.)



To examine each axilla while sitting up or standing and with arm only slightly raised so one can easily feel in this

Breast Self Examination Examine up to the collarbone, out to armpit, in to middle of chest and down to bottom of rib cage.

area. Raising arm straight up tightens the tissue in this area and makes it harder to examine.

Mammography

Mammograms are x-rays of the breast that may help define the nature of a lump. Mammograms are also recommended for screening to find early cancer. Usually, it is possible to tell from the mammogram whether a lump in the breast is breast cancer, but no test is 100% reliable. Mammograms are thought to miss as many as 10-15% of breast cancers. A false-positive mammogram is one that suggests malignancy when no malignancy is found on biopsy. A false-negative mammogram is one that appears normal when in fact cancer is present. A mammogram alone is often not enough to evaluate a lump.

Ultrasound

Ultrasound of the breast is often done to evaluate a breast lump. It can demonstrate whether a mass is filled with fluid (cystic) or solid. Cancers are usually solid, while many cysts are benign. Ultrasound might also be used to guide a biopsy or the removal of fluid.

MRI

MRI may provide additional information and may clarify findings which have been seen on mammography or ultrasound. MRI is not routine for screening for cancer but may be recommended in special situations.

Biopsy

The only way to diagnose breast cancer with certainty is to biopsy the tissue in question. A number of biopsy techniques are available.

- □ Fine-needle aspiration is used most commonly when a fluid-filled mass is identified and cancer is not likely.
- □ Core-needle biopsy is performed with a special needle with ultrasound or mammogram guidance. This technique is being used more and more because it is less invasive than surgical biopsy. It obtains only a sample of tissue rather than removing an entire lump. Occasionally, if the mass is easily felt, cells may be removed with a needle without additional guidance.

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□ Surgical biopsy is done by making an incision in the breast and removing the piece of tissue. Certain techniques allow removal of the entire lump.

If a cancer is diagnosed on biopsy, the tissue will be tested for hormone receptors. In general, the more receptors, the more sensitive the tumor will be to hormone therapy.

Breast cancer grade

The grade helps predict a woman's prognosis. In general, a lower grade number indicates a slower-growing cancer that is less likely to spread, while a higher number indicates a faster-growing cancer that is more likely to spread.

Histologic tumor grade (sometimes called the Bloom-Richardson grade, Scarff-Bloom-Richardson grade, or Elston-Ellis grade) is based on the arrangement of the cells in relation to each other: whether they form tubules; how closely they resemble normal breast cells (nuclear grade); and how many of the cancer cells are in the process of dividing (mitotic count). This system of grading is used for invasive cancers but not for in situ cancers.

- □ **Grade 1** (well differentiated) cancers have relatively normal-looking cells that do not appear to be growing rapidly and are arranged in small tubules.
- □ **Grade 2** (moderately differentiated) cancers have features between grades 1 and 3.
- □ **Grade 3** (poorly differentiated) cancers, the highest grade, lack normal features and tend to grow and spread more aggressively.

The tumor grade is most important in patients who have small tumors and no lymph node involvement. Patients with small, well-differentiated tumors may require no further treatment after the tumor is removed, while patients with moderately or poorly differentiated tumors usually receive additional hormonal or chemotherapy.

Treatment of breast cancer

Treatments can be classified into broad groups :

Local therapy :

Local therapy is intended to treat a tumor at the site without affecting the rest of the body. Surgery and radiation therapy are examples of local therapies.

Systemic therapy :

Systemic therapy refers to drugs which can be given by mouth or directly into the bloodstream to reach cancer cells anywhere in the body. Chemotherapy, hormone therapy, and targeted therapy are systemic therapies.

Surgery for breast cancer :

Most women with breast cancer have some type of surgery. Operations for local treatment include breast-conserving surgery, mastectomy, and axillary lymph node sampling and removal. Women who have breast surgery may also decide to have breast reconstruction, either at the same time or later on.

Breast-conserving surgery :

In these types of surgery, only a part of the affected breast is removed, although how much is removed depends on the size and location of the tumor and other factors.

Lumpectomy removes only the breast lump and a surrounding margin of normal tissue. Radiation therapy is usually given after a lumpectomy. If adjuvant chemotherapy is to be given as well, the radiation is usually delayed until the chemotherapy is completed.

Partial (segmental) mastectomy or quadrantectomy removes more breast tissue than a lumpectomy. For a quadrantectomy, one-quarter of the breast is removed. Radiation therapy is usually given after surgery. Again, this may be delayed if chemotherapy is to be given as well.

For most women with stage I or II breast cancer, breast conservation therapy (lumpectomy/partial mastectomy plus radiation therapy) is as effective as mastectomy. Survival rates of women treated with these 2 approaches are the same. However, breast conservation therapy is not an option for all women with breast cancer.

Radiation therapy can sometimes be omitted as a part of breast-conserving therapy. Women who may consider lumpectomy without radiation therapy typically have all of the following characteristics:

- □ they are age 70 years or older
- they have a tumor 2 cm or less that has been completely removed
- □ the tumor is hormone receptor-positive, and the women is getting hormone therapy
- □ they have no lymph node involvement.

Mastectomy :

Mastectomy involves removing all of the breast tissue, sometimes along with other nearby tissues.

In a simple or total mastectomy the surgeon removes the entire breast, including the nipple, but does not remove axillary lymph nodes or muscle tissue from beneath the breast. Sometimes this is done for both breasts (a double mastectomy), especially when it is done as preventive surgery in women at very high risk for breast cancer.

A modified radical mastectomy involves removing the entire breast and some of the axillary lymph nodes. This is the most common surgery for women with breast cancer who are having the whole breast removed.

