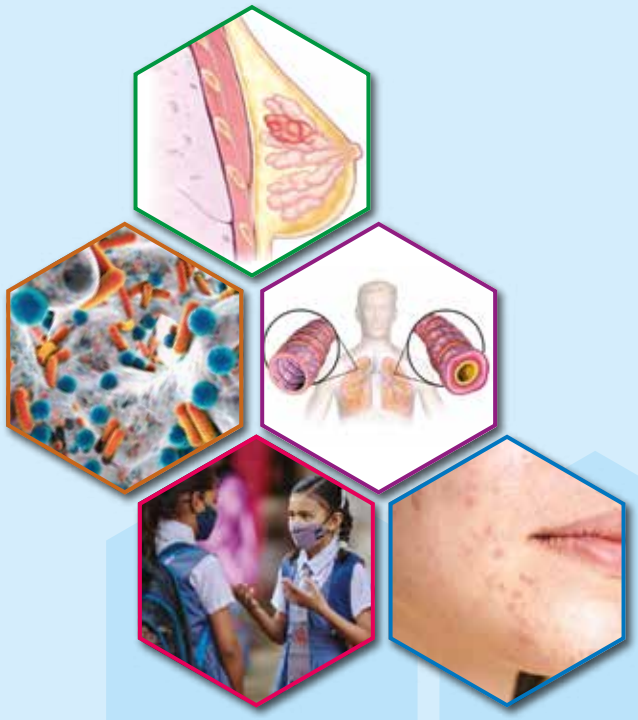
April 2023 Vol 28 No. 1 ISSN 1681-5552

the SQUARE Healthcare bulletin

Since 1993

- Antimicrobial Resistance
- Breast Cancer
- Acute Respiratory Distress Syndrome
- Post COVID Syndrome
- Psoriasis



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the SQUARE
healthcare bulletin

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Editorial

Dear Doctor,

Welcome to this addition of 'the *SQUARE'* healthcare bulletin!

Firstly, let us take the opportunity to offer you all our best wishes from our editorial team!

This issue contains a blend of selected articles. At the beginning, we focused on "Antimicrobial Resistance" which poses a worldwide public health threat and has become a huge obstacle to the effective control of related infectious diseases. We have highlighted on "Breast Cancer", that occurs in every country of the world in women at any age after puberty but with increasing rates in later life. We have presented a feature on "Acute Respiratory Distress Syndrome" is a common yet complex syndrome that develops in critically ill patients. Here, we have also included a topic on "Post COVID Syndrome" is a complex, multifactorial illness that describes the residual effects of the acute COVID-19 infection. Besides, in this issue we have presented a feature on "Psoriasis" is a chronic, noncontagious, multisystem, inflammatory disorder. You will also find our regular feature, "Test Yourself" in this issue.

We carefully tried to make this issue interesting and informative. We hope you will find this issue useful too!

On behalf of the management of SQUARE we wish you all a healthy, prosperous lives!

Thank you

Omar Akramur Rab

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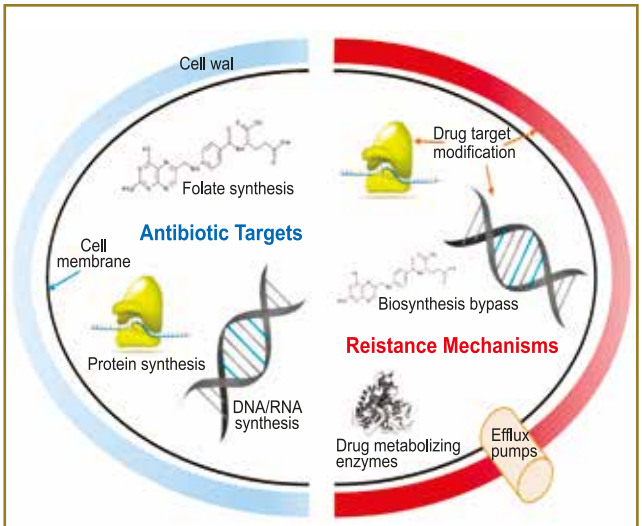
Key title: the *SQUARE* (Dhaka)
Abbreviated key title: *SQUARE* (Dhaka)

Antimicrobial Resistance

Antimicrobial resistance (AMR) is a complex issue of global concern. Antibiotics are a pillar of modern medicine, used for treatment and prevention of bacterial infection. These are played a significant role in increasing life expectancy witnessed in the second half of the 20th century. The discovery of antibiotics has been regarded to be the bedrock of many of the greatest medical advances of the 20th century. The era of antibiotic discovery made the therapeutic and surgical aspects of clinical medicine relatively safer. Antimicrobial resistance (AMR) is a challenge to human wellbeing all over the world and is one of the more serious public health concerns. AMR has the potential to emerge as a serious healthcare threat if left unchecked and could put into motion to another pandemic. Apart from being an emerging threat in the clinical space, AMR also increases treatment complexity, posing a real challenge to the existing guidelines in the management of antibiotic resistance. The attribute of resistance development has been linked to many genetic elements, some of which have complex transmission pathways between microbes. Beyond this, new mechanisms underlying the development of AMR are being discovered. Apart from the genetic aspects of AMR, other practices, including misdiagnosis, exposure to broad-spectrum antibiotics and lack of rapid diagnosis, add to the creation of resistance.

Microbial pathogens continue to evolve and develop resistance and this, combined with the extreme decline in antibiotic research has only increased the magnitude of AMR and its impacts on global healthcare costs and outcomes. The rampant upswing in the use of antibiotics with over-the counter options fueled AMR. This also adds to the risk of re-emergence of many diseases; like the emergence of extensively drug-resistant tuberculosis (XDR-TB). However, infections by multidrug-resistant bacteria are on the rise globally, causing the specter of untreatable infections to become a reality. World Health Organization (WHO, Geneva, Switzerland) report in 2017, confirmed that the entire world would will run out of antibiotics, as the existing drugs in clinical use were developed through modifications to the existing classes and have shown to have short impact cycles.

The European Commission has documented the occurrence of AMR-related deaths to be around 33,000/year in the European Union (EU), costing about €1.5 billion/year in healthcare costs. The 2019 antibiotic resistance threat report published by the Center for Disease Control and Prevention estimated the occurrence of AMR to be over 2.8 million/year in the USA, including over 35,000 deaths. The report also further detailed threats under urgent, serious, concerning and watch list categories; carbapenem resistance was considered urgent. The emergence of carbapenem-resistant bacteria raises a serious concern, as these are categorized as the “last-resort” antibiotics for treating multidrug resistance infections. Increasing global antimicrobial resistance (AMR) is a major threat to human and animals and endangering decades of improvements in health-care outcomes and also undermines food safety.

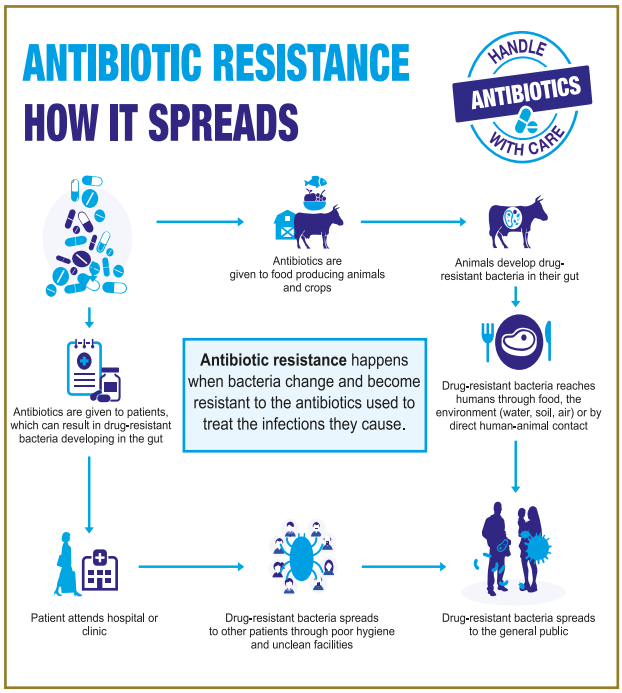


Molecular mechanisms of antimicrobial resistance (AMR)

Factors Contributing to AMR

Throughout history, the development of antibiotic resistance has been documented to be a natural process to enable survival of the bacteria, but has been fueled by human activities, including the misuse of antibiotics in the medical, veterinary and agricultural sectors, which include the inappropriate prescribing of antibiotics, their overuse in the livestock sector and insufficient hygiene practices in hospital, all contribute to the rise of AMR. Global trade and travel are also accelerating the spread.

- AMR, apart from adding to the challenge around disease management, also impacts the patient. It has been documented to compromise the human immune system and increase complications and vulnerability after complicated surgeries involving cancer, knee replacement, dialysis, etc. Further, individuals with comorbid conditions have an increased risk of severe adverse outcomes with AMR. Conditions which necessitate the use of "last-resort" antibiotics also significantly increase treatment costs to the patient, prolonging in-hospital stay and admission rates.



