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MEDICUS

The essence of medical practice

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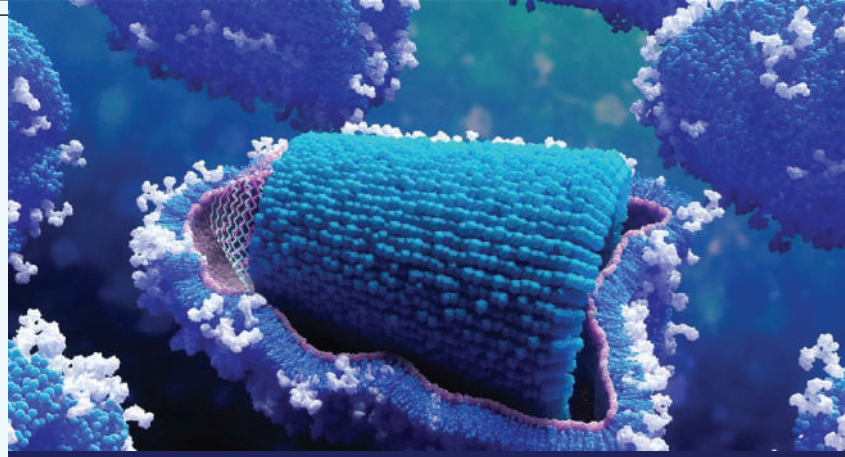


DISEASE HISTORY

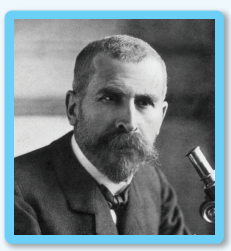
Rabies

Rabies is one of the oldest known diseases in history with cases dating back to 4000 years ago. Researchers estimate that 30,000 to 70,000 deaths are attributable to rabies each year, with less developed countries affected more. Rabies virus, scientific name Rabies lyssavirus, is a neurotropic virus that causes rabies in animals, including humans. The virus is most commonly spread through the bite of an infected mammal, including domestic and wild ones, but transmission can occur from saliva through broken skin or mucous membranes. Following viral transmission, the rhabdovirus travels through the peripheral nervous system targeting the central nerves, which then leads to encephalomyelitis.

In the past, people were so scared of rabies that after being bitten by a potentially rabid animal, many would commit suicide. Virtually all infections with rabies resulted in death until two French scientists, Louis Pasteur and Émile Roux, developed the first rabies vaccination in 1885. On July 6, 1885, Louis Pasteur and his colleagues injected the first of 14 daily doses containing progressively inactivated rabies virus into 9-year-old Joseph Meister, who had been severely bitten by a rabid dog 2 days before. The immunization was successful and the Pasteur rabies immunization procedure was rapidly adopted throughout the world.

Another era in vaccine development is now beginning-an era based on the practical application of recombinant-DNA technology and other novel genetic manipulations of rabies and other viruses and microorganisms. These new technologies promise even more potent and safer vaccines, as well as lower costs, improved stability and easier delivery throughout the world to people at risk.

Louis Pasteur
(27 December, 1822 - 28 September, 1895)



Émile Roux
(17 December, 1853 - 3 November, 1933)

References: 1. ncbi.nlm.nih
2. CDC

Asthma

Asthma is a major noncommunicable disease (NCD), affecting both children and adults and is the most common chronic disease among children. Asthma is included in the WHO Global Action Plan for the Prevention and Control of NCDs and the United Nations 2030 Agenda for Sustainable Development.

It is caused by inflammation and muscle tightening around the airways, which makes it harder to breathe. Asthma is often underdiagnosed and undertreated, particularly in low and middle income countries. People with under-treated asthma can suffer from sleep disturbance, tiredness during the day and poor concentration. If symptoms are severe, people with asthma may need to receive emergency health care and they may be admitted to hospital for treatment and monitoring. In the most severe cases, asthma can lead to death.

Symptoms of asthma can vary from person to person. Symptoms sometimes get significantly worse. This is known as an asthma attack. Symptoms are often worse at night or during exercise. Common symptoms of asthma include:

- A persistent cough, especially at night
- Wheezing when exhaling and sometimes when inhaling
- Shortness of breath or difficulty breathing, sometimes even when resting
- Chest tightness, making it difficult to breathe deeply

Some people will have worse symptoms when they have a cold or during changes in the weather. Other triggers can include dust, smoke, fumes, grass and tree pollen, animal fur and feathers, strong soaps and perfume.

Many factors have been linked to an increased risk of developing asthma, although it is often difficult to find a single direct cause. Such as:

- Family history
- Allergic conditions, such as eczema and rhinitis (hay fever)
- Urbanization
- Events in early life affecting the developing lungs (low birth weight, prematurity, exposure to tobacco smoke and other sources of air pollution, viral respiratory infections)
- Exposure to a range of environmental allergens and irritants (air pollution, house dust, mites, moulds and occupational exposure to chemicals, fumes or dust)
- Obesity

Although asthma can be a serious condition, it can be managed with the right treatment. Reducing tobacco smoke exposure is important for both primary prevention of asthma and disease management. The most common treatment is to use an inhaler, which delivers medication directly to the lungs. Inhalers can help control the disease and enable people with asthma to enjoy a normal, active life.

There are two main types of inhaler:

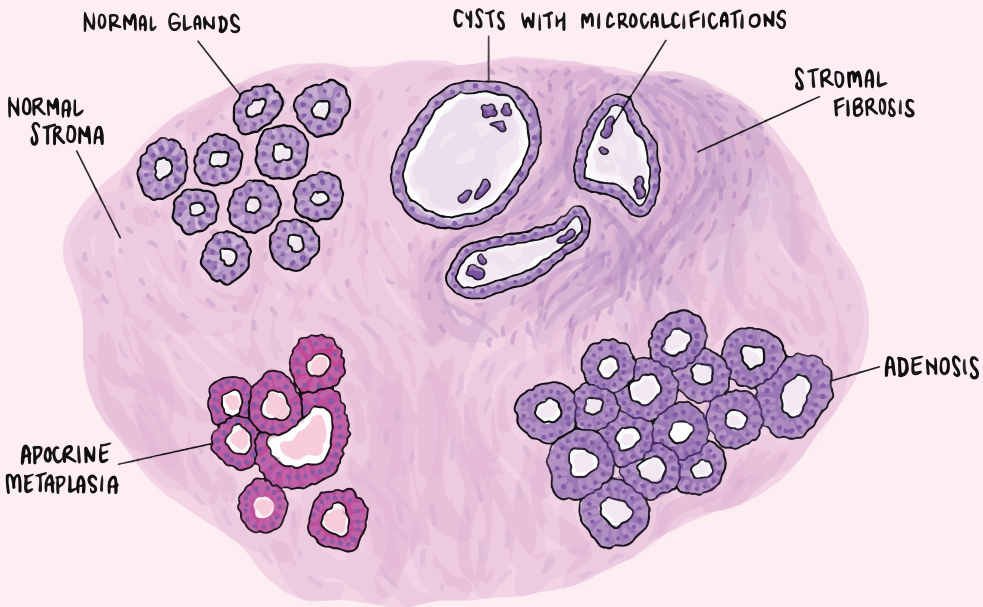
Bronchodilators (such as salbutamol): Open the air passages and relieve symptoms.