For some women who have smaller tumors, one option may be a newer procedure known as a skin-sparing mastectomy, where most of the skin over the breast (other than the nipple and areola) is left intact.

A radical mastectomy is an extensive operation where the surgeon removes the entire breast, axillary lymph nodes, and

the pectoral muscles under the breast. This surgery was once very common. But because of the disfigurement and side effects it causes and because a modified radical mastectomy has been proven to be as effective as a radical mastectomy, it is rarely done today.

Axillary lymph node dissection (ALND) :

To determine if the breast cancer has spread to axillary lymph nodes, some of these lymph nodes may be removed and looked at under the microscope. This is an important part of staging and determining treatment and outcomes. When the lymph nodes are affected, there is an increased likelihood that cancer cells have spread through the bloodstream to other parts of the body.

As noted above, axillary lymph node dissection is part of a radical or modified radical mastectomy procedure. It may also be done along with a breast-conserving procedure, such as lumpectomy. Anywhere from about 10 to 40 (though usually less than 20) lymph nodes are removed.

The presence of cancer cells in the lymph nodes under the arm is an important factor in considering adjuvant therapy. Axillary dissection is used as a test to help guide other breast cancer treatment decisions.

Radiation therapy :

Radiation therapy is treatment with high-energy rays or particles that destroy cancer cells. This treatment may be used to kill any cancer cells that remain in the breast, chest wall, or underarm area after breast-conserving surgery. Radiation may also be needed after mastectomy in cases with either a cancer larger than 5 cm in size, or when cancer is found in the lymph nodes.

Chemotherapy :

Chemotherapy is treatment that may be given intravenously or by mouth. The chemotherapy is given in cycles, with each period of treatment followed by a recovery period. Treatment usually lasts for several months.

Adjuvant chemotherapy :

Systemic therapy given to patients after surgery who have no evidence of cancer spread is called adjuvant therapy. When used as adjuvant therapy after breast-conserving surgery or mastectomy, chemotherapy reduces the risk of breast cancer coming back.

Even in the early stages of the disease, cancer cells may break away from the primary breast tumor and spread through the bloodstream. These cells don't cause symptoms, they don't show up on imaging tests, and they can't be felt during a physical exam. But if they are allowed to grow, they can establish new tumors in other places in the body. The goal of adjuvant chemotherapy is to kill undetected cells that have traveled from the breast.

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Neoadjuvant chemotherapy :

Chemotherapy given before surgery is called neoadjuvant therapy. The major benefit of neoadjuvant chemotherapy is that it can shrink large cancers so that they are small enough to be removed by lumpectomy instead of mastectomy. Another possible advantage of neoadjuvant chemotherapy is to see how the cancer responds to chemotherapy. If the tumor does not shrink, different chemotherapy drugs may be try.

Chemotherapy for advanced breast cancer :

Chemotherapy can also be used as the main treatment for women whose cancer has already spread outside the breast and underarm area at the time it is diagnosed, or if it spreads after initial treatments. The length of treatment depends on whether the cancer shrinks, how much it shrinks, and how a patient tolerates treatment.

Hormone therapy :

Hormone therapy is another form of systemic therapy. It is most often used as an adjuvant therapy to help reduce the risk of cancer recurrence after surgery, although it may also be used for more advanced breast cancers. Ovaries are the main source of the hormone estrogen up until menopause. After menopause, smaller amounts are still made in the body's fat tissue, where a hormone made by the adrenal gland is converted into estrogen.

Estrogen promotes the growth of about 2 out of 3 of breast cancers - those containing estrogen receptors (ER-positive cancers) and/or progesterone receptors (PR-positive cancers). Because of this, several approaches to blocking the effect of estrogen or lowering estrogen levels are used to treat ER-positive and PR-positive breast cancers. Hormone therapy does not help patients whose tumors are both ER- and PR-negative.

Tamoxifen and Toremifene :

These anti-estrogen drugs work by temporarily blocking estrogen receptors on breast cancer cells, preventing estrogen from binding to them. Patient with ER- or PR-positive cancers, taking tamoxifen after surgery for 5 years reduces the chances of the cancer coming back by about half. Tamoxifen can also be used to treat metastatic breast cancer, as well as to reduce the risk of developing breast cancer in women at high risk.

Toremifene is used mainly in post-menopausal women with advanced cancers that are ER-positive (or whose ER status is unknown).

Fulvestrant :

Fulvestrant is a drug that also acts on the estrogen receptor, but instead of blocking it, this drug eliminates it. It is often effective even if the breast cancer is no longer responding to tamoxifen. It is given by injection once a month. It is currently only approved for use in post-menopausal women with advanced breast cancer that no longer responds to tamoxifen or toremifene.

Aromatase inhibitors :

Three drugs that stop estrogen production in postmenopausal women have been approved to treat both early and advanced breast cancer: letrozole, anastrozole and exemestane. They work by blocking an enzyme (aromatase) responsible for making small amounts of estrogen in postmenopausal women. They cannot stop the ovaries of premenopausal women from making estrogen, so they are only effective in post-menopausal women.

Several studies have compared these drugs with tamoxifen as adjuvant hormone therapy in post-menopausal women. Using these drugs, either alone or after tamoxifen, has been shown to better reduce the risk of cancer recurrence compared to using just tamoxifen alone for 5 years.

For post-menopausal women whose cancers are estrogen and/or progesterone receptor-positive, most doctors now recommend using an aromatase inhibitor at some point during adjuvant therapy. But several important questions have not yet been answered. For example, it's not clear if starting adjuvant therapy with one of these drugs is better than giving tamoxifen and then switching to an aromatase inhibitor. If tamoxifen is given first, it's not clear how long it should be given. The optimal length of treatment with aromatase inhibitors has not yet been determined, nor has it been shown if any one of these drugs is better than the others. Studies now being done should help answer these questions.