- The mounting evidence around antibiotic usage practice being a crucial risk towards AMR necessitates the need to include habitual and appropriately guided clinical management practices. Knowledge about vaccinations, transmission and prevention strategies are the key in public health education. Elaborate care practices for wounds and infections among patients with comorbid conditions can reduce the burden on hospital admission and control infection spread.
- Communicating the need for antibiotics based on diagnosis and recommended clinical management protocol is also a crucial aspect in AMR. A lack of diagnostic tools and regulatory guidelines and self-treatment with over-the-counter antibiotics for ailments such as the common cold and flu are common in developing countries, adding severely to the burden of AMR.
- Apart from changes in antibacterial use and consumption patterns across different global economies, modern day travelling has also been a major contributor towards dissemination of new infections and antibiotic resistance across the world. The recent coronavirus disease (COVID-19) pandemic is the best example. One documented study among European travelers from India identified the presence of Carbapenemase Producing Enterobacteriaceae (CPE), even among those with no contact with the Indian healthcare system during their stay.

Factors Contributing to AMR Transmission

Transmission of highly drug resistant microbes has been documented to occur inter and intra species. Identifying the reservoirs and best practices around causes for transmission will be fundamental to control future pandemics. Pandemics and epidemics involving COVID-19 are examples involving viruses which spread material between species. Any public healthcare measure that can control the dissemination and use of antibacterial agents is the first step in controlling AMR. High-quality global surveillance systems are needed to provide warnings associated with changes in antimicrobial use and avoidance of the time lag in knowledge transmission is a key to prevent a global health crisis by AMR.

Bacterial Resistance Mechanisms

Bacteria have a remarkable genetic flexibility that allows them to respond to a wide array of environmental threats, including the presence of antibiotic molecules that may jeopardize their existence. Bacteria's are sharing the same ecological niche with antimicrobial-producing organisms have evolved ancient mechanisms to withstand the effect of the harmful antibiotic molecule and consequently, their intrinsic resistance permits them to thrive in its presence. There are many mechanisms that bacteria exhibit to protect themselves from antibiotics and understanding the mechanisms by which bacteria resist antibiotics will become critical to solve the crisis.

Misuse of antibiotics may contribute to the development of resistant bacteria; an incomplete course of antibiotics risks not entirely eradicating the colony thus allowing the development of resistant bacteria. Mechanisms of drug resistance fall into several broad categories, including active efflux pumps, drug inactivation/alteration, modification of drug binding sites/targets, changes in cell permeability resulting in reduced intracellular drug accumulation, biofilm formation and others.

Efflux Pumps

Efflux pumps are transporter proteins involved in the removal of toxic substances from the interior of the cell to the external environment. Efflux pumps in bacteria are major contributors to drug resistance; they extrude a broad spectrum of antibiotics to the exterior of the organism. Hence, infections caused by these pathogens can be difficult to treat. Some efflux pumps are specific for a single drug while others are capable of transporting multiple substrates. The genes of efflux pumps can be intrinsic or acquired. The intrinsic efflux mechanism of resistance is chromosomally encoded and is activated by environmental signals or by mutation in regulatory genes.

Antibiotic Inactivation

Bacteria uses several mechanisms of rendering antimicrobials inactive such as the enzymatic hydrolysis of antibiotics, group transfer and redox process. The production of β- lactamases that hydrolyze the β-lactam ring of penicillins is the classical example of antibiotic inactivation. The enzymes can often be excreted by the bacteria, inactivating antibiotics before they reach their target within the bacteria. The second mechanism of antibiotic inactivation involves enzyme mediated structural alteration of the drug via transfer of a functional group such as an acyl, ribosyl, phosphoryl or thiol group. The modified antibiotic is unable to bind to the target due to the resultant change in the structure and the reaction is irreversible. The third mechanism of antibiotic inactivation is by redox reaction.

Target Modification

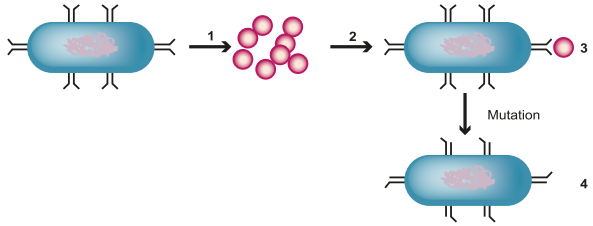
Modification of the antibiotic target site makes the antibiotic unable to bind properly. Microorganisms cannot evade antimicrobial action by dispensing with them entirely because of the vital cellular functions of the target sites. In this mechanism, bacteria found ways to alter the targets of antimicrobial agents. The classical example of drug target modification is the staphylococcal mechanism of variously altering the Penicillin Binding Protein (PBP) which is the target of β-lactam antibiotics.

Reducing Entry of Antimicrobial Agents

Mostly antimicrobial compounds always require access into the bacterial cell to reach their target site. Porin channels are the passageways by which antibiotics normally cross the bacterial outer membrane. Some bacteria protect themselves by prohibiting these antimicrobial compounds from entering to their cell walls.

Mutation

Mutation is a spontaneous change in the DNA sequence within the gene that may lead to a change in the trait which it codes for. A single base pair change may lead to a corresponding change in one or more of the amino acids for which its codes, which can then change the enzyme or cell structure that consequently changes the affinity or effective activity of the targeted antimicrobials. In prokaryotic genomes, mutations frequently occur due to base changes caused by exogenous agents, DNA polymerase errors, deletions, insertions and duplications.



A diagram to show how mutations lead to antibiotics being unable to bind to their target.

Biofilm Formation

Complex microbial communities containing bacteria and fungi are called biofilms. Microorganisms synthesize and secrete a protective matrix that attaches the biofilm firmly to a living or nonliving surface. A biofilm can be described as bacteria embedded in a thick, slimy barrier of sugars and proteins. The biofilm barrier protects the microorganisms from external

threats. The high cell density in biofilms increases the absolute numbers of resistant mutants that can be selectable under antimicrobial pressure.

Strategies to Combat Antibiotic Resistance

Antibiotic-resistant bacteria are spread globally in the same way as other bacteria. This means they can be transferred between people, animals and foodstuffs and they can spread in our environment. These links between the various sectors mean that efforts to combat antibiotic resistance must be made from a broad perspective. Prudent use of antibiotics in healthcare, animal health and agricultural settings is essential to slow the emergence of resistance and extend the useful lifetime of effective antibiotics.

Resistant bacteria can spread quickly and represent a reservoir of bacteria that can spread further to both man and animals. Animals can get infections that are difficult to treat as a result of resistant bacteria. To prevent overuse and misuse of antibiotics, a formalized, practical guideline for appropriate antibiotic prescribing should be developed and followed by formulary implementation of the guidelines contained therein. The development of quick and effective molecular diagnostic techniques for identification and epidemiological surveillance of resistance genes of antibiotic resistant pathogens can improve current control strategies. Reducing use of antibiotic in agriculture, especially in food animals, is also important. Changing policies to use of antibiotics in livestock can include ban or restriction on using veterinary important antibiotics, promising financial incentives for developing livestock specific antibiotics, making drug licensing rules more stringent and imposing penalties.

Effective strategies are required to address the problem of antibiotic resistance. Therefore, appropriate use of antibiotics, vaccination, education, research, development of novel antibiotics, policy, regulations, surveillance of antimicrobial resistance and antibiotic use have a great role in minimization of antibiotic resistance. Antibiotic Resistance Genes (ARGs) surveillance is an essential part of the Global Antimicrobial Resistance Surveillance System launched by the WHO is the year 2015 as the first collaborative effort towards standardizing AMR surveillance. It provides a structural framework to collect, analyze and share AMR data and documents the status of existing and new AMR surveillance systems. It encourages a shift from an isolate-based data system to epidemiological and clinical-level data. It aims to generate standardized data at standards that are comparable between nations, serve as a guideline in forming policies, track the spread and emergence of ARGs and guide as resource allocation to handle the AMR threats.

Addressing This Threat Needs Aggressive Action Towards:

- Preventing infections and controlling transmission.
- Improving antibiotic use to slow the development of resistance through high quality surveillance and usage guidelines.
- Stopping the spread of resistant microbes when they do develop through antimicrobial stewardship programs.

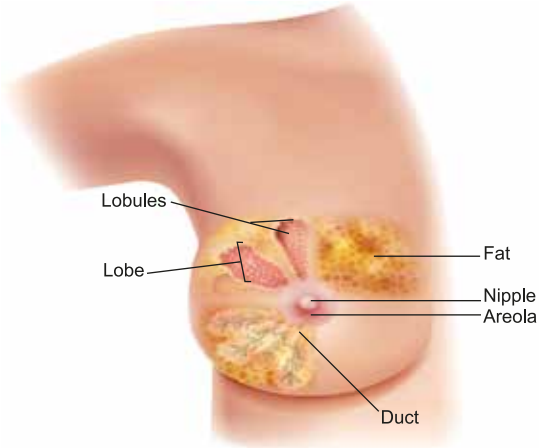
Conclusion

Resistance towards antibiotics is an inevitable part of microbial evolution. This emphasizes the need for surveillance of ARGs as the key aspect in future policy making. Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. Infections caused by antibiotic resistant organism are difficult and sometimes impossible to treat. The only way forward is continuous education, surveillance, data analysis and research to tackle the ever-emerging AMR crisis. The prudent use of antibiotics in healthcare, animal health and agricultural settings is essential to slow the emergence of resistance and extend the useful lifetime of effective antibiotics.