Steroids (such as beclometasone): Reduce inflammation in the air passages, which improves asthma symptoms and reduces the risk of severe asthma attacks and death.

People with asthma may need to use their inhaler every day. Using an inhaler can be difficult, especially for children and during emergency situations. Using a spacer device makes it easier to use an aerosol inhaler. This helps the medicine to reach the lungs more easily.

People with asthma and their families need education to understand more about their asthma. This includes their treatment options, triggers to avoid and how to manage their symptoms at home. Healthcare providers may give an asthma action plan to help people with asthma to take greater control of their treatment.

Reference: WHO



REVIEW ARTICLE

Benign Breast Disease in Women

INTRODUCTION

Benign breast disease in women is a very common finding. An understanding of the hormonal and growth factor control of breast development and function is the key to the rational and systematic evaluation and treatment of patients. A firm understanding of benign breast disease is important since sequential steps are necessary to distinguish lesions which impart a high risk of subsequent breast cancer from those which do not.

BREAST PHYSIOLOGY IN WOMEN

Hormones and growth factors act upon stromal and epithelial cells to regulate mammary gland development, maturation and differentiation. Broadly summarized, estrogen mediates development of ductal tissue; progesterone facilitates ductal branching and lobulo-alveolar development and prolactin regulates milk protein production. At puberty, estradiol and progesterone levels increase to initiate breast development. A complex tree-like structure results and comprises 5 to 10 primary milk ducts originating at the nipple, 20 to 40 segmental ducts and 10 to 100 sub-segmental ducts ending in glandular units called terminal duct lobular units (TDLUs). During the menstrual cycle the increments in estrogen and progesterone stimulate cell proliferation during the luteal phase (Figure1). Cycle dependent apoptosis balances proliferation. In response to enhanced proliferation, the breast can increase by as much as 15% in size during the luteal phase.

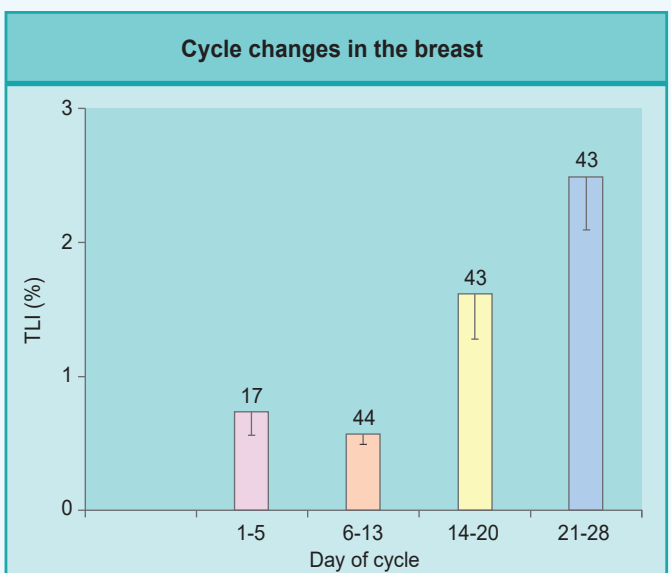


Figure 1. Influence of the cycle phase on breast total labeling index (TLI) of women less than 34 years of age according to whether cycles were natural or regulated by oral contraceptives (OC).

AGE RELATED CHANGES IN BREAST MORPHOLOGY

Anatomic and histologic structures of the breast undergo substantial change during the period from early adolescence to menopause. The normal histologic appearance represents a spectrum ranging from a predominance of ducts, lobules and intra- and inter-lobular

stroma to patterns with a predominance of fibrous change and cyst formation, a process formerly called fibrocystic disease (Figure 2). The term "fibrocystic changes" is now preferred since up to 50 to 60 percent of normal women may have this pattern histologically. During the early reproductive years, stromal hyperplasia may occur and produces juvenile breast hypertrophy or rarely, the more significant problems of unilateral or bilateral macromastia. In the middle reproductive years, glandular breast tissue continues to undergo changes in response to cyclic increments in plasma levels of estradiol and progesterone and if substantial, is called adenosis. Ductal changes remain uncommon while stromal hyperplasia may occur resulting in areas of ill-defined fullness ("lumpy-bumpy" consistency) on physical exam or in firm areas requiring biopsy.

In the late reproductive period, glandular tissue may become hyperplastic with sclerosing adenosis or lobular hyperplasia. Ductal tissue also may undergo hyperplastic change with an increase in number of ductal cells but without alterations in their appearance. This change, when associated with a 2% or greater prevalence of Ki67 positive cells, is associated with an approximately two fold increase of subsequent breast cancer. Based on the number of mutations required for cancer, current opinion suggests that breast cancer is a process that takes many years to develop with the age of menarche as the earliest factor influencing this process. The progression from the earliest neoplastic changes to invasive breast cancer is considered to take a median of 16 years with a range of 1 to 30 years based on doubling time. After the onset of menopause, glandular tissue undergoes involution and stroma and fatty tissue (i.e. approximately 97%) replace glandular elements. The degree of involution is inversely related to the risk of subsequent breast cancer.

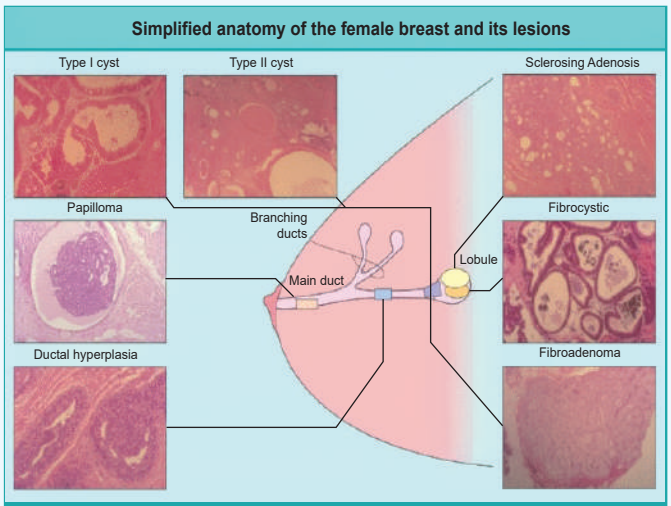


Figure 2. Simplified anatomy of the female breast illustrating the major structural components of the breast, the anatomic location of various lesions and the histology of those lesions and corresponding sites of origin of potential lesions.