Ovarian ablation :

In pre-menopausal women, removing or shutting down the ovaries, which are the main source of estrogens, effectively makes the woman 'post-menopausal'. This may allow some other hormone therapies to work better.

Ovarian ablation can be done surgically (and permanently) by removing the ovaries. This operation is called an oophorectomy. It also can be done with drugs called luteinizing hormone-releasing hormone (LHRH) analogs, such as goserelin or leuprolide. These drugs block the mechanism that causes the ovaries to make estrogens. They are now being tested as adjuvant therapies along with tamoxifen or an aromatase inhibitor in pre-menopausal women.

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Viral gastroenteritis is a common illness, affecting populations worldwide. Epidemiologic studies have shown that it is the second most frequent illness encountered by American families. It affects all age groups at all times of the year, although some individual viruses may target specific age groups during certain seasons. Viral acute gastroenteritis is more frequent than both bacterial and parasitic diarrhoea, causing high morbidity as well as mortality in children in developing countries. In industrialized countries, morbidity

occurs mostly as outbreaks in young children attending day care centers and in the elderly.



Viral gastroenteritis causes considerable mortality in the developing world;

Fig.: Etiologic Agents Associated for gastroenteritis (1991-2000, n=231)

rotavirus alone is estimated to be responsible for 600,000 to 800,000 deaths per year , which is approximately one-quarter of all deaths due to infectious diarrhea. In the United States, viral gastroenteritis causes only a few hundred deaths per year, principally due to rotavirus and norovirus (also called Norwalk-like virus [NLV]). However, morbidity is considerable with approximately 50,000 hospitalizations annually due to rotavirus and a similar number due to norovirus. During Hurricane Katrina, norovirus was responsible for a large outbreak of acute gastroenteritis among evacuees, with substantial secondary spread to medical personnel, police officers, and volunteers who had direct contact with patients.

Difination

Viral gastroenteritis is an infection caused by a variety of viruses that results in vomiting or diarrhea or both. It is often called the "stomach flu," although it is not caused by the influenza viruses.

Causes of viral gastroenteritis

There are four viral agents that are known to be medically important causes of viral gastroenteritis :

- □ Norovirus
- □ Rotavirus
- □ Enteric adenovirus
- □ Astrovirus

Viral gastroenteritis is not caused by bacteria (such as *Salmonella* or *Escherichia coli*) or parasites (such as Giardia), or by medications or other medical conditions, although the symptoms may be similar. Type A Rotavirus (RVA) is the most frequent etiologic agent of gastroenteritis in children under 5 years of age. Each year, RVA causes approximately

111 million episodes of gastroenteritis requiring only home care, 25 million clinic visits, 2 million hospitalizations, and 352,000-592,000 deaths (median, 440,000 deaths) in children under five years of age.

Pathophysiology

Viral spread from person to person occurs by fecal-oral transmission of contaminated food and water. Some viruses, like noroviruses, may be transmitted by an airborne route. Clinical manifestations are related to intestinal infection, but the exact mechanism of the induction of diarrhea is not clear.

The most extensive studies have been done with rotavirus. Rotaviruses attach and enter mature enterocytes at the tips of small intestinal villi. They cause structural changes to the small bowel mucosa, including villus shortening and mononuclear inflammatory infiltrate in the lamina propria.

The current knowledge on the mechanisms leading to diarrheal disease by rotavirus is as follows :

- Rotavirus infections induce maldigestion of carbohydrates, and their accumulation in the intestinal lumen, as well as a malabsorption of nutrients and a concomitant inhibition of water reabsorption, can lead to a malabsorption component of diarrhea.
- Rotavirus secretes an enterotoxin, NSP4, which leads to a Ca2+ -dependent Cl- secretory mechanism. Mobilization of intracellular calcium associated with NSP4 expressed endogenously or added exogenously is known to induce transient chloride secretion.

Morphologic abnormalities can be minimal, and studies demonstrate that rotavirus can be released from infected epithelial cells without destroying them. Viral attachment and entry into the epithelial cell without cell death may be enough to initiate diarrhea. The epithelial cell synthesizes and secretes numerous cytokines and chemokines, which can direct the host immune response and potentially regulate cell morphology and function. Studies also suggest that one of the nonstructural viral proteins may act as an enterotoxin, promoting active chloride secretion mediated through increases in intracellular calcium concentration. Toxinmediated diarrhea would explain the observation that villus injury is not necessarily linked to diarrhea.

Clinical features of viral gastroenteritis

History

The clinical spectrum of acute viral gastroenteritis ranges from asymptomatic infection to severe dehydration and death. Viral gastroenteritis typically presents with short prodrome, with mild fever and vomiting, followed by 1-4 days of nonbloody, watery diarrhea. Viral gastroenteritis is usually self-limited.

Viral Gastroenteritis



- □ The history should focus on severity and dehydration. The onset, frequency, quantity, and duration of diarrhea and vomiting are important factors in assessing the status. Oral intake, urine output, and weight loss are important considerations. Viruses are the suspected cause of acute gastroenteritis when vomiting is prominent, when the incubation period is longer than 14 hours, and when the entire illness is over in less than 3 days. Travel history (including cruise ships), eating history, and daycare history are important epidemiological factors.
- □ A viral cause should be suspected when the warning signs of bacterial infection (ie, high fever, bloody diarrhea, severe abdominal pain, >6 stools/24 h) are absent and an alternative diagnosis is not suggested by epidemiologic clues from the history (eg, travel, sexual practices, antibiotic use).
- □ Factors associated with severe and prolonged disease are immunodeficiency and immune suppression, comorbid disease, and malnutrition.
- Death results from dehydration and acidosis.
- Ruling out other diagnoses is important. Mucus or overt blood in the stool almost always indicates bacterial or parasitic infection.