References

- Biomed J Sci & Tech Res 24(5)-2020.
- Antibiotics 2022, 11, 1082.
- WHO. (2021). Factsheet: Antimicrobial Resistance.
- Eng. BMC Infect. Dis. 2016, 16, 465.

Breast cancer arises in the epithelium of the ducts (85%) or lobules (15%) in the glandular tissue of the breast. Initially, the cancerous growth is confined to the duct or lobule ("in situ") where it generally causes no symptoms and has minimal potential for spread (metastasis).



This diagram of the breast shows the location of the lobules, lobe, duct, areola, nipple and fat.

Over time, these in situ (stage 0) cancers may progress and invade the surrounding breast tissue (invasive breast cancer) then spread to the nearby lymph nodes (regional metastasis) or to other organs in the body (distant metastasis). If a woman dies from breast cancer, it is because of widespread metastasis.

Types of Breast Cancer

There are several different types of breast cancer, which develop in different parts of the breast.

Breast cancer is often divided into either:

- Non-invasive breast cancer (carcinoma in situ) found in the ducts of breast (Ductal Carcinoma in Situ or DCIS) which has not spread into the breast tissue surrounding the ducts. Non-invasive breast cancer is usually found during a mammogram and rarely shows as a breast lump.
- Invasive breast cancer - where the cancer cells have spread through the lining of the ducts into the surrounding breast tissue. This is the most common type of breast cancer.

Other, less common types of breast cancer include:

- Invasive (and pre-invasive) lobular breast cancer
- Inflammatory breast cancer
- Paget's disease of the breast
- Secondary, or metastatic, breast cancer

Scope of Breast Cancer

In 2020, there were 2.3 million women diagnosed with breast cancer and 685 000 deaths globally. As of the end of 2020, there were 7.8 million women alive who were diagnosed with breast cancer in the past 5 years, making it the world's most prevalent cancer. There are more lost disability-adjusted life years (DALYs) by women to breast cancer globally than any other type of cancer. Breast cancer occurs in every country of the world in women at any age after puberty but with increasing rates in later life.

Breast cancer mortality changed little from the 1930s through to the 1970s. Improvements in survival began in the 1980s in countries with early detection programmes combined with different modes of treatment to eradicate invasive disease.

Breast Cancer Risk

Breast cancer is not a transmissible or infectious disease. Unlike some cancers that have infection-related causes, such as human papillomavirus (HPV) infection and cervical cancer, there are no known viral or bacterial infections linked to the development of breast cancer.

Approximately half of breast cancers develop in women who have no identifiable breast cancer risk factor other than gender (female) and age (over 40 years). Certain factors increase the risk of breast cancer including increasing age, obesity, harmful use of alcohol, family history of breast cancer, history of radiation exposure, reproductive history (such as age that menstrual periods began and age at first pregnancy), tobacco use and postmeno-pausal hormone therapy.

Behavioural choices and related interventions that reduce the risk of breast cancer include

- prolonged breastfeeding;
- regular physical activity;
- weight control;
- avoidance of harmful use of alcohol;
- avoidance of exposure to tobacco smoke;
- avoidance of prolonged use of hormones; and
- avoidance of excessive radiation exposure.

Unfortunately, even if all of the potentially modifiable risk factors could be controlled, this would only reduce the risk of developing breast cancer by at most 30%.

Female gender is the strongest breast cancer risk factor. Approximately 0.5-1% of breast cancers occur in men. The treatment of breast cancer in men follows the same principles of management as for women.

Family history of breast cancer increases the risk of breast cancer, but the majority of women diagnosed with breast cancer do not have a known family history of the disease. Lack of a known family history does not necessarily mean that a woman is at reduced risk.

Certain inherited "high penetrance" gene mutations greatly increase breast cancer risk, the most dominant being mutations in the genes BRCA1, BRCA2 and PALB-2. Women found to have mutations in these major genes could consider risk reduction strategies such as surgical removal of both breasts. Consideration of such a highly invasive approach only concerns a very limited number of women, should be carefully evaluated considering all alternatives and should not be rushed.

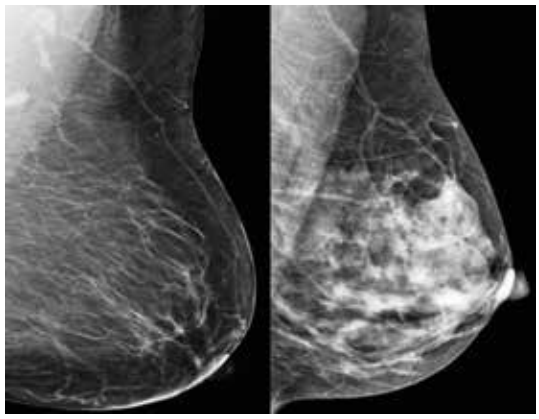
Signs and Symptoms

Breast cancer most commonly presents as a painless lump or thickening in the breast. It is important that women finding an abnormal lump in the breast consult a health practitioner without a delay of more than 1-2 months even when there is no pain associated with it. Seeking medical attention at the first sign of a potential symptom allows for more successful treatment.

Generally, symptoms of breast cancer include:

- a breast lump or thickening;
- alteration in size, shape or appearance of a breast;
- dimpling, redness, pitting or other alteration in the skin;
- change in nipple appearance or alteration in the skin surrounding the nipple (areola); and/or
- abnormal nipple discharge.

There are many reasons for lumps to develop in the breast, most of which are not cancer. As many as 90% of breast masses are not cancerous. Non-cancerous breast abnormalities include benign masses like fibroadenomas and cysts as well as infections. Breast cancer can present in a wide variety of ways, which is why a complete medical examination is important. Women with persistent abnormalities (generally lasting more than one month) should undergo tests including imaging of the breast and in some cases tissue sampling (biopsy) to determine if a mass is malignant (cancerous) or benign.



The image on the left shows a mostly fatty breast and the image on the right shows a dense breast

Advanced cancers can erode through the skin to cause open sores (ulceration) but are not necessarily painful. Women with breast wounds that do not heal should have a biopsy performed.

Breast cancers may spread to other areas of the body and trigger other symptoms. Often, the most common first detectable site of spread is to the lymph nodes under the arm although it is possible to have cancer-bearing lymph nodes that cannot be felt.

Over time, cancerous cells may spread to other organs including the lungs, liver, brain and bones. Once they reach these sites, new cancer-related symptoms such as bone pain or headaches may appear.

Breast Cancer Screening

Mammogram

For many women, mammograms are the best way to find breast cancer early, when it is easier to treat and before it is big enough to feel or cause symptoms. Having regular mammograms can lower the risk of dying from breast cancer. At this time, a mammogram is the best way to find breast cancer for most women of screening age.

Breast Magnetic Resonance Imaging (MRI)

A breast MRI uses magnets and radio waves to take pictures of the breast. Breast MRI is used along with mammograms to screen women who are at high risk for getting breast cancer. Because breast MRIs may appear abnormal even when there is no cancer, they are not used for women at average risk.

Women with a higher-than-average risk of developing breast cancer may be offered screening and genetic testing for the condition. As the risk of breast cancer increases with age, all women who are 50 to 70 years old are invited for breast cancer screening every 3 years. Women over the age of 70 are also entitled to screening.

Treatment

Breast cancer treatment can be highly effective, achieving survival probabilities of 90% or higher, particularly when the disease is identified early. Treatment generally consists of surgery and radiation therapy for control of the disease in the breast, lymph nodes and surrounding areas (locoregional control) and systemic anti-cancer therapy to treat and/or reduce the risk of the cancer spreading (metastasis). Anti-cancer medicines include endocrine (hormone) therapy, chemotherapy and in some cases targeted biologic therapy (antibodies).

In the past, all breast cancers were treated surgically by mastectomy. When cancers are large, mastectomy may still be required. Today, the majority of breast cancers can be treated with a smaller procedure called a “lumpectomy” or partial mastectomy, in which only the tumor is removed from the breast. In these cases, radiation therapy to the breast is generally required to minimize the chances of recurrence in the breast.

Lymph nodes are removed at the time of cancer surgery for invasive cancers. Complete removal of the lymph node bed under the arm (complete axillary dissection) in the past was thought to be necessary to prevent the spread of cancer. A smaller lymph node procedures called “sentinel node biopsy” is now preferred as it has fewer complications. It uses dye and/or a radioactive tracer to find the first few lymph nodes to which cancer could spread from the breast.

Medical treatments for breast cancers, which may be given before (“neoadjuvant”) or after (“adjuvant”) surgery, is based on the biological subtyping of the cancers. Cancer that express the estrogen receptor (ER) and/or progesterone receptor (PR) are likely to respond to endocrine (hormone) therapies such as tamoxifen or aromatase inhibitors. These medicines are taken orally for 5-10 years and reduce the chance of recurrence of these “hormone-positive” cancers by nearly half. Endocrine therapies can cause symptoms of menopause but are generally well tolerated.

Cancers that do not express ER or PR are “hormone receptor negative” and need to be treated with chemotherapy unless the cancer is very small. The chemotherapy regimens available today are very effective in reducing the chances of cancer spread or recurrence and are generally given as outpatient therapy. Chemotherapy for breast cancer generally does not require hospital admission in the absence of complications.