SPECIFIC BENIGN BREAST LESIONS

A wide variety of benign breast lesions have been described and the histologic appearance fully characterized. On a practical basis, these can be subdivided into those associated with no substantial increased risk of breast cancer (i.e. < 1.49%), those with an increase of 1.5-2% and those with a >2% increase (Table 1).

Table 1. Relative risk of breast cancer imparted by specific benign breast lesions

Subtypes	Description	Relative risk ±95 Confidence intervals
Diagnostic subtypes	Non-proliferative disease	1.17 (0.94-1.47)
	Proliferative disease without atypia	1.76 (1.58-1.95)
	Benign breast disease not otherwise specified	2.07 (1.64-2.61)
	Atypical hyperplasia not otherwise specified	3.93 (3.24-4.76)
Histologic subtypes	Adenosis	2.00 (1.46-2.74)
	Atypical ductal hyperplasia	3.28 (2.54-4.23)
	Atypical lobular hyperplasia	3.92 (2.81-5.47)
	Cysts not otherwise specified	1.55 (1.26-1.90)
	Fibroadenoma	1.41 (1.11-1.80)
	Papilloma	2.06 (1.38-3.07)

MAMMOGRAPHIC DENSITY AND BREAST CANCER RISK

The percent breast density on mammography correlates with breast cancer risk as shown on Figure 3. When comparing the lowest density category with highest, the relative risk is increased by 5.3 fold. Recent studies examined the histologic composition of dense and non-dense breast tissue. When dense lesions are biopsied and compared to areas of low density, they are found to contain a higher proportion of stroma and glandular tissue and lesser amount of fat. Notably, dense lesions contain more of the enzyme aromatase, when quantitated by an immunologic histologic score after staining with an aromatase monoclonal antibody. These findings are likely associated with a higher local production of estradiol and could explain the higher incidence of breast cancer with both of these lesions. Taking these observations together, determination of breast density assessed by Bi-RADS criteria or quantitated with a computer assisted method of determining breast density, provides the most powerful means of predicting risk of breast cancer over time (Figure 3).

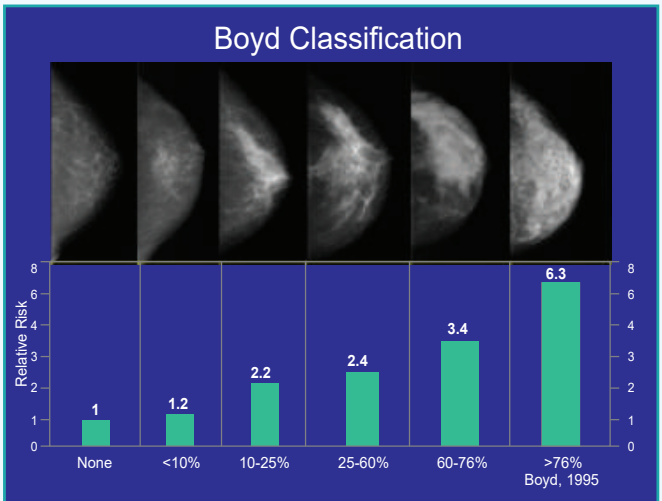


Figure 3. The percentage of breast tissue which is dense on a mammogram is determined by computer assisted analysis and classified as none, 75%. The relative risk of breast cancer increases with each step of increased breast density.

ETIOLOGY OF BENIGN BREAST DISORDERS

Clinical observations in women receiving estrogens and anti-estrogens suggest that hormonal events play a role in the etiology of benign breast lesions. In post-menopausal women receiving estrogens ± progestins for >8 years, the prevalence of benign breast lesions increased by 1.7 fold. In the Women's Health Initiative study (WHI), the use of estrogen plus progestin was associated with a 74% increase in the risk of benign proliferative breast disease. The anti-estrogen, tamoxifen, when used for breast cancer prevention, was associated with a 28 percent reduction in prevalence of benign breast lesions, including adenosis, cysts, duct ectasia, and hyperplasia. Underlying and acquired genetic changes are also associated with benign breast lesions. Loss of heterozygosity (LOH), a finding caused by deletions of small segments of DNA is commonly found in benign breast lesions. Women frequently have multi-focal lesions, each of which exhibit loss of heterozygosity (LOH) of differing regions of DNA. Women with BRCA1/2 mutations are found to have a high frequency of multiple benign or malignant breast lesions when bilateral mastectomy specimens are meticulously examined. These findings support the current theory of an underlying predisposition to mutations in some patients as the cause of multiple breast lesions. In the past, this phenomenon was termed a "field effect" and more recently, a "mutator phenotype".

CLINICAL MANIFESTATIONS

Clinical presentations of benign breast disease are divided into those with pain, lumps or breast discharge (Table 2).

Table 2. Common Benign Breast Disorders in Women

Symptom or Finding	Possible Causes or Disorders
Breast pain	
Cyclic pain	Hormonal stimulation of normal breast lobules before menses
Noncyclic pain	Stretching of Cooper's ligaments Pressure from brassiere Fat necrosis from trauma Hidradenitis suppurativa Focal mastitis Periductal mastitis Cyst Mondor's disease (sclerosing periphlebitis of breast veins)

Symptom or Finding	Possible Causes or Disorders
Nonbreast pain	
Chest-wall pain	Tietze's syndrome (costochondritis) Localized lateral chest-wall pain Diffuse lateral chest-wall pain Radicular pain from cervical arthritis
Non-chest-wall pain	Gallbladder disease Ischemic heart disease
Nipple discharge	
Presence of galactorrhea	
From multiple ducts bilaterally	Hyperprolactinemia from pituitary tumor, hypothyroidism, drugs
Absence of galactorrhea	
From one duct- elicited or spontaneous and bloody, with occult blood or serosanguineous	Intraductal papilloma Ductal carcinoma in situ Paget's disease of breast
From multiple ducts- elicited and bloody or nonbloody, bilateral, black or clear	Fibrocystic changes Ductal ectasia
Discrete solitary lump	
Age < 30 years	
Firm, rubbery lump	Most common lesions: Fibroadenoma
Age 30 – 50 years	
Firm, discrete lump	Most common lesions: Fibroadenoma, cyst, fibrocystic changes, usual ductal hyperplasia, atypical ductal hyperplasia, atypical lobular hyperplasia
Age > 50 years	
Firm, discrete lump	Most common lesions: cyst, ductal carcinoma in situ, invasive cancer
Diffuse lumpiness ("lumpy- bumpy")	
Absence of discrete lump	Fibrocystic changes