In 1982, the Kaplan criteria were established to distinguish outbreaks due to norovirus from outbreaks of bacterial etiology. The criteria are highly specific (99%) and moderately sensitive (68%). The 4 criteria indicative of an outbreak due to norovirus are as follows : 4

- □ Vomiting in 50% of affected persons in the outbreak
- □ Mean incubation period of 24-48 hours
- □ Mean duration of illness of 12-60 hours
- □ Lack of identification of a bacterial pathogen in stool culture

Physical Examination

The physical examination can be helpful in determining the etiology of gastroenteritis and in assessing the presence and degree of dehydration.

- □ Temperature, blood pressure and pulse, and body weight can provide evidence of severity of the condition.
- □ Temperature may be slightly elevated. High fever suggests bacterial infection. Tachycardia, thready pulse, and hypotension suggest severe dehydration.
- □ The degree of weight loss may be related to dehydration and the duration of the diarrhea.
- □ The mucous membranes and the skin should be examined carefully. Dry mouth, no tears, skin tenting, dry skin, and capillary refill are all signs of dehydration.
- The mental status in elderly patients and infants may be abnormal, especially when blood pressure and circulation are compromised.
- The abdominal examination may demonstrate mild tenderness. Severe abdominal pain and tenderness suggest bacterial infection or an abdominal emergency.

The affected person may also have headache. In general, the symptoms begin 1 to 2 days following infection with a virus that causes gastroenteritis and may last for 1 to 10 days, depending on which virus causes the illness; however, most episodes last from 1-3 days.

Prognosis

People who get viral gastroenteritis almost always recover completely without any long-term problems. Gastroenteritis is a serious illness, however, for persons who are unable to drink enough fluids to replace what they lose through vomiting or diarrhea. Infants, young children, and persons who are unable to care for themselves, such as the disabled or elderly, are at risk for dehydration from loss of fluids. Immune compromised persons are at risk for dehydration because they may get a more serious illness, with greater vomiting or diarrhea. They may need to be hospitalized for treatment to correct or prevent dehydration.

Incubation period

The incubation period is 24 – 72 hours.

Infectious period

During illness and for at least 48 hours after symptoms have disappeared.

Spread of virus

The viruses that cause gastroenteritis are spread through close contact with infected persons (for example, by sharing food, water or eating utensils). Individuals may also become infected by eating or drinking contaminated foods or beverages. Viral

Viral Gastroenteritis

gastroenteritis may also be spread through coughing and sneezing. Fig.: Person-to-Person Spread



Diagnosis

Generally, viral gastroenteritis is diagnosed by a physician on the basis of the symptoms and medical examination of the patient. A faecal examination can sometimes identify the virus and should be performed also to rule out bacterial infection following laboratory tests need-

- □ Examination of stool for toxins, (e.g. Clostridium difficile toxin)
- □ Stool cultures for the organisms that causes the disease, (e.g. Salmonella, Shigella, Campylobacter and enterotoxic Escherichia coli)
- □ Microscopy for parasites and their ova and cysts
- □ EIA for viruses

Differential diagnosis

It is important to consider infectious gastroenteritis as a

diagnosis of exclusion. A few loose stools and vomiting may be the result of systemic infection such as pneumonia, septicemia, urinary tract infection and even meningitis. Surgical conditions such as appendicitis, intussusception Gastroenteritis viruses and rarely, even Hirschsprung's disease may mislead the clinician.



rotavirus, B = adenovirus, CNorovirus and D = Astrovirus. The virus particles are shown at the same magnification to allow size comparison.

Noninfectious

Non-infectious causes to consider are poisoning with heavy metals (e.g. arsenic, cadmium), seafood (e.g. ciguatera, scombroid, toxic encephalopathic shellfish poisoning) or mushrooms (e.g. Amanita phalloides). Secretory tumours (e.g. carcinoid, medullary tumour of the thyroid, vasoactive intestinal peptide-secreting adenomas) and endocrine disorders (e.g. thyrotoxicosis and Addison's disease) are disorders that can cause diarrhea. Also, pancreatic insufficiency, short bowel syndrome, Whipple's disease, coeliac disease, and laxative abuse should be excluded as possibilities.

Infectious

Infectious gastroenteritis is caused by a wide variety of bacteria and viruses. Bacteria commonly causing gastroenteritis are- Salmonella, E. coli, campylobacter, shigella. Pseudomembranous colitis is an important cause of diarrhea in patients often recently treated with antibiotics. Viruses causing gastroenteritis include rotavirus, norovirus, adenovirus and astrovirus.

If gastroenteritis in a child is severe enough to require admission to a hospital, then it is important to distinguish between bacterial and viral infections. Bacteria, Shigella and *Campylobacter*, for example, and parasites like Giardia can be treated with antibiotics, but viruses do not respond to antibiotics and infected children usually make a full recovery after a few days. Children admitted to hospital with gastroenteritis routinely are tested for rotavirus And to develop surveillance data relevant to the epidemiological effects of rotavirus vaccination programs. These children are routinely tested also for norovirus, which is extraordinarily infectious and requires special isolation procedures to avoid transmission to other patients. Other methods, electron microscopy and polyacrylamide gel electrophoresis, are used in research laboratories.

Treatment

No specific antiviral drugs are useful for treating viral gastroenteritis. It is a common illness which may be particularly serious in young children. There are several treatments which are useful for gastroenteritis of any cause. Seek medical advice if any of the following symptoms occur:

- □ signs of dehydration, such as thirst and decreased urination, lethargy, dry mouth sunken eyes, feeling faint on standing
- □ fever
- abdominal pain, especially if severe
- □ bloody diarrhoea
- □ any symptoms in a child less than 12 months of age.