Breast cancers may independently overexpress a molecule called the HER-2/neu oncogene. These “HER-2 positive” cancers are amenable to treatment with targeted biological agents such as Trastuzumab. These biological agents are very effective but also very expensive, because they are antibodies rather than chemicals. When targeted biological therapies are given, they are combined with chemotherapy to make them effective at killing cancer cells.

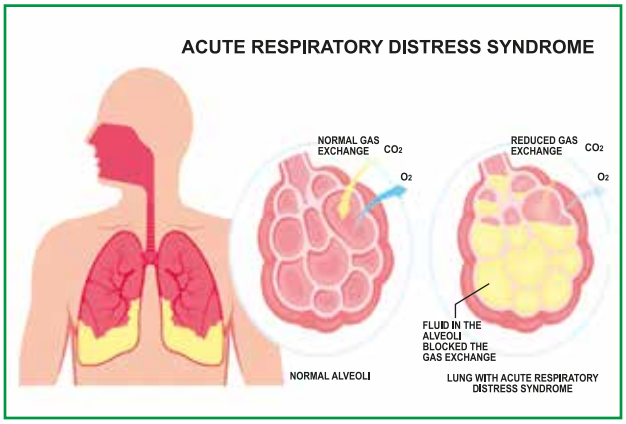
Radiotherapy also plays a very important role in treating breast cancer. With early stage breast cancers, radiation can prevent a woman having to undergo a mastectomy. With later stage cancers, radiotherapy can reduce cancer recurrence risk even when a mastectomy has been performed. For advanced stage of breast cancer, in some circumstances, radiation therapy may reduce the likelihood of dying of the disease.

Effectiveness of breast cancer therapies depends on the full course of treatment. Partial treatment is less likely to lead to a positive outcome.

References

- www.who.int/news-room/fact-sheets/detail/breast-cancer
- www.cdc.gov/cancer/breast/basic_info
- www.nhs.uk/conditions/breast-cancer

Acute respiratory distress syndrome (ARDS) is an important cause of acute respiratory failure that is often associated with multiple organ failure. Several clinical disorders can precipitate ARDS, including pneumonia, sepsis, aspiration of gastric contents and major trauma. Physiologically, ARDS is characterized by increased permeability pulmonary edema, severe arterial hypoxemia and impaired carbon dioxide excretion. Since the original description of acute respiratory distress syndrome (ARDS) in 1967, considerable progress has been made in understanding the pathogenesis and pathophysiology of acute lung injury (ALI).



ARDS occurs when lungs are severely injured, often by infection or trauma. Many people who get ARDS are already in the hospital due to an infection or trauma. But if the symptoms suggest ARDS, patients should be referred to the nearest ER immediately. ARDS causes fluid to leak into the lungs, making it difficult to get oxygen into the bloodstream. Treatment is improving and more people are surviving ARDS now than in the past. Survival can depend on age and the presence of other medical problems. In the early stages of ARDS, fluid from the smallest blood vessels in the lungs starts to leak into the alveoli-the tiny air sacs where oxygen exchange takes place. The lungs become smaller and stiffer and it becomes hard to breathe. The amount of oxygen in the blood falls. This is called hypoxemia. The body becomes starved for oxygen. This harms the brain and other tissues and leads to organ failure. ARDS patients need help to open closed airspaces, get oxygen into the blood and make it easier to breath. A ventilator and extra oxygen are used for these reasons and maintained until the injury resolves.

Pathophysiology

ARDS is a form of fluid accumulation in the lungs not explained by heart failure (noncardiogenic pulmonary edema). It is typically provoked by an acute injury to the lungs that results in flooding of the lungs' microscopic air sacs responsible for the exchange of gases such as oxygen and carbon dioxide with capillaries in the lungs. Additional common findings in ARDS include partial collapse of the lungs (atelectasis) and low levels of oxygen in the blood (hypoxemia). The clinical syndrome is associated with pathological findings including pneumonia, eosinophilic pneumonia, cryptogenic organizing pneumonia, acute fibrinous organizing pneumonia and diffuse alveolar damage (DAD). Of these, the pathology most commonly associated with ARDS is DAD, which is characterized by a diffuse inflammation of lung tissue. The triggering insult to the tissue usually results in an initial release of chemical signals and other inflammatory mediators secreted by local epithelial and endothelial cells.

Neutrophils and some T-lymphocytes quickly migrate into the inflamed lung tissue and contribute in the amplification of the phenomenon. The typical histological presentation involves diffuse alveolar damage and hyaline membrane formation in alveolar walls. Although the triggering mechanisms are not completely understood, recent research has examined the role of inflammation and mechanical stress.

In addition, in broncho-alveolar lavage fluids of ARDS, it can be observed trichomonads, which are unicellular flagellated parasites of the order Trichomonadida. These trichomonads occur in an amoeboid form, without flagellum, which makes it difficult to identify them under the microscope. The colonization of the alveolar spaces by the parasite is a secondary phenomenon, frequent beyond D5, probably favored by the local hypoxia of the DAD. The amoeboid transformation is an argument in favor of a deleterious action of the parasite, which nevertheless remains conjectural.

Acute Respiratory Distress Syndrome

Histopathology

The key histologic changes in ARDS reveal the presence of alveolar edema in areas of a diseased lung. The type I pneumocytes and vascular endothelium are injured, which results in the leaking of proteinaceous fluid and blood into the alveolar airspace. Other findings may include alveolar hemorrhage, pulmonary capillary congestion, interstitial edema and hyaline membrane formation. None of these changes are specific to the disease.

Causes

ARDS results from lung injury. The exact nature of the injury is not always clear. Common injuries are:

- Sepsis, a life-threatening condition occurs when immune system must work aggressively to fight off infection or trauma
- Inhaling harmful substances
- Pneumonia
- Trauma to the head, chest or other areas of the body
- Blood transfusions
- Pancreatitis
- Near drowning

Risk factors

Most people who develop ARDS are already in the hospital because of injury or illness. While it is not clear who will develop ARDS, certain factors may increase the risk for ARDS including:

- Advanced age
- A history of tobacco use
- A history of alcoholism
- Presence of chronic lung disease
- High-risk surgery

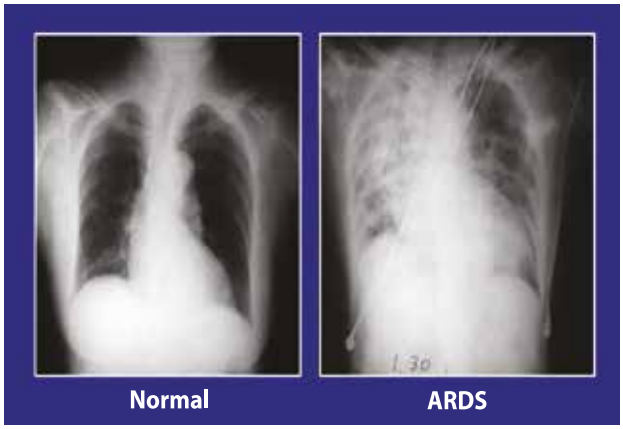
Symptoms

Symptoms of ARDS includes:

- Severe shortness of breath
- Rapid, shallow breathing
- Tiredness, drowsiness or confusion
- Feeling faint

Diagnosis

- There's no specific test to identify ARDS. The diagnosis is based on the physical exam, chest X-ray and oxygen levels. It's also important to rule out other diseases and conditions for example, certain heart problems that can produce similar symptoms.



Imaging

- Chest X-ray: A chest X-ray can reveal which parts of lungs and how much of the lungs have fluid and whether heart is enlarged.
- Computerized tomography (CT): A CT scan combines X-ray images taken from many different directions into cross-sectional views of internal organs. CT scans can provide detailed information about the structures within the heart and lungs.

Lab tests

A test using blood from an artery of wrist can measure the oxygen level. Other types of blood tests can check for signs of infection or anemia. If doctor suspects that there is a lung infection, secretions from the airway may be tested to determine.

Heart tests

Because the signs and symptoms of ARDS are similar to those of certain heart problems, may be recommended heart tests such as:

- Electrocardiogram
- Echocardiogram

Prognosis

- Without prompt treatment, many people who have ARDS will not survive. However, depending upon the underlying disorder, with appropriate treatment, about 60 to 75% of people with ARDS survive.

- People who respond promptly to treatment usually recover completely with few or no longterm lung abnormalities. Those whose treatment involves long periods on a ventilator are more likely to develop lung scarring. Such scarring may decrease over a few months after the person is taken off the ventilator. Lung scarring, if extensive, can impair lung function permanently in ways that are noticeable during certain day-to-day activities. Less extensive scarring may impair lung function only when the lungs are stressed, such as during exercise or an illness.
- Many people lose large amounts of weight and muscle during the illness. Rehabilitation in the hospital can help them regain their strength and independence.

Treatment

There is no cure for ARDS at this time. Treatment focuses on supporting the patient while the lungs heal. The goal of supportive care is getting enough oxygen into the blood and delivered to the body to prevent damage and removing the injury that caused ARDS to develop.