Clinical Examination of a Patient with Benign Breast Disease

History

- Characterize symptoms
- Identify risk factors for breast cancer
  - ❑ Age (at menarche, at first live birth)
  - ❑ Number of relatives with breast cancer or ovarian cancer (age at diagnosis)
  - ❑ Number of previous breast biopsies
  - ❑ Presence of atypical hyperplasia or lobular carcinoma in situ on previous breast biopsy
  - ❑ Weight gain after menopause
  - ❑ Waist-to-hip ratio
  - ❑ Results of bone-density testing
- If patient is postmenopausal
  - ❑ Age at menopause
  - ❑ Duration of use of estrogen or progestin therapy

Physical examination

- Palpate the four breast quadrants while patient is sitting and lying down

- ❑ Identify discrete lumps and examine for regional nodes
- ❑ Determine whether consistency is doughy with vague nodularity - findings consistent with fibrocystic changes
- ❑ Determine whether a discrete lesion has distinctly marginated borders- a finding consistent with fibroadenoma

- Examine overlying skin, areola and axilla
- Determine degree of symmetry (asymmetry suggests underlying disease)
- Examine nipple and seek to elicit discharge
  - ❑ Determine whether galactorrhea is present
  - ❑ Determine whether discharge is from one duct or from multiple ducts
  - ❑ Determine whether discharge is viscous, watery, grossly bloody, serosanguineous, clear, blue-black or green
  - ❑ Determine whether occult blood is present
- Seek to elicit chest-wall pain
  - ❑ Examine costochondral junctions (Tietze's syndrome)
  - ❑ Examine lateral chest wall while patient is lying on her side (at 90 degrees) to move breast away from chest wall
  - ❑ Compare pain elicited by squeezing breast tissue with pain elicited by palpation of chest wall

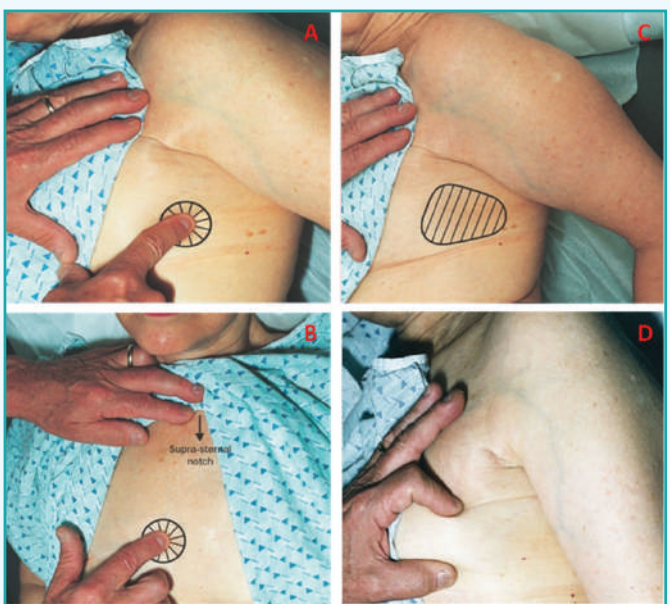


Figure 4. A. Focal chest wall pain—lateral. The patient is turned 90° on her side so that breast tissue is no longer under the area of palpation. The index finger elicits a focal area of pain. B. Focal chest wall pain over costochondral junctions anteriorly. C. Diffuse lateral chest wall pain. With the patient turned over 90 degrees on her side, pain is elicited over a wider area of the chest wall. D. Verification that squeezing breast tissue does not elicit pain ensures that the pain is not related to the breast but represents chest wall pain.

gynecologist or surgeon with expertise in breast diseases should be involved in the evaluation of patients with breast disorders. MRI mammography, ductography or ultrasound may be utilized (Figures 5 and 6). The method of documenting whether breast pain is chest wall related is illustrated on Figure 4 A-D. Imaging has become an integral part of the management of benign breast disorders.

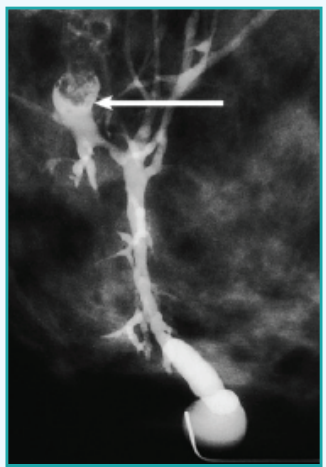


Figure 5. Galactogram illustrating space occupying lesion. A catheter is inserted into the duct from which the bloody discharge emerges. Contrast material is then injected through the catheter. The various branches of the duct are outlined.

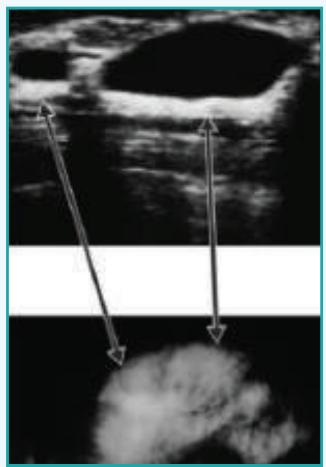


Figure 6. Upper panel illustrates by ultrasound a non-dense black area representing cyst fluid. The lower panel is the corresponding area on mammogram showing a dense area. With the combination of mammogram and ultrasound, the lesion can be shown to be a cyst.

IMAGING STUDIES

Mammography is useful for evaluation of palpable lesions, particularly in those over 35. Digital mammography is preferred because of its ability to penetrate through dense breast tissue which is commonly found in younger women. Ultrasound is often used as initial evaluation of a palpable mass in women under age 35. If a simple cyst is present, no further evaluation is necessary (Figure 6). If not, mammography may also be necessary to fully evaluate the lump. If the mass has findings suggestive of a fibroadenoma by ultrasound and mammography, short term followup and re-imaging can be considered (usually performed in 6 months). Experts are divided as to the necessity to biopsy all fibroadenomas. MRI is more sensitive than digital mammography but false positives are more common. Routine yearly MRI is now recommended for women whose lifetime risk of breast cancer is > 20%. As an illustration of its sensitivity, 3% of the contralateral breasts in women with diagnosed breast cancer are found to have a second lesion in the opposite breast when examined by MRI.

TREATMENT OF BENIGN BREAST DISEASE IN WOMEN

The initial step in evaluating pain is to distinguish true breast pain from chest wall pain (Figure 4). Several well designed, randomized, controlled, double blind, cross over trials have validated the efficacy of medical therapy for cyclic mastalgia. Based upon these studies, we categorize therapies as definitely effective, definitely ineffective, possibly effective and insufficiently studied. Danazol, bromocriptine and tamoxifen have been proven to be effective. Linoleic acid in the form of evening primrose oil has been shown effective in two randomized trials but not in the third, the largest trial. Its role in treatment therefore remains uncertain. Vitamin E is considered definitely ineffective and iodine and vaginal progesterone possibly effective. Medroxyprogesterone acetate, caffeine avoidance and progesterone have not been sufficiently studied. Several other therapies have not been examined in randomized controlled trials but are likely to be beneficial since they are based upon physiologic principles. For example, precise fitting of a bra to provide support for pendulous breasts has been reported to relieve pain in observational studies. GnRH agonist analogues are used to lower LH, FSH and estradiol levels and to create a temporary post-menopausal state. Onset of menopause is known to reduce the frequency of breast pain. This therapy is reserved for patients in whom all other measures fail and the pain is considered severe. Reduction of the dosage of estrogens in post-menopausal women or addition of an androgen to estrogen replacement therapy appears to be beneficial in reducing breast pain. The approach to non-breast pain is outlined in Figure 7.