The following are general recommendations for the treatment of gastroenteritis:

Patient should give plenty of fluids. Oral rehydration solution is highly recommended. It is available at pharmacies and should be administered following the instructions on the packaging. For mildly unwell children, diluted juice or carbonated (fizzy) drinks (one part to three parts of water) or cordial (even more diluted) can be given.

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- □ Medicines to prevent vomiting or diarrhea should not be given (especially in children) except where specifically advised by a doctor.
- □ Breast-fed babies should continue to be breastfed with extra fluids between feeds.
- □ Children on formula or solid diets should not have food withheld for more than 24 hours.

Control of spread

Control of spread masures are focused on minimising the spread of the virus within and between wards and departments as viruses are very infectious. Practicing good hygiene will reduce the risk of acquiring the virus and spreading of gastroenteritis.

Contact precautions-

- Gloves and long sleeved gowns must be worn at all times while in the patient's room.
- Gloves and gowns must be removed before leaving the room.
- Hands should be wash or disinfact immediately after removing gloves and gown and leaving the room.

Prevention

Persons can reduce their chance of getting infected by frequent handwashing, prompt disinfection of contaminated surfaces with household chlorine bleach-based cleaners, and prompt washing of soiled articles of clothing. If food or water is thought to be contaminated, it should be avoided. Immunity to noroviruses is short-term, lasting only a few months, so it is possible to be reinfected. To complicate matters more, however, some individuals presumably immune because of high levels of antibodies to the norovirus may still be susceptible to infection. Since there are many strains of noroviruses and immunity is specific for each strain, it is possible to have an episode of gastroenteritis immediately after another if the infecting strains are different; however, this probably occurs infrequently. Overall, the status of immunity to the viruses causing gastroenteritis--particularly as it relates to susceptibility to infection--is incomplete.

Vaccine for viral gastroenteritis

Currently there is a licensed rotavirus vaccine available that protects against severe diarrhea from rotavirus infection in infants and young children. Studies into a norovirus vaccine are underway.

□ In April 2008, the United States Food and Drug Administration (FDA) approved a new vaccine for rotavirus gastroenteritis. This vaccine is a monovalent vaccine derived from the most common human rotavirus strain that has been attenuated by serial passage and is administered in 2 oral doses, 1-2 months apart.

- The trial of rotavirus vaccine reported the following results :
 - Rotavirus vaccine was highly protective against severe rotavirus gastroenteritis (85%) and hospitalization for severe rotavirus gastroenteritis (85%).
 - The vaccine was also protective against gastroenteritis of any cause (40%) and hospitalization for gastroenteritis of any cause (42%).
 - Infants vaccinated with Rotarix had fewer serious adverse events or required hospitalization because of gastrointestinal events.
 - The vaccine proved to be safe with respect to the risk of intussusceptions. The observed risk estimate was below the initial risk increase of 4 per 100,000 that led to the withdrawal of the RotaShield vaccine, and it was also below the subsequent consensus risk estimate of 1 per 100,000 for that vaccine.
- The rotavirus vaccine strain replicates well in the gut after the first dose and provides cross-protection against most other serotypes. RotaTeq, on the other hand, is not so broadly cross-protective and grows less well in human intestines. In addition, the vaccine strains are infrequently shed in the stool, and 3 doses are required.
- Recommendations from the American Academy of Pediatrics and the CDC for the use of rotavirus vaccine are pending.
- □ Research on a vaccine for calicivirus infection is proceeding rapidly. Baculovirus-produced antigens spontaneously form virus-like particles without RNA that are immunogenic and possibly protective. Genomes also can be inserted into edible foodstuffs (eg, potatoes, bananas).
- □ Proper hygiene is still the first preventative step in viral gastroenteritis. Hand washing to prevent fecal-oral transmission is very important. It also includes properly handling food and using clean water supplies.
- On a community level, proper sanitation, clean water supplies, and surveillance programs for outbreaks are important steps in prevention.

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Dyslexia

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Dyslexia has been around for a long time and has been defined in different ways. For example, in 1968, the World Federation of Neurologists defined dyslexia as "a disorder in children who, despite conventional classroom experience, fail to attain the language skills of reading, writing, and spelling commensurate with their intellectual abilities." According to the U.S. National Institutes of Health, dyslexia is a learning disability that can hinder a person's ability to read, write, spell, and sometimes speak. The severity of dyslexia can vary from mild to severe. The sooner dyslexia is treated, the more favorable the outcome; however, it is never too late for people with dyslexia to learn to improve their language skills.

Dyslexia is impairment in human brain's ability to translate written images received from individual eyes into meaningful language. Also called specific reading disability, dyslexia is the most common learning disability in children, affecting 5 percent or more of all elementary-age children.

Dyslexia may occur in children with normal vision and normal intelligence. Children with dyslexia usually have normal speech, but often have difficulty interpreting spoken language and writing

Types of dyslexia

There are several types of dyslexia that can affect the child's ability to spell as well as read.

Primary dyslexia :

This type of dyslexia is a dysfunction of, rather than damage to, the left side of the brain (cerebral cortex) and does not change with age. Individuals with this type are rarely able to read above a fourth-grade level and may struggle with reading, spelling, and writing as adults. Primary dyslexia is passed in family lines through their genes (hereditary). It is found more often in boys than in girls.

Secondary or developmental dyslexia :

This type caused by hormonal development during the early stages of fetal development. Developmental dyslexia diminishes as the child matures. It is also more common in boys.