Ventilator support

All patients with ARDS will require extra oxygen. Oxygen alone is usually not enough and high levels of oxygen can also injure the lung. A ventilator is a machine used to open airspaces that have shut down and help with the work of breathing. The ventilator is connected to the patient through a mask on the face or a tube inserted into the windpipe.

Prone positioning

ARDS patients are typically in bed on their back. When oxygen and ventilator therapies are at high levels and blood oxygen is still low, ARDS patients are sometimes turned over on their stomach to get more oxygen into the blood. This is called proning and may help improve oxygen levels in the blood for a while. It is a complicated task and some patients are too sick for this treatment

Sedation and medications to prevent movement

To relieve shortness of breath and prevent agitation, the ARDS patient usually needs sedation. Sometimes added medications called paralytics are needed up front to help the patient adjust to the ventilator. These medications have significant side effects and their risks and benefits must be continuously monitored.

Fluid management

Fluid management may include a diuretic to increase urination in hopes of removing excess fluid from the body to help prevent fluid from building up in the lungs. This must be done carefully, because too much fluid removal can lower blood pressure and lead to kidney problems.

Extracorporeal membrane oxygenation (ECMO)

ECMO is a very complicated treatment that takes blood outside the body and pumps it through a membrane that adds oxygen, removes carbon dioxide and then returns the blood to the body. This is a high-risk therapy with many potential complications. It is not suitable for every ARDS patient.

Recovering from ARDS

ARDS patients may require ventilation for long periods of time. On average this is 7 to 14 days. Beyond this time, tracheostomy may be done. Usually it may take weeks more to recover from ventilator support. This tube can easily be removed once the patient is free of the need for a ventilator. It is important to note that most people survive from ARDS. They will not require oxygen on a long-term basis and will regain most of their lung function. Others will struggle with muscle weakness and may require re-hospitalization or pulmonary rehabilitation to regain their strength.

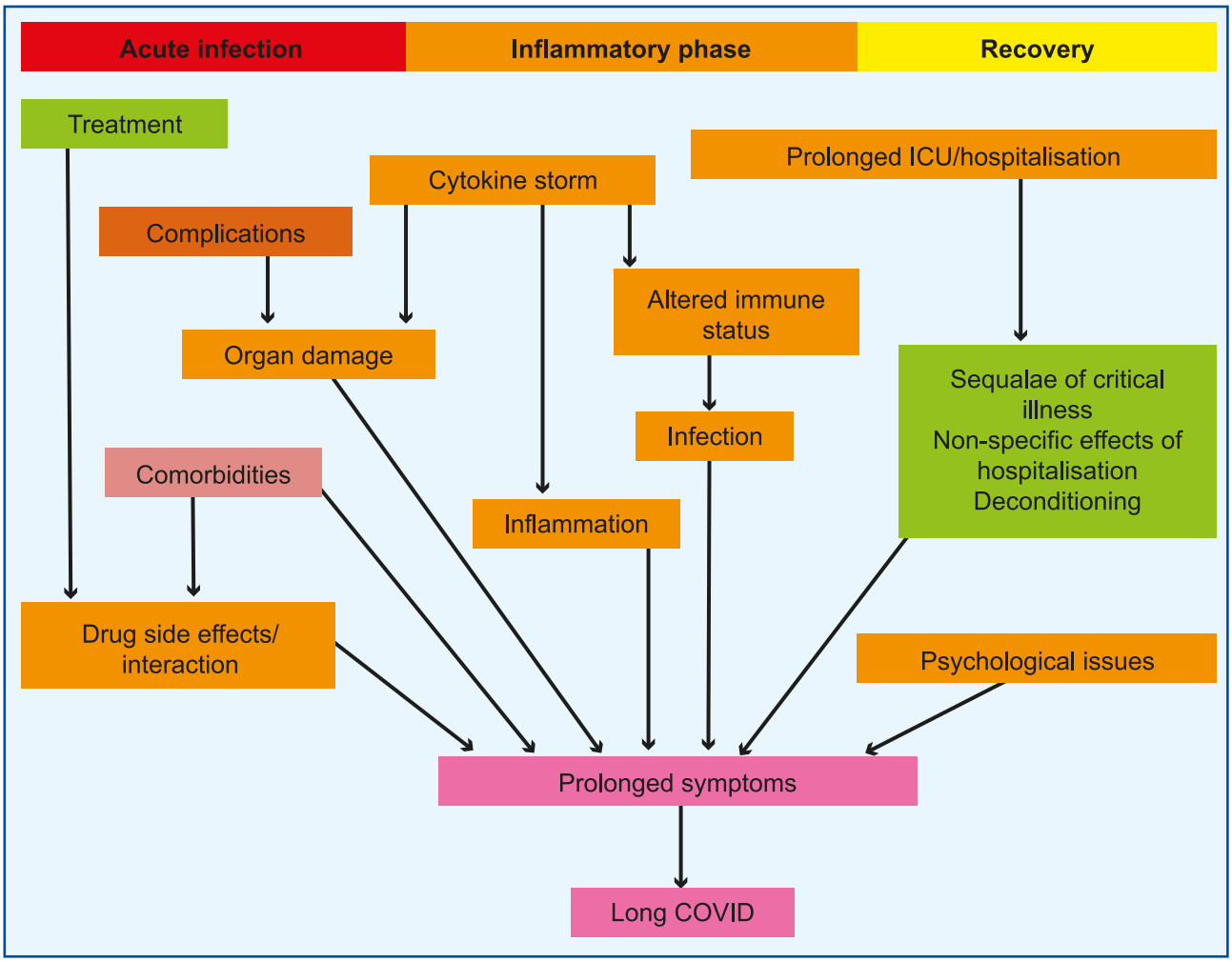
References

- www.medscape.com
- www.medicalnewstoday.com
- The Lancet, 01 April, Vol 401 No.10382

Post COVID Syndrome

SARS CoV-2 infection (COVID-19) is a major pandemic resulting in substantial mortality and morbidity worldwide. Of the individuals affected, about 80% had mild to moderate disease and among those with severe disease, 5% develop critical illness. A few of those who recovered from COVID-19 develop persistent or new symptoms lasting weeks or months; this is called “long COVID”, “Long Haulers” or “Post COVID syndrome.”

“Long COVID” is a term used to describe presence of various symptoms, even weeks or months after acquiring SARS-CoV-2 infection irrespective of the viral status. It can be continuous or relapsing and remitting in nature.



Pathophysiology of “Long COVID”

The exact mechanism behind the persistence of symptoms has to be identified. Reason for the persistence of symptoms can be the sequelae of organ damage, varying extent of injury (organ damage) and varying time required for the recovery of each organ system, persistence of chronic inflammation (convalescent phase) or immune response/auto antibody generation, rare persistence of virus in the body, nonspecific effect of hospitalization, sequelae of critical illness, post-intensive care syndrome, complications related to corona infection or complications related to co morbidities or adverse effects of medications used.

Symptoms of long COVID

The most common symptoms of long COVID are:

- Extreme tiredness (fatigue)
- Shortness of breath
- Loss of smell
- Muscle aches

However, other symptoms may include:

- Lack of memory and concentration ("brain fog")
- Chest pain or tightness

- Insomnia
- Heart palpitations
- Dizziness
- Joint pain
- Depression and anxiety
- Tinnitus, earaches
- Loss of appetite
- High temperature, cough, headaches, sore throat, changes to sense of smell or taste.

Some tests to find out more about the symptoms and rule out other things that could be causing them-

These might include:

1. Blood tests
2. Checking blood pressure and heart rate
3. Chest X-ray
4. Measuring oxygen levels

Complications associated with long COVID-19

COVID-19 is a multi-systemic disease, which may occur with complications at presentation or developing during the acute phase of illness.

Cardiovascular abnormalities

A study of 100 patients showed that 78% had abnormal findings based on cardiac magnetic resonance imaging results 2-3 months after the onset of COVID-19 and 60% had evidence of myocardial inflammation independent of the severity and overall course of their acute illness. The possibility of cardiovascular abnormalities occurring in patients with long COVID was supported by another study which reported that up to 40% of COVID-19 patients presented with pericarditis or myocarditis > 70 days after infection.

Pulmonary abnormalities

A study conducted lung function tests in a sample of 57 patients 30 days after discharge for acute COVID-19 and reported a decrease in diffusing capacity of the lung for carbon monoxide (DLCO) in 53% and diminished respiratory muscle strength in 49% of patients. In another study, lung function abnormalities were detected in approximately a quarter of patients at three months after hospital discharge. The commonest lung function abnormality (16.36%) was DLCO. A higher level of D-dimer at admission was significantly associated with DLCO% < 80% suggesting that D-dimer might be a potential biomarker for the prediction of DLCO decline patients with COVID-19. The patients with lung function abnormalities, 12 also had radiological changes, including evidence of lung fibrosis. At six months of follow-up, also found lung diffusion impairment among 34% (114/334) of patients previously hospitalized for acute COVID-19.

Neurological abnormalities

The occurrence of encephalitis, seizures and other conditions such as major mood swings and cognitive impairment (brain fog) have been reported in patients up to two to three months after the onset of acute illness. Magnetic resonance imaging scanning of previously hospitalized patients with COVID-19 suggested possible disruption to micro-structural and functional brain integrity at three months of follow-up.