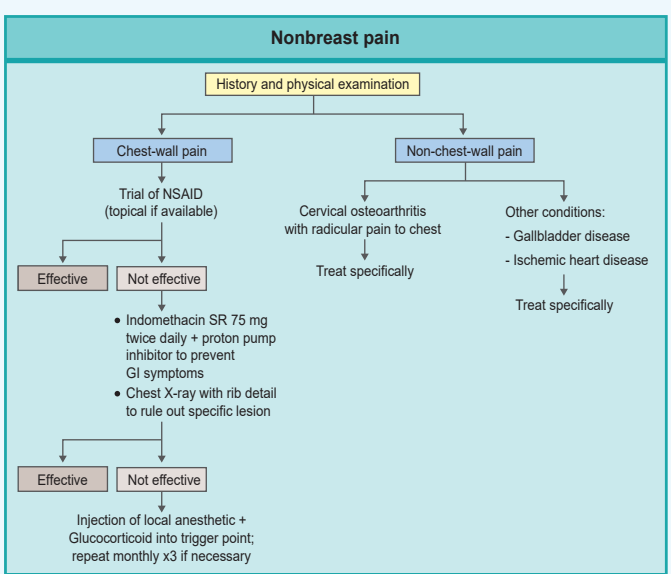


Figure 7. Algorithm to treat non-breast pain

WOMEN AT HIGH RISK FOR BREAST CANCER

A major consideration for women who present with breast problems is whether they have a higher than normal risk of developing breast cancer. Certain breast lesions such as fibrocystic changes are associated with no increased risk of subsequent breast cancer. A 1.5 to 2- fold greater risk of development of breast cancer over a 20 year period of follow-up occurs with proliferative lesions including ductal hyperplasia, lobular hyperplasia without atypia, sclerosing adenosis, diffuse papillomatosis and complex fibroadenomas. A recent report also suggested that radial scars increase relative risk by 1.8, a risk similar to that found in proliferative disease without atypia. The presence of dense breast tissue on mammography has also been reported to be a predictor of increased incidence of breast cancer. Two components of this finding must be considered: one, the presence of high breast density makes it more difficult to read mammograms and masks the sensitivity of finding a breast cancer initially but identifies it later and two, there is an increased risk of breast cancer associated with increased breast density. According to classic twin studies, heritability accounts for approximately 60% of the variation in breast density. Breast cancer risk is also increased in association with high plasma estradiol and testosterone levels in postmenopausal women and 20 kg or more weight gain in the pre-menopausal years. Another risk factor is use of hormone replacement therapy. This risk is probably increased further in women starting this therapy shortly after the menopause. Starting this therapy a long time after experiencing menopause (long gap) is associated with a lesser relative risk. The use of estrogen alone was associated with a trend toward reduction of risk of breast cancer at five years and a statistically significant reduction in those adhering to therapy.

BREAST CANCER PREVENTION

Patients with benign breast lesions imparting an increased risk of breast cancer can be offered tamoxifen (or raloxifene) as a prevention strategy. The risk of breast cancer is determined using the Gail or Tyrer-Cuzick model and the benefits versus risks of tamoxifen evaluated. Current recommendations suggest that women with a five year risk of breast cancer of over 1.67 percent and no contraindications to tamoxifen should be informed about the possibility of taking tamoxifen for five years. A recent overview has shown a 38 percent reduction of the relative risk of breast cancer with tamoxifen but benefits may be offset by increased risks of thromboembolic phenomena, endometrial cancer and maturation of cataracts. The Star trial addressed whether raloxifene might be preferable to tamoxifen and demonstrated relative equivalence. However, of interest was the fact that tamoxifen prevented more non-invasive breast cancers than did raloxifene. More intensive and frequent screening with multimodality imaging may be required in high risk patients. Atypical hyperplasia lesions appear to be more amenable to breast cancer prevention as reviewed from non-head-to-head studies showing prevention ranging from 62 to 75% reduction in four separate randomized studies when compared to a 38% reduction in women selected to be at high risk based on reproductive factors.

Reference: ncbi.nlm.nih.gov

Dementia

Dementia is the loss of cognitive functioning such as, thinking, remembering and reasoning to such an extent that it interferes with a person's daily life and activities. Some people with dementia cannot control their emotions and their personalities may change. Dementia ranges in severity from the mildest stage, when it is just beginning to affect a person's functioning; to the most severe stage, when the person must depend completely on others for basic activities of daily living such as feeding oneself. There are several different forms of dementia, including Alzheimer's disease, which is the most common.

Dementia affects millions of people and is more common as people grow older but it is not a normal part of aging.

SIGNS AND SYMPTOMS

Signs and symptoms of dementia result when once-healthy neurons (nerve cells) in the brain stop working, lose connections with other brain cells and die. While everyone loses some neurons as they age, people with dementia experience far greater loss.

The signs and symptoms can vary depending on the type and may include:

- Experiencing memory loss, poor judgment and confusion
- Difficulty speaking, understanding and expressing thoughts or reading and writing
- Wandering and getting lost in a familiar neighborhood
- Trouble handling money responsibly and paying bills
- Repeating questions
- Taking longer to complete normal daily tasks
- Losing interest in normal daily activities or events
- Hallucinating or experiencing delusions or paranoia
- Acting impulsively
- Not caring about other people's feelings
- Losing balance and problems with movement

CAUSES OF DEMENTIA

Dementia is the result of changes in certain brain regions that cause neurons (nerve cells) and their connections to stop working properly. Researchers have connected changes in the brain to certain forms of dementia and are investigating why these changes happen in some people but not others. For a small number of people, rare genetic variants that cause dementia have been identified.

DIFFERENT TYPES OF DEMENTIA

Various neurodegenerative disorders and factors contribute to the development of dementia through a progressive and irreversible loss of neurons and brain functioning. Types of dementia include:

Alzheimer's disease: The most common dementia diagnosis among older adults. It is caused by changes in the brain, including abnormal build-ups of proteins known as amyloid plaques and tau tangles.

Frontotemporal dementia: A rare form of dementia that tends to occur in people younger than 60. It is associated with abnormal amounts or forms of the proteins tau and TDP-43.