Traumatic dyslexia :

Usually occurs after some form of brain trauma or injury to the area of the brain that controls reading and writing. It is rarely seen in today's school-age population.

Visual dyslexia :

It is characterized by number and letter reversals and the inability to write symbols in the correct sequence.

Auditory dyslexia :

It involves difficulty with sounds of letters or groups of letters. The sounds are perceived as jumbled or not heard correctly.

Famous dyslexics are :

1. Hans Christian Andersen. 2. Harry Belafonte. 3. Alexander Graham Bell. 4. George Burns. 5. Stephen J. Cannell. 6. Cher. 8. Leonardo Da Vinci. 7. Winston Churchill. 9. Walt Disney. 10. Albert Einstein. 11. Henry Ford. 12. Danny Glover. 13. Whoopi Goldberg. 14. Bruce Jenner. 15. William Lear. 16. Jay Leno. 17. Greg Louganis. 18. General George Patton. 19. Nelson Rockefeller. 20. Woodrow Wilson.

The positive aspects of having dyslexia

The Dyslexic has a nice collection of capabilities, which are in fact advantages when used in the right context.

These capabilities with the potential to be advantages are often underestimated or even unknown. Einstein used his ability to daydream to come up with relativity theory, whilst children are often discouraged to daydream, thus this capability risks not being fully developed. Where using ones capabilities leads to happiness, not using them has not a neutral effect, it has even a negative effect: it results in unhappiness.

By giving more attention on those advantages and nurture them, some one can use them to alleviate the disadvantages, boost the dyslexics' self-confidence. Not every dyslexic develops the same strengths. However, by knowing them and nurture them, so they can be fully develop and contribute to the development of the dyslexic child.



Wrong perception of letters and numbers

Here are the basic abilities all dyslexics share:

- 1. They can utilize the brain's ability to alter and create perceptions (the primary ability).
- 2. They are highly aware of the environment.

Dyslexia

- 3. They are more curious than average.
- 4. They think mainly in pictures instead of words.
- 5. They are highly intuitive and insightful.
- 6. They think and perceive multi-dimensionally (using all the senses).
- 7. They can experience thought as really

Causes of dyslexia

Between 2 - 8% of elementary-age children have some degree of reading disability. Developmental reading disorder (DRD) is not caused by vision problems, but rather with the brain's ability to recognize and process symbols. Children with DRD may have trouble rhyming and separating the sounds in spoken words. These abilities appear to be critical in the process of learning to read.

A child's initial reading skills are based on word recognition, which involves being able to separate out the sounds in words and associate them with letters and groups of letters. More developed reading skills require the linking of words into a coherent sentence. Because DRD children have difficulty connecting the sounds of language to the letters of words, they may consequently have difficulty understanding sentences.

Symptoms

Dyslexia can be difficult to recognize before children enters school, but some early clues may indicate a problem. If any young child begins talking late, adds new words slowly and has difficulty rhyming, he or she may be at increased risk of dyslexia. Common symptoms are –

Possible family history of learning disorder Difficulty learning to recognize written words

Difficulty learning to recognize written words

was?? saw??

Thank you,

Whole Word

Child can't read and can't make real sense of word

Difficulty rhyming

- Difficulty determining the meaning (idea content) of a simple sentence
- May occur in combination with writing or arithmetic learning problems

Children with dyslexia commonly have problems processing and understanding what they hear. They may have difficulty comprehending rapid instructions, following more than one command at a time or remembering the sequence of things. Reversals of letters (b for d) and a reversal of words (saw for was) are typical among children who have dyslexia. Reversals are also common for children age 6 and younger who don't have dyslexia. But with dyslexia, the reversals persist

Parents responsibility

It is important to consult with pediatrician if any one concerned about individual child's development. Additionally, meeting with children's teachers is an important step toward getting more answers.

Ideally, every school has a team that meets on a regular basis to discuss problems a specific child might be having. These teams are made up of the principal, classroom teacher, and one or a combination of the following depending on the staffing of the school: school psychologist, nurse, speech therapist, reading specialist, and other pertinent professionals. A parent should always be included as a part of this team. The teams are commonly referred to as Child Study Teams, Student Study Teams, or Student Support Teams. Any parent or teacher who suspects a learning problem may request a meeting with this team to discuss the child's problem. The parent may request this even if the teacher feels the child is doing well. Sometimes a decision to test the child will be made. The parent or teacher may request testing, but it cannot be done without the parents' written permission.

If the child attends a private school which lacks the appropriate professionals to evaluate a suspected learning problem, he should be referred to the public-school system for evaluation. If testing is not satisfactorily conducted in the public-school system for private or public school students, the parent will need to locate the appropriate health professionals for assessment.

Because testing can sometimes be stressful for children, especially if they are unhappy about their school performance, alternative strategies are usually tried before testing is done. Once the assessment plan has been discussed with the parents and they have granted permission, the school team completes the testing and holds a meeting with the parents to discuss the test results.

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The assessment plan for each child depends on the specific problems the child is having. Each plan should include testing in five areas: cognition (intelligence), academic performance, communication, sensory/motor, and health and developmental. The testing will be done by the various members of the school team or the professionals consulted by the parent. Typically, the school or clinical psychologist determines whether or not the child has dyslexia. Since there are different forms of dyslexia, such as learning disability in reading, written language, or math, the psychologist diagnoses the specific type. Another form known as expressive language delay can be diagnosed by a speech therapist.

Medical testing

The inner-ear mechanisms responsible for dyslexia or ADD and related syndromes must first be demonstrated before medical treatment can be initiated. Most important, the pattern of diagnostic inner-ear-determined signs and symptoms characterizing each patient is essential for choosing the combination of medications most likely to be helpful.