Renal complications

In one study, approximately one-third of previously hospitalized patients, who had acute kidney injury during the acute phase of COVID-19, did not fully regain renal function at discharge or post-hospitalization follow-up.

Endocrine disorders

Two studies reported newly diagnosed diabetes mellitus in patients after hospitalization. However, more research is required to fully understand the etiology.

Mental disorder

In the longer term, depression and anxiety and reduced quality of life were observed at one year after infection with COVID-19. In addition, a study found that up to 40% of patients who had SARS continued to experience fatigue and psychiatric illnesses for nearly 3.5 years after the acute infection. These findings are similar to those from a six-month follow-up study of previously hospitalized patients with COVID-19, which showed that patients mainly struggled with fatigue or muscle weakness, sleep difficulties and anxiety or depression.

This suggests that in the longer term, patients with long COVID may also experience a similar disease trajectory to that of patients.

Management of long COVID

Treatment options are currently limited as there is insufficient understanding of the mechanisms that underpin long COVID. While there are still uncertainties about the optimal management of patients with long COVID, a number of countries have produced clinical guidelines to assist clinicians. Patients may require multidisciplinary care involving the long-term monitoring of ongoing symptoms, to identify potential complications for clinical intervention and the need for physical rehabilitation, mental health and social services support.

Physical rehabilitation

Patients with severe acute COVID-19 who are managed in intensive care units may develop muscle weakness, deconditioning, myopathies and neuropathies, which are the physical domains of post-intensive care syndrome. It is recommended that appropriate rehabilitation to prevent this syndrome should start in intensive care units as soon as sedation and clinical stability permit. Pulmonary rehabilitation may help improve patients' breathing, exercise capacity, muscle strength, quality of life and functional outcome. Early mobilization would help to improve functional, cognitive and respiratory conditions in these patients and may shorten hospital stay.

Non-hospitalized patients with long COVID may also require physical rehabilitation, especially those with cardiopulmonary problems who may need significant rehabilitation, in order to improve their ability to engage in activities of daily living. However, identifying this group of patients may be challenging due to under-recognition and under-investigation of symptoms. There is also a risk that non-hospitalized patients with long COVID with mild-to-moderate symptoms, who are likely to represent a significant proportion of long COVID sufferers, may not be prioritized for follow-up care.

Management of pre-existing co-morbidities

A significant proportion of patients who experience severe acute COVID-19 have underlying co-morbidities. It is therefore essential that these are adequately managed in order to avoid clinical deterioration and the need for readmission in these patients.

Mental health support

There is a need to ensure that appropriate mental health support is available and accessible to those patients who require such services. Patients may be screened as part of their follow-up care and those identified as requiring extra support referred for specialist management. However, care should be taken not to patients as physical manifestations of COVID-19 may distort responses to assessment tools.

Social services support

Due to persistent symptoms, a significant number of patients with long COVID are unable to return to work and may require long-term governmental financial support. Some patients may be unable to cope with day-to-day living especially if they also suffer significant social isolation and or stigmatization. These groups of patients would benefit from social services support.

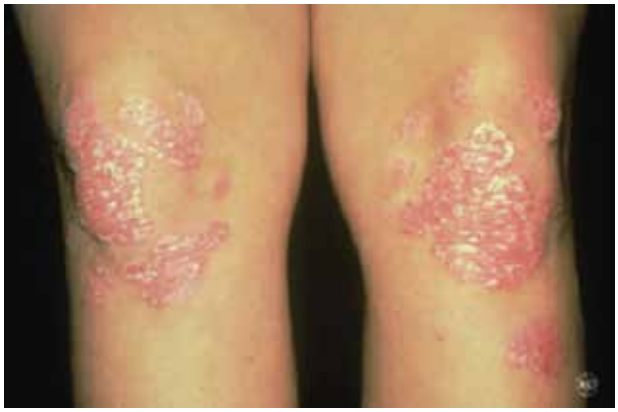
Conclusion

The wide range of potential symptoms and complications patients with long COVID may experience highlights the need for a deeper understanding of the clinical course of the condition. There is an urgent need for better, more integrated care models to support and manage patients with long COVID-19 in order to improve clinical outcomes. Resilient healthcare systems are required to ensure efficient and effective responses to future health challenges.

References

- www.ncbi.nlm.nih.gov.com
- www.nhs.uk/conditions/coronavirus-covid-19
- pubmed.ncbi.nlm.nih.gov

Psoriasis is a complex, chronic, multifactorial, inflammatory disease that involves hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. Environmental, genetic and immunologic factors appear to play a role. The disease most commonly manifests on the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal clefts and glans penis. In up to 30% of patients, the joints are also affected.



Plaque psoriasis

Etiology

Psoriasis involves hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. The cause of the loss of control of keratinocyte turnover is unknown. However, environmental, genetic and immunologic factors appear to play a role.

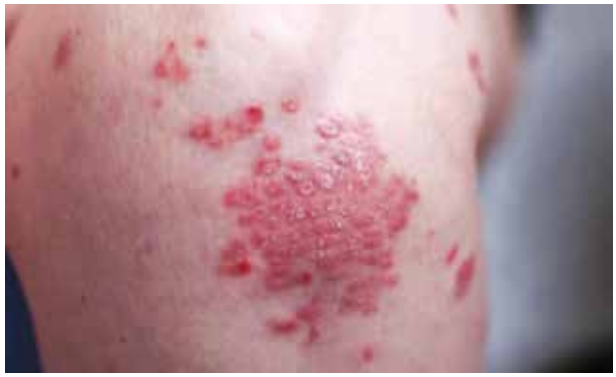
Environmental factors

Many factors besides stress have also been observed to trigger exacerbations, including cold, trauma, infections (eg, streptococcal, staphylococcal, human immunodeficiency virus), alcohol and drugs (eg, iodides, steroid withdrawal, aspirin, lithium, beta-blockers, botulinum A, antimalarials). One study showed an increased incidence of psoriasis in patients with chronic gingivitis. Satisfactory treatment of the gingivitis led to improved control of the psoriasis but did not influence long term incidence, highlighting the multifactorial and genetic influences of this disease.

Genetic factors

Patients with psoriasis have a genetic predisposition for the disease. The gene locus is determined. The triggering event may be unknown in most cases, but it is likely immunologic. The first lesion commonly appears after an upper respiratory tract infection.

Psoriasis is associated with certain human leukocyte antigen (HLA) alleles, the strongest being human leukocyte antigen Cw6 (HLA-Cw6). In some families, psoriasis is an autosomal dominant trait. Additional HLA antigens that have shown associations with psoriasis and psoriatic subtypes include HLA-B27, HLA-B13, HLA-B17 and HLA-DR7.



Guttate psoriasis

A multicenter meta-analysis confirmed that deletion of two late cornified envelope (LCE) genes, LCE3C and LCE3B, is a common genetic factor for susceptibility to psoriasis in different populations.

Obesity is another factor associated with psoriasis. Whether it is related to weight alone, genetic predisposition to obesity, or a combination of the two is not certain. Onset or worsening of psoriasis with weight gain and/or improvement with weight loss is observed.

Immunologic factors

Evidence suggests that psoriasis is an autoimmune disease. Studies show high levels of dermal and circulating TNF-α. Treatment with TNF-α inhibitors is often successful. Psoriatic lesions are associated with increased activity of T cells in the underlying skin.

Psoriasis is related to excess T-cell activity. Experimental models can be induced by stimulation with streptococcal super antigen, which cross-reacts with dermal collagen. This small peptide has been shown to cause increased activity among T cells in patients with psoriasis but not in control groups. Some of the newer drugs used to treat severe psoriasis directly modify the function of lymphocytes.

Also of significance is that 2.5% of those with HIV develop worsening psoriasis with decreasing CD4 counts. This is paradoxical, in that the leading hypothesis on the pathogenesis of psoriasis supports T-cell hyperactivity and treatments geared to reduce T-cell counts help reduce psoriasis severity. This finding is possibly explained by a decrease in CD4 T cells, which leads to over activity of CD8 T cells, which drives the worsening psoriasis. The HIV genome may drive keratinocyte proliferation directly.

Guttate psoriasis often appears following certain immunologically active events, such as streptococcal pharyngitis, cessation of steroid therapy and use of antimalarial drugs.

Epidemiology

According to the National Institutes of Health (NIH), approximately 2.2% of the United States population has psoriasis. Internationally, the incidence of psoriasis varies dramatically. Overall, approximately 2-3% of people are affected by psoriasis worldwide. Psoriasis can begin at any age, yet there is a bimodal peak between age 20-30 years and 50-60 years. Approximately 10-15% of new cases begin in children younger than 10 years. The median age at onset is 28 years.

Psoriasis appears to be slightly more prevalent among women than among men; however, men are thought to be more likely to experience the ocular disease.

The incidence of psoriasis is dependent on the climate and genetic heritage of the population. It is less common in the tropics and in dark-skinned persons. Psoriasis prevalence in African Americans is 1.3% compared with 2.5% in whites.

Psoriasis, even severe psoriasis, may occur in the pediatric age group, with a prevalence of 0.5-2% of children. Both biologic and immunomodulating therapies may be used safely and effectively.