Lewy body dementia: A form of dementia caused by abnormal deposits of the protein alpha-synuclein, called Lewy bodies.

Vascular dementia: A form of dementia caused by conditions that damage blood vessels in the brain or interrupt the flow of blood and oxygen to the brain.

Mixed dementia: A combination of two or more types of dementia.

Other conditions that cause dementia or dementia-like symptoms include:

- Normal pressure hydrocephalus
- Creutzfeldt-Jakob disease
- Huntington's disease
- Chronic traumatic encephalopathy
- HIV-associated dementia
- Heavy alcohol use over a long period of time
- Head injury such as a concussion from a fall or accident
- Emotional problems such as stress, anxiety and depression
- Delirium

In addition, medical conditions such as tumors, vitamin deficiencies, medication side effects or problems with the thyroid, kidney or liver can also cause serious memory problems that resemble dementia. Some causes of dementia symptoms can be halted or even reversed with treatment. For example, normal pressure hydrocephalus often resolves with treatment.

DIAGNOSIS

To diagnose dementia, doctors first assess whether a person has an underlying, potentially treatable, condition that may relate to cognitive difficulties. A physical examination to measure blood pressure and other vital signs, as well as laboratory tests of blood and other fluids to check levels of various chemicals, hormones and vitamins, can help uncover or rule out possible causes of symptoms.

A review of a person's medical and family history can provide important clues about risk for dementia. Typical questions might include asking about whether dementia runs in the family, how and when symptoms began, changes in behavior and personality and if the person is taking certain medications that might cause or worsen symptoms.

The following procedures also may be used to diagnose dementia:

Cognitive and neurological tests: It is used to evaluate thinking and physical functioning. These tests include assessments of memory, problem solving, language skills and math skills, as well as balance, sensory response and reflexes.

Brain scans: These tests can identify strokes, tumors and other problems that can cause dementia. Scans also identify changes in the brain's structure and function. The most common scans are:

- Computed tomography (CT)
- Magnetic resonance imaging (MRI)
- Positron emission tomography (PET)

Psychiatric evaluation: If someone is experiencing behavioral or mood changes, a psychiatric evaluation may be recommended to help determine if depression or another mental health condition is causing or contributing to a person's symptoms.

Genetic tests: Some forms of dementia are caused by a person's genes. In these rare cases, a genetic test ordered by a doctor can help people know if they have the altered genes.

Cerebrospinal fluid (CSF) tests: Doctors collect CSF by performing a lumbar puncture, also called a spinal tap. Measuring the levels of proteins or other substances in CSF may be used to help diagnose Alzheimer's or other types of dementia.

Blood tests: Blood test to measure levels of beta-amyloid, a protein that accumulates abnormally in people with Alzheimer's.

TREATMENT AND CARE

Treatment of dementia depends on its cause. In the case of most progressive dementias, including Alzheimer's disease, there is no cure, but two treatments: Aducanumab and Lecanemab which demonstrate that removing beta-amyloid, one of the hallmarks of Alzheimer's disease, from the brain reduces cognitive and functional decline in people living with early Alzheimer's. Others can temporarily slow the worsening of dementia symptoms and improve quality of life for those living with Alzheimer's and their caregivers. The same medications used to treat Alzheimer's are among the drugs sometimes prescribed to help with symptoms of other types of dementias. Non-drug therapies can also alleviate some symptoms of dementia.

Non-drug Approaches

Non-drug approaches to managing behavior symptoms promote physical and emotional comfort.

Many of these strategies aim to identify and address needs that the person with Alzheimer's may have difficulty expressing as the disease progresses. Non-drug approaches should always be tried first.

Steps to developing successful non-drug treatments include:

- Recognizing that the person is not just "acting mean or ornery," but is having further symptoms of the disease.
- Identifying the cause and how the symptom may relate to the experience of the person with Alzheimer's.
- Changing the environment to resolve challenges and obstacles to comfort, security and ease of mind.

RISK AND PREVENTION

Some risk factors for dementia, such as age and genetics, cannot be changed. But researchers continue to explore the impact of other risk factors on brain health and prevention of dementia. Adopting multiple healthy lifestyle choices, including healthy diet, not smoking, regular exercise and cognitive stimulation, may decrease the risk of cognitive decline and dementia.

Early detection of symptoms is important as some causes can be successfully treated. However, in many cases, the cause of dementia is unknown and cannot be effectively treated. Still, obtaining an early diagnosis can help with managing the condition and planning ahead. In the early stages of dementia, it may be possible for people to continue with their everyday activities. As the disease progresses, people will need to adopt new strategies to help adjust.

References: 1. Alzheimer's Association
2. National Institute on Aging

CASE REVIEW

A Suspected Case of Lyme Disease Causing Complete Heart Block

INTRODUCTION

Lyme disease is a tick-borne multisystem disease caused by Borrelia burgdorferi (other causative organisms being Borrelia mayonii, Borellia afzelii and Borellia garinii). Clinical manifestations of Lyme disease can be categorized into three phases

- Early localized (usually within 7–14 days)
- Early disseminated (within days to several weeks)
- Late disease (several weeks to months)

Lyme carditis usually manifests during the early disseminated phase, occurring within a few weeks from the exposure. Despite being a relatively less frequent complication of Lyme disease, carditis can present with life-threatening presentations, such as bradycardia, heart block, ventricular fibrillation, asystole etc. It is thought to be caused by cross-reactive antibodies (IgM and IgG) damaging the heart; however, the exact mechanism is not entirely understood. The most common presentation of Lyme carditis is atrioventricular conduction block (AV block), which can vary from prolonged PR interval to complete AV dissociation. Lyme disease can be diagnosed by detecting Borrelia-specific IgM and IgG antibodies. Our case describes a unique presentation of Lyme carditis associated with a positive IgM but a negative IgG; an uncommon finding.

CASE REPORT

A 37-year-old previously healthy male presented to the emergency department with two episodes of syncope without prodromal symptoms in the past 5 days. During these days, he had increasingly frequent episodes of dizziness and near-syncope. He also reported fever, chills, muscle aches, and bilateral lower extremity erythematous rash that had developed 3 weeks earlier that had resolved by the time of presentation. The patient reported removing several ticks from his left thigh and groin. SARS-CoV-2 tests were negative for active infection and he had no history of recent travel. An initial electrocardiogram (ECG) revealed complete heart block with a heart rate of 55 bpm (ECG shown in Fig. 1), so a temporary pacemaker was urgently inserted. Laboratory testing was positive for B.burgdorferi IgM and IgG antibodies on enzyme-linked immunosorbent assay (ELISA) screen and confirmatory western blot. Based on these data, Lyme carditis was diagnosed and he was started on intravenous ceftriaxone. An echocardiogram showed diastolic tricuspid and mitral regurgitation (Echocardiography shown in Fig. 2). After 9 days the complete heart block resolved. Follow up ECG on day 10 showed first degree atrioventricular (AV) node block with a PR interval of 280 ms and a heart rate of 64 bpm (ECG shown in Fig. 3). The patient was then transitioned to oral doxycycline 100 mg PO BID to complete total 4-week course of antimicrobials and was discharged.