In western world, medical treatment is provided by The Medical Dyslexic and ADD Treatment Center, only medical testing, especially of the inner-ear (CV) system, is performed — exceptions aside. (Educational and psychological testing are most helpful when tutoring is performed. Also, additional visual and related testing is provided to facilitate other therapeutic modalities and ensure diagnostic reliability). As a result, descriptions of the following non-invasive diagnostic tests and measurements are provided to help you understand the primary procedures performed at this center:

Electronystagmography (ENG) :

The ENG is a standardized neurophysiologic test in which eye movements are induced and measured under various testing conditions. Fine and reflexive eye movements are controlled by the cerebellum and the vestibular system. As a result, the ENG can help determine whether or not an innerear abnormality exists.

Audiological testing :

Audiological testing attempts to determine the presence or absence of middle ear and related problems. It evaluates (1) the pressure of the middle ear system, (2) the compliance or distensibility of the middle ear, (3) the acoustic reflexes of the ear drum, and (4) the ability of the patient to hear and distinguish different pitches at varying volumes.

Posturography :

Posturography testing assesses overall balance function (sensory integration), vision dependence, proprioception

Dyslexia

(internal senses) dependence, symmetry of weight bearing, lateral sway, and overall assessment of vestibular deficits. And its computer generated scores serve as an objective measure of medication-triggered improvements. Also, many of the symptoms of an inner-ear disorder (e.g., imbalance, dizziness, motion sickness, etc.) can sometimes result from other illnesses as well (i.e., extreme stress and anxiety, dysfunction of cerebral and other related CNS structures). Posturography aids in this differentiation since a vestibular dysfunction produce a specific, quantifiable frequency and pattern of movement which is distinct from that caused by other disorders.

Optokinetic testing:

Since the inner-ear controls the eye's ability to rapidly track and efficiently fixate targets, a dysfunction results in "clumsy eye movements." The result is rapid or pathological blurring scores as well as impaired fixation and movement illusions of stationary figures. By utilizing medical instruments proven capable of diagnosing inner-ear/cerebellar dysfunctionincluding a simple, rapid and accurate 3D Optical Scanner for detecting the eye tracking disorder characterizing all dyslexics — it is possible to determine those with dyslexia in almost 100% of individuals tested.

How the 3D optical scanner works

When a sequence of elephants are accelerated across a computer screen, the eye is physiologically forced to track this sequence at a proportional speed so that clear vision can be maintained. Since inner-ear impaired dyslexics were found to have defective or clumsy eye movements, their eyes will not be able to "run" as fast as the elephants. As a result, they will blur-out the elephant sequence at speeds sharply reduced from those of normal children or adults.



3D optical screening of children

The blurring-speed is then a diagnostic indicator of an innerear/cerebellar dysfunction which predisposes children to dyslexia. Most important, this test is independent of the

Dyslexia

following typical variables complicating the usual "pencil and paper" tests, i.e., language, culture, socioeconomic status, prior tutoring, etc. Thus this test can be used to effectively screen young children before they begin to fail and before they begin to feel dumb, ugly, stupid, brainless, etc.

Neurological testing:

This consists of a series of standardized neurological tests commonly administered to assess the status of the integrated function of the cerebellar-vestibular (CV) system as well as other central nervous system (CNS) structures. Difficulties with any of these tests indicate a dysfunction within the CV or CNS systems.

'Bender Gestalt' & 'Good Enough' figure drawings :

The copying of Bender-Gestalt and Good Enough designs significantly tests CV-determined and regulated visual-spatial processing and graphomotor abilities. These drawings highlight CV-based difficulties with tilting, articulation of related parts, angle formation, rhythmicity and overall maturity of graphomotor coordination and output.

Treatment

Before any treatment is started, an evaluation must be done to determine the child's specific area of disability. While there are many theories about successful treatment for dyslexia, there is no actual cure for it. The school will develop a plan with the parent to meet the child's needs. If the child's current school is unprepared to address this condition, the child will need to be transferred to a school, if available in the area, which can appropriately educate the dyslexic child. The plan may be implemented in a Special Education setting or in the regular classroom. An appropriate treatment plan will focus on strengthening the child's weaknesses while utilizing the strengths. A direct approach may include a systematic study of phonics. Techniques designed to help all the senses work together efficiently can also be used. Specific reading approaches that require a child to hear, see, say, and do something (multisensory), such as the Slingerland Method, the Orton-Gillingham Method, or Project READ can be used. Computers are powerful tools for these children and should be utilized as much as possible. The child should be taught compensation and coping skills. Attention should be given to optimum learning conditions and alternative avenues for student performance.

In addition to what the school has to offer, there are alternative treatment options available outside the school setting. Although alternative treatments are commonly recommended, there is limited research supporting the effectiveness of these treatments. In addition, many of these treatments are very costly, and it may be easy for frustrated parents to be misled by something that is expensive and sounds attractive.

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Perhaps the most important aspect of any treatment plan is attitude. The child will be influenced by the attitudes of the adults around him. Dyslexia should not become an excuse for a child to avoid written work. Because the academic demands on a child with dyslexia may be great and the child may tire easily, work increments should be broken down into appropriate chunks. Frequent breaks should be built into class and homework time. Reinforcement should be given for efforts as well as achievements. Alternatives to traditional written assignments should be explored and utilized.