Signs and Symptoms

Signs and symptoms of psoriasis may include the following:

- Worsening of a long-term erythematous scaly area
- Sudden onset of many small areas of scaly redness
- Recent streptococcal throat infection, viral infection, immunization, use of antimalarial drug, or trauma
- Pain (especially in erythrodermic psoriasis and in some cases of traumatized plaques or in the joints affected by psoriatic arthritis)
- Pruritus (especially in eruptive, guttate psoriasis)
- Afebrile (except in pustular or erythrodermic psoriasis, in which the patient may have high fever)
- Dystrophic nails, which may resemble onychomycosis
- Long-term, steroid-responsive rash with recent presentation of joint pain
- Joint pain (psoriatic arthritis) without any visible skin findings
- Conjunctivitis or blepharitis

Ocular findings occur in approximately 10% of patients. The most common ocular symptoms are redness and tearing due to conjunctivitis or blepharitis.

The nonocular symptoms are related to rash and psoriatic arthritis. The rash can be uncomfortable or even painful. Psoriatic arthritis can cause stiffness, pain, throbbing, swelling, or tenderness of the joints. The distal joints, such as the fingers, toes, wrists, knees and ankles, are most often affected.

Diagnosis

The diagnosis of psoriasis is clinical and the type of psoriasis present affects the physical examination findings.

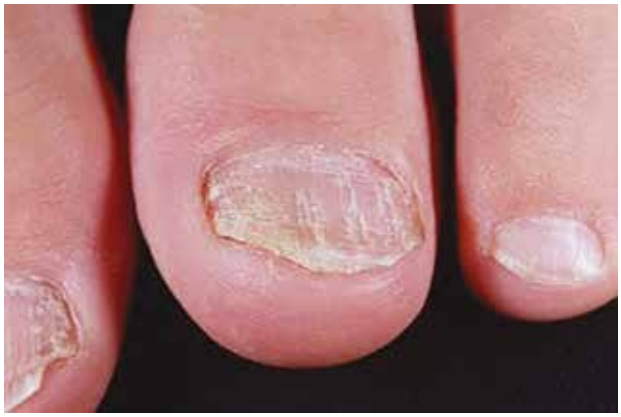
Physical Examination

Findings on physical examination depend on the type of psoriasis present.

The most common skin manifestations are scaling, salmon-colored/erythematous macules, papules and plaques. Typically, the macules are seen first and these progress to maculopapules and ultimately well-demarcated, noncoherent, silvery plaques overlying a glossy homogeneous erythema. The area of skin involvement varies with the form of psoriasis.

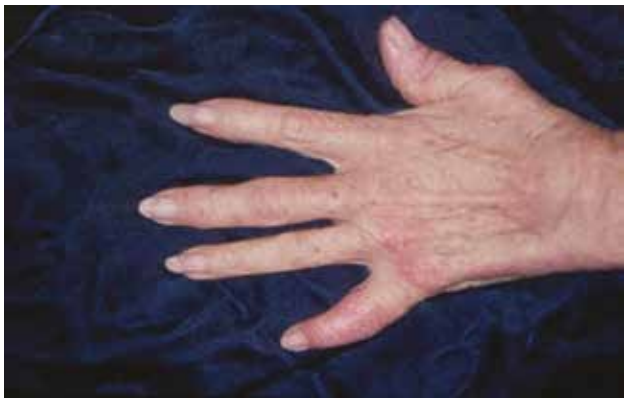
Chronic stationary psoriasis (psoriasis vulgaris) is the most common type of psoriasis. This involves the scalp, extensor surfaces, genitals, umbilicus and lumbosacral and retroauricular regions.

Plaque psoriasis is characterized by raised, inflamed lesions covered with a silvery white scale. The scale may be scraped away to reveal inflamed skin beneath. This is most common on the extensor surfaces of the knees, elbows, scalp and trunk.



Nail psoriasis

Guttate psoriasis presents as small salmon-pink papules, 1-10 mm in diameter, predominately on the trunk; the lesions may be scaly (see the image below). It frequently appears suddenly, 2-3 weeks after an upper respiratory infection (URI) with group A beta-hemolytic streptococci.



Psoriatic Arthritis

Inverse psoriasis occurs on the flexural surfaces, armpit, groin, under the breast and in the skin folds. It is characterized by smooth, inflamed lesions without scaling due to the moist nature of the area where this type of psoriasis is located.

Pustular psoriasis presents as sterile pustules appearing on the palms and soles or diffusely over the body. Pustular psoriasis may cycle through erythema, pustules, then scaling. The diffuse variant is termed von Zumbusch variant, which is accompanied by fever and intense ill feeling in addition to the widespread pustules.

Erythrodermic psoriasis presents as generalized erythema, pain, itching and fine scaling; various pustular forms also exist. It typically encompasses nearly the entire body surface area. It may be accompanied by fever, chills, hypothermia and dehydration secondary to the large body surface area involvement. Patients with severe pustular or erythrodermic psoriasis may require hospital admission for metabolic and pain management. Older patients with erythrodermic psoriasis may experience cardiac instability and hypotension due to massive vascular shunting in the skin.

Scalp psoriasis affects approximately 50% of patients. It presents as erythematous raised plaques with silvery white scales on the scalp.

Nail psoriasis may cause pits on the nails, which often become thickened and yellowish; this is considered the most common nail finding. Oil spots, caused by exocytosis of leukocytes beneath the nail plate, are considered the most specific nail finding in psoriasis. Nails may separate from the nail bed, known as onycholysis, due to the parakeratosis of the distal nail bed. Psoriatic nails may be indistinguishable from fungal nails and, at the same time, may be more prone to developing onychomycosis because of the nail separation and subungual debris.

Psoriatic arthritis affects approximately 10-30% of those with skin symptoms. The arthritis is usually in the hands and feet and, occasionally, the large joints. It produces stiffness, pain and progressive joint damage.

Oral psoriasis may present with whitish lesions on the oral mucosa, which may appear to change in severity daily. It may also present as severe cheilosis with extension onto the surrounding skin, crossing the vermillion border. Geographic tongue is considered by many to be an oral form of psoriasis.

Eruptive psoriasis involves the upper trunk and upper extremities. Most often, it is seen in younger patients.

Ocular Manifestations

In addition to skin manifestations, psoriasis may also affect the lid, conjunctiva, or cornea and give rise to ocular manifestations, including ectropion and trichiasis, conjunctivitis and conjunctival hyperemia and corneal dryness with punctate keratitis and corneal melt.

Blepharitis is the most common ocular finding in psoriasis. Erythema, edema and psoriatic plaques may develop and they can result in madarosis, cicatricial ectropion, trichiasis and even loss of the lid tissue.

A chronic nonspecific conjunctivitis is fairly common. It usually occurs in association with eyelid margin involvement. Psoriatic plaques can extend from the lid onto the conjunctiva. Chronic conjunctivitis can lead to symblepharon, keratoconjunctivitis sicca and trichiasis. Nodular episcleritis and limbal lesions resembling phlyctenules also can be seen.

Corneal disease is relatively rare. Most often, it is secondary to lid or conjunctival complications, such as dryness, trichiasis, or exposure. The most common finding is punctate keratitis. Filaments, epithelial thickening, recurrent erosions, vascularization, ulceration and scarring can occur. The vascularization tends to be superficial, peripheral and interpalpebral or inferior. Rarely, peripheral infiltration and melting can occur in the absence of trichiasis and exposure.

In one case, recurrent nasolacrimal duct occlusion was observed, presumably caused by washing of the scales into the lacrimal sac.

Usually, anterior uveitis can be seen in association with psoriatic arthritis. Acute psoriatic uveitis tends to be bilateral, prolonged and more severe than nonpsoriatic cases.

Complications

Complications of psoriasis may include the following:

- Secondary infections
- Possible increased risk of lymphoma
- Possible increased risk of cardiovascular and ischemic heart disease
- Psoriatic arthritis
- Mitral valve prolapse
- Possibly inflammatory bowel disease

Laboratory Studies

Laboratory studies and findings for patients with psoriasis may include the following:

- Test result for rheumatoid factor (RF) is negative.
- Erythrocyte sedimentation rate (ESR) is usually normal (except in pustular and erythrodermic psoriasis).
- Uric acid level may be elevated in psoriasis (especially in pustular psoriasis), causing confusion with gout in psoriatic arthritis.
- Fluid from pustules is sterile with neutrophilic infiltrate.
- Perform fungal studies. (This is especially important in cases of hand and foot psoriasis that seem to be worsening with the use of topical steroids.)

If starting systemic therapies such as immunological inhibitors, consider obtaining baseline laboratory studies (ie, complete blood cell count, blood urea nitrogen /creatinine, liver function tests, hepatitis panel, tuberculosis screening and pregnancy test).

Other Tests

Although most cases of psoriasis are diagnosed clinically, some, particularly the pustular forms, can be difficult to recognize. In these cases, dermato logic biopsy can be used to make diagnosis. Biopsy of the skin lesion may reveal basal cell hyperplasia, proliferation of subepidermal vasculature, absence of normal cell maturation and keratinization. A large number of activated T cells are present in the epidermis. Biopsy of acral skin may be less useful as chronic eczematous dermatitis may be psoriasiform and psoriasis of the palms and soles may show spongiosis more often associated with eczema.