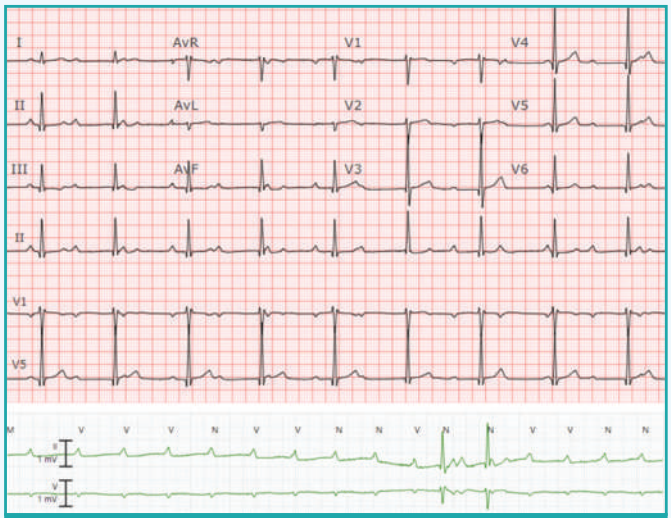


Fig. 1. Initial ECG showing normal sinus rhythm with complete heart block with a narrow QRS complex (top) and a rhythm strip showing complete heart block with many non-conducted P-waves and prolonged ventricular pauses.

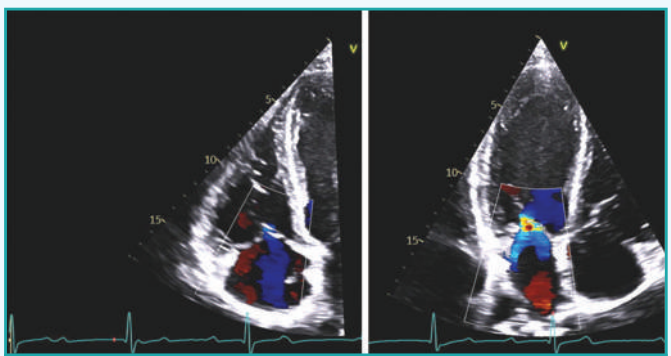


Fig. 2. Echocardiography from apical 4-chamber views showing tricuspid regurgitation (left) and mitral regurgitation (right) during diastole. Red marker on the ECG denotes where in the cardiac cycle the image was taken.

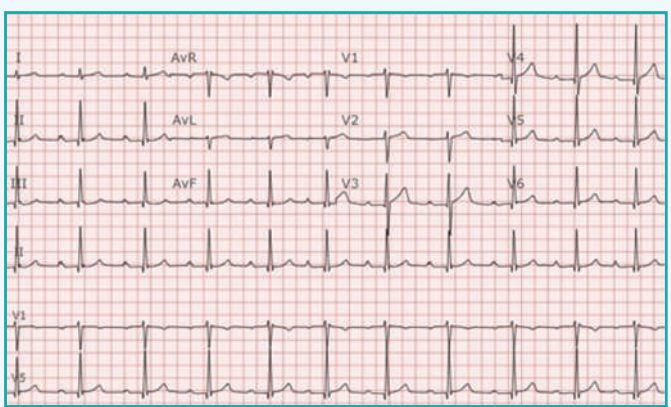


Fig. 3. Follow up ECG showing normal sinus rhythm with first degree AV block and a PR interval of 280 ms.

DISCUSSION

Lyme carditis is an uncommon manifestation of Lyme disease that primarily affects males between 20 and 40 years old, consistent with our case, and women 25–29 years old. Cardiac involvement is a rare complication of the early dissemination stage of Lyme disease; it is estimated that 4–10% of patients in the United States with untreated Lyme disease develop carditis and it may be isolated or accompanied by cutaneous erythema migrans, joint (arthritis), or neurologic (neuroborreliosis) manifestations. Some estimates show the prevalence of asymptomatic carditis as high as 30%; while in other cases symptoms of Lyme carditis are heterogenous and non-specific, including lightheadedness, syncope, dyspnea, palpitations, and chest pain. Preceding history of flu-like symptoms, EM, and travel usually occur 1–2 months prior to cardiac syndrome presentation, contributing to lack of recall in several cases.

The most common finding in Lyme carditis is AV block with symptoms such as light-headedness, syncope or near-syncope, shortness of breath, palpitations, and chest pain. Heart block in Lyme carditis can be acute onset and rapidly fluctuating. In up to 90% of cases, Lyme carditis presents as AV block, typically intermittent and shifting from first to third-degree in severity . Among cases of Lyme carditis with high-grade (second-degree type 2 or third-degree) AV block, almost half progressed to complete heart block and 20% included second-degree AV block . Progression of first-degree AV block to complete AV block appears most likely when the PR interval exceeds 300 ms . Other conduction abnormalities of Lyme carditis include left and right bundle branch blocks, diffuse ST segment depression with prominence in the anterolateral leads, and T wave flattening or inversion, typically in the inferolateral leads. Additionally, sick sinus syndrome, atrial fibrillation, isolated tachycardia-bradycardia syndrome, supraventricular and ventricular tachycardias, ventricular fibrillation, pericarditis, myocarditis, endocarditis, pericardial effusion, small vessel vasculitis, cardiomegaly and sudden cardiac death have been reported related to Lyme carditis.

DIAGNOSIS

Prompt recognition of Lyme carditis is important to avoid life threatening complications from the disease and unnecessary treatment such as permanent pacing. Although, appropriately diagnosing Lyme carditis is challenging, requiring confirmation of the association between a patient's historical, clinical, and laboratory data.

Patients presenting with AV block should be asked about possible tick exposure, history of erythema migrans rash, recent travel to a

high-incidence Lyme disease area and other constitutional symptoms of Lyme disease like fever, fatigue, malaise, chills, muscle and joint pain. Clinicians should be familiar with the prevalence of Lyme disease in their geographical location. A primarily clinical strategy for diagnosis of Lyme carditis in the setting of AV block can lead to failure to recognize Lyme disease, especially as the geographical distribution of Lyme disease changes related to climate change and northern migration of Ixodes ticks and host animals. Moreover, Lyme carditis can be difficult to recognize in cases where classic signs of Lyme disease are not obvious upon patient presentation and EM rash or tick bite difficult to recall. To address these challenges with the timely diagnosis of Lyme carditis, the Suspicious Index in Lyme Carditis (SILC) has been proposed. This risk score emphasizes important demographic and clinical parameters suggestive of Lyme disease, and patients are classified based on these criteria as low, intermediate, or high risk for the presence of Lyme carditis.