Teachers are learning to deliver information to students in a variety of ways that are not only more interesting but helpful to students who may learn best by different techniques. Interactive technology is providing interesting ways for students to feedback on what they have learned, in contrast



to traditional paper-pencil Practice to differentiate similar letters

Prognosis

tasks

Marked improvement in reading and understanding can be achieved with remedial instruction. However, difficulties with reading may persist throughout adulthood

Possible complications

- □ Problems in school, including behavior problems (an indirect result, such as a reaction to teasing by other children) and loss of self-esteem
- □ Problems with reading in adulthood, which may result in occupational problems in certain careers, particularly if the problem was not addressed early

Prevention

Learning disorders tend to run in families. DRD is one kind of learning disorder. Affected families should make every effort to recognize existing problems early.

For families without a previous history of learning disabilities, an intervention can begin as early as preschool or kindergarten if teachers detect early signs. Early intervention will provide the best possible outcome.

References

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- 2. Mavoclinic.com
- Wikipedia. 3.
- 4. Medicine net.com

Test Yourself

Test 2	Yourself - 25	-
1. c 2	Correct Answers :	1.
CONG		
	Dr. Abdul Latif, HMO Neuro-Surgery Ward (W-28) CMCH	2.
	Dr. Kazi Anichur Rahman, MBBS, M.S. (P-II) Jr. Consultant, BICO & Eye Hospital Alekharchar, Comilla	
	Dr. Mostaque Hossain IMO, Ward-13 RMCH	3.
	Dr. Md. Shah Mizanur Rahman 382, Beldarpara Rajshahi – 6100	
	Dr. Mahmuda Rahman (Elora), MBBS Medical Officer Islami Bank Hospital Barisal	
	Dr Hossain Rashid Chowdhury , MBBS, RMO Upazilla Health Complex Hathazari, Chittagong	4.
	Dr Nasima Akter, FCPS Nibedita M/C 11/A Dhanmondi Dhaka	5.
	Dr. Md. Monir Hossain, MBBS MD-II (Pediatric Unit) DMCH	
	Dr. Samaresh Dutta, MBBS, PGT (Child) Medical Officer Khulna Shishu Hospital Ratan Sen Saroni Khulna	6.
	Dr. Marzina Arefin Medical Officer, SOPD Mohammad Ali Hospital Bogra	

Test Yourself - 26

1. All the following are true for "breast cancer" except:

- a. DCIS is the most common type of invasive breast cancer.b. Papillary carcinoma tends to be diagnosed in younger
- women. c. Medullary carcinoma accounts in about 3% - 5% of breast cancer.
- d. Mucinous carcinoma is also called colloid carcinoma.

2. All the following are true for "chronic cough" except:

- Chronic cough affects 10% -20% of adult, according to recent study.
- b. GERD is one of the etiologic causes of chronic cough.
- c. UACS is considered one of the rare causes of chronic cough.
- d. Upper and lower respiratory tract infection, asthma and GERD are the most common causes of chronic cough in children.
- The below mentioned points are true for "viral gastroenteritis" except:
 - a. It affects all age groups.
 - b. There are five medically important viral agents that cause viral gastroenteritis.
 - c. The incubation period is 24-72 hours.
 - d. Rotavirus vaccine is administered orally in three doses, three months apart.

I. All the following points are true for "dyslexia" except:

- a. There are two types of dyslexia that affects the children.
- b. Albert Einstein, Leonardo Da Vinci are among the famous dyslexics.
- c. Dyslexia can be difficult to recognize before the child enters school.
- d. Learning disorders do not tend to run in families.

5. The following are correct regarding "breast cancer" except:

- a. In stage IIB, the tumor is larger than 2cm or 5cm.
- b. In stage IIA, the tumor is more than 5cm and has spread to axillary lymph nodes.
- c. Biopsy is the only definitive way to diagnose breast cancer.
- d. Letrozole, Anastrozole are among the drugs that are approved to treat both early and advanced breast cancer.

All the following points are true for "chronic cough" except:

- a. Sinusitis, tuberculosis, pertussis and cystic fibrosis are some of the causes of chronic cough in children.
- b. Chest imaging is best reserved for evaluation of cough in smokers.
- As UACS is the most common cause of chronic cough, it should be treated first.
- d. In children, asthmatic symptoms may be caused by GERD.

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

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"SQUARE" in International Business

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SQUARE Pharmaceuticals Ltd., the market leader of Bangladesh Pharmaceutical Industry since 1985, participated in the Annual Scientific Conference of the Pharmaceutical Society of Kenya (PSK) held from 30 May to 2 June 2008 in Mombasa, Kenya. PSK is the professional body working for

countries participated in the conference. *SQUARE* participated in the conference with an exhibition stand and presentation on Company Profile & its Products followed by the video presentation on "*SQUARE*"s manufacturing facilities". The participants were highly impressed to see the



SQUARE's Participation in the PSK Conference, Mombasa, Kenya

the welfare & growth of Pharmacy as a profession in the fields of Policy & Regulations, Practice and Research as well in the provision of quality and accessible pharmaceutical care.

Pharmacists from all over Kenya & some other surrounding

world class manufacturing facilities of *SQUARE* and expressed their hope that *SQUARE* can play a great role in ensuring time-demanded healthcare services to the people of Kenya by providing quality medicine at an affordable price.









Effervescent tablet for water purification

- World Health Organization (WHO) approves NaDCC tablet
- U.S. Environmental Protection Agency approves NaDCC tablet
- ✓ UNDP specifies the use of effervescent NaDCC tablet
- The Unicef Supply Catalogue Product List includes NaDCC tablet



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Medical Services Department, *SQUARE PHARMACEUTICALS LTD*. Corporate Headquarters, Square centre 48, Mohakhali Commercial Area, Dhaka-1212, Tel : 8833047-56, 8859007 Fax : 880 -2-882 8608 / 882 8609 E-mail : info@squaregroup.com, Web Page : http://www.squarepharma.com.bd, Omar Akramur Rab <oar@squaregroup.com>

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