Radiographs of affected joints can be helpful in differentiating types of arthritis. Joint x-rays can facilitate the diagnosis of psoriatic arthritis. Bone scans can identify joint involvement early.

Conjunctival impression cytology has demonstrated an increased incidence of squamous metaplasia, neutrophil clumping and snakelike chromatin.

When the scales are removed, small droplets of blood appear within a few seconds from exposed vessels in the dermal papillae; this is known as the Auspitz sign.

Procedures

Punch biopsy of the skin may act as a confirmatory workup procedure.

Histologic Findings

Histopathology findings include the following:

- Regular acanthosis of the epidermis
- Parakeratosis
- Kogoj spongiotic pustules
- Munro micro abscesses

Management

Pharmacotherapy

Medications used in the management of psoriasis include the following:

- Topical corticosteroids (eg, triamcinolone acetonide 0.025-0.1% cream, betamethasone 0.025-0.1% cream)
- Topical aryl hydrocarbon receptor (AhR) agonists
- Ophthalmic corticosteroids (eg, prednisolone acetate 1% ophthalmic, dexamethasone ophthalmic)
- Intramuscular corticosteroids (eg, triamcinolone): Requires caution because the patient may have a significant flare as the medication wears off; 3 months should elapse between injections
- Intralesional corticosteroids: May be useful for resistant plaques and for the treatment of psoriatic nails
- Coal tar 0.5-33%
- Keratolytic agents (eg, anthralin, urea): Use of these medications may facilitate more direct steroid contact with the skin
- Vitamin D analogs (eg, calcitriol ointment, calcipotriene, calcipotriene and betamethasone topical ointment)
- Topical retinoids (eg, tazarotene aqueous gel and cream 0.05% and 0.1%)
- Antimetabolites (eg, methotrexate)
- Immunomodulators (eg, tacrolimus topical 0.1%, cyclosporine, alefacept, ustekinumab)
- TNF inhibitors (eg, infliximab, etanercept, adalimumab)
- Phosphodiesterase-4 inhibitors (eg, apremilast, roflumilast topical)
- Interleukin inhibitors (eg, ustekinumab, secukinumab, tildrakizumab, guselkumab, risankizumab, ixekizumab, brodalumab)
- Artificial tears

The American Academy of Dermatology (AAD) guidelines recommend treatment with methotrexate, cyclosporine and acitretin, with consideration of contraindications and drug interactions.

Other Therapies

Management of psoriasis may also involve the following nondrug therapies:

- Light therapy with solar or ultraviolet radiation
- Stress reduction
- Biofeedback
- Climatotherapy
- Adjuncts, such as sunshine, sea bathing, moisturizers, oatmeal baths
- Punctal occlusion (and ocular lubricants): For keratoconjunctivitis sicca
- Bandage contact lens: To retard corneal melting

Surgical Option

Ocular manifestations such as trichiasis and cicatricial ectropion usually require surgical treatment. Progression of corneal melting, inflammation and vascularization may require lamellar or penetrating keratoplasty.

Differential Diagnoses

- Adult Blepharitis
- Allergic Contact Dermatitis
- Atopic Dermatitis
- Atopic Keratoconjunctivitis (AKC)
- Cutaneous Squamous Cell Carcinoma
- Diaper Dermatitis (Diaper Rash)
- Dry Eye Disease (Keratoconjunctivitis Sicca)
- Gout and Pseudogout
- Lichen Planus
- Lichen Simplex Chronicus
- Mycosis Fungoides
- Nummular Dermatitis (Nummular Eczema)
- Onychomycosis
- Pityriasis Alba

- Pityriasis Rosea
- Pustular Eruptions
- Reactive Arthritis
- Seborrheic Dermatitis
- Sicca Keratoconjunctivitis
- Subcorneal Pustulosis
- Syphilis
- Tinea in Emergency Medicine

Follow up

Close follow-up is necessary to design an optimal treatment plan in accordance with the severity of disease.

Severity of psoriasis can be classified as follows:

- Mild - Less than 2% of the body is affected
- Moderate - From 3-10% of the body is affected
- Severe - More than 10% of the body is affected

Of note, the palm of the patient's hand is equal to 1% body surface area.

Diet

Ample literature suggests that weight loss can help psoriasis, but other attempts to show improvement with more specific diets, such as a gluten-free diet, are less conclusive. Studies of very-low-calorie diets and the "Mediterranean Diet" have both shown improvement in anecdotal reports and small studies. Nutritional supplements have shown limited benefit, with the exception of fish oil. Vitamin D itself has also been reported to be of benefit in small studies. Much more work needs to be done before enthusiastic support of any particular supplement or dietary plan may be offered.

Activity

Any restrictions on activity would relate to concomitant arthritis and how well it is being controlled. Natural sunlight can help psoriasis and may explain why it is relatively rare on the face. It has been suggested that a more active lifestyle can help psoriasis, but whether this is an independent factor or more related to better weight control is less certain.

Prevention

No specific strategies prevent psoriasis, although healthy lifestyles that avoid obesity and reduced alcohol use can make control easier and increase the chances of at least temporary remission. Whenever possible, patients who are currently being treated for psoriasis or have a history of psoriasis should avoid over-the-counter and prescription medications known to exacerbate it. This includes the use of over-the-counter NSAIDs such as ibuprofen and naproxen.

Prognosis

Although psoriasis is usually benign, it is a lifelong illness with remissions and exacerbations and is sometimes refractory to treatment. It progresses to arthritis in about 10% of cases. About 17-55% of patients experience remissions of varying lengths.

Mild psoriasis does not appear to increase risk of death. However, men with severe psoriasis died 3.5 years earlier compared with men without the disease. Women with severe psoriasis died 4.4 years earlier compared with women without the disease.

Psoriasis is associated with smoking, alcohol, metabolic syndrome, lymphoma, depression, suicide, potentially harmful drug and light therapies and possibly melanoma and nonmelanoma skin cancers.

Quality of life

Psoriasis can significantly influence a person's quality of life. The physical and mental disability experienced with this disease can be comparable or in excess of that found in patients with other chronic illnesses such as cancer, arthritis, hypertension, heart disease, diabetes and depression.

While the clinical presentation of psoriasis and whatever improvements are made during therapy, is usually measured using the PASI (Psoriasis Area and Severity Index) score, measurement of the effect on the quality of life of the psoriasis patient may be better assessed by the DLQI (Dermatology Life Quality Index) or the CDLQI (Children's Dermatology Life Quality Index). Measurements using these tools generally show improved quality of life with more aggressive treatment such as systemic agents.

Studies show that psoriasis of the palms and soles tend to have greater impact on the patient's quality of life compared to those with more extensive psoriatic involvement not involving the palms and soles.

References

- Medscape, Sep 14, 2022.
- Healthline, Nov 17, 2021.

Test Yourself - 52

Correct Answers :

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

CONGRATULATIONS!

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Test Yourself - 53

1. **The followings are true for 'Acute Respiratory Distress Syndrome (ARDS)' except:**
   a. It is typically provoked by an acute injury to the lungs.
   b. The key histologic changes in ARDS reveal the presence of alveolar edema in areas of a diseased lung.
   c. Without prompt treatment, many people who have ARDS will survive.
   d. Pneumonia, pancreatitis, sepsis are among the causes of ARDS.

2. **All the followings are correct for 'Psoriasis' except:**
   a. Patients with psoriasis have a genetic predisposition for the disease.
   b. It appears to be slightly more prevalent among men than among women.
   c. Chronic stationary psoriasis is the most common type of psoriasis.
   d. Guttate psoriasis frequently appears suddenly.

3. **All the below are true for 'Antimicrobial Resistance (AMR)' except:**
   a. Misuse of antibiotics may contributes to the development of resistant bacteria.
   b. Efflux pumps in bacteria are not major contributors of drug resistance.
   c. The attribute of resistance development has been linked to many genetic elements.
   d. Modification of the antibiotic target site makes the antibiotic unable to bind properly.

4. **All the followings are correct for 'Breast Cancer' except:**
   a. Family history of breast cancer increases the risk of breast cancer.
   b. It most commonly presents as a painless lump or thickening in the breast.
   c. Mammograms are the best way to find breast cancer early, when it is easier to treat.
   d. It may not spread to other areas of the body and trigger other symptoms.

5. **The followings are right for 'Psoriasis' except:**
   a. Psoriatic arthritis affects about 50-80% of those with skin symptoms.
   b. Blepharitis is the most common ocular finding in psoriasis.
   c. Though it is usually benign, it is a lifelong illness with remissions and exacerbations.
   d. It can significantly influence a person's quality of life.

6. **All the followings are correct for 'Antimicrobial Resistance (AMR)' except:**
   a. Modern day travelling has also been a major contributor towards dissemination of new infections and antibiotic resistance across the world.
   b. Antibiotic resistant bacteria are spread globally in the same way as other bacteria.
   c. New resistance mechanism are emerging and spreading globally, threatening the ability to treat common infectious diseases.
   d. WHO report in 2007, confirmed that the entire world will run out of antibiotics.

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