Laboratory tests are helpful to support the diagnosis, even if not required in patients with potential tick exposure in a Lyme disease endemic area with history of one or more skin lesions compatible with EM. During the early disseminated phase, most patients present with IgM and IgG seropositivity against B. burgdorferi. The most frequent assays used are ELISA and Western blotting. In addition, 12-lead ECG and telemetry should be performed in cases with high clinical suspicion of Lyme carditis and real-time ambulatory cardiac telemetry may also be particularly useful for such patients. Other tests like echocardiography and chest radiography are useful for evaluation of heart size, heart function, and the presence of pericardial effusion and pulmonary congestion. Most cases of Lyme carditis exhibit structural and functional cardiac abnormalities that are mild and transient. In patients with AV block, diastolic mitral and tricuspid regurgitation due to dissociation of atrial and ventricular systole are often detected as in this case. Current guidelines do not recommend routine endomyocardial biopsy for diagnosis given the potential focality of myocarditis and the high risk of the procedure, although it can be considered in specific cases.

MANAGEMENT

The cornerstone of management of Lyme carditis is supportive care and antimicrobial therapy. Heart block due to Lyme carditis is mostly reversible and correct diagnosis avoids permanent pacemaker placement and its long-term complications. Adults with mild Lyme carditis, presenting only with first-degree AVB, with PR < 300 ms, can be treated with outpatient oral antibacterials, generally doxycycline 100 mg oral twice daily for 14–21 days. Inpatient care is recommended for patients with severe AV block with a PR interval > 300 ms, second or third degree AVB, in whom continuous ECG monitoring is recommended. In these patients, antibacterial therapy with IV ceftriaxone 2 g once daily is suggested, with conversion to oral therapy upon evidence of clinical improvement.

It has been reported that 35–59% of patients with high-grade AV block, (secondary degree type 2 or type 3 complete heart block) undergo temporary pacing, either transcutaneous or transvenous . More than 90% of patients with high grade heart block show resolution within one week of beginning antibacterial therapy, therefore temporary rather than permanent pacemaker placement is preferred . To further evaluate patients in whom temporary pacing was required and for whom restoration of 1:1 AV conduction occurs, stress ECG has been suggested to assess AV conduction stability at higher heart rates . Although there are case reports demonstrating the need for permanent pacing in Lyme carditis despite correct antibacterial therapy, this is rare.

CONCLUSION

Timely diagnosis and treatment of heart block due to Lyme carditis can lead to immediate and life-saving temporary pacing during initiation of antibiotic therapy, while avoiding unnecessary permanent pacemaker placement. Clinical suspicion for Lyme carditis should be high for young patients with unexplained high grade heart block, particularly in Lyme disease endemic areas. The pathogenesis of this condition is not well understood but it is likely to result from a complex interplay of host, pathogen and disease related factors.

References: 1. Oxford Medical Case Reports
2. sciencedirect.com

World Cancer Day

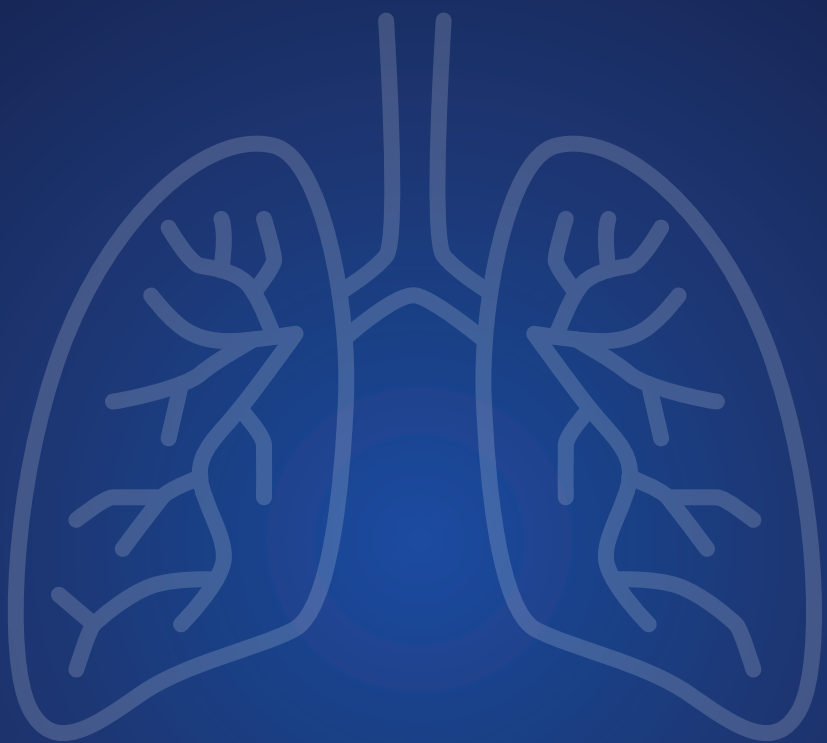
4 February, 2024

Together, we challenge those in power

World Cancer Day is an initiative of the Union for International Cancer Control (UICC), the largest and oldest international cancer organization. World Cancer Day was born on the 4 February 2000 at the World Summit Against Cancer for the New Millennium in Paris.

This World Cancer Day, the power of working together will be recognized. Together, the leaders will be made sure to know the demand of a commitment to prioritizing cancer, to creating innovative strategies designed to confront inequity and to investing resources to achieve a just and cancer-free world. The leaders will be called to eliminate health inequities by addressing their root causes, ensuring that everyone has access to quality health services when, where and how they need them.

Reference: World cancer day



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INFO QUIZ CARD

(BMDC registered doctors only)

AMM / FM Territory Code……..

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Read the questions, tick (√) the correct answers and hand over the Info Quiz Card attached to the Info Medicus to your nearest ACI representative by 31st December 2023.

1. **Below which type of dementia can be inherited?**
   (a) Diffuse Vascular Dementia (b) Alzheimer's Disease
   (c) Fronto Temporal Dementia (d) Lewy Body Dementia

2. **Which is the most common type of benign breast disease?**
   (a) Adenoma (b) Fibroma (c) Fibroadenoma (d) Non-invasive ductal carcinoma

3. **Which one is the characteristic finding of life-threatening asthma?**
   (a) PEF < 33% (b) O2 saturation > 92% (c) Hypertension (d) Tachycardia

4. **Which of the following disease is associated with Jarisch-Herxheimer reaction?**
   (a) Lyme disease (b) Kala-azar (c) Malaria (d) Measles

5. **People with Hodgkin lymphoma have abnormal lymphocytes; what are they called?**
   (a) Atypical squamous cells (b) Reed-Sternberg cells
   (c) Pencil cells (d) CMV-infected cells