NAME: OMIGIE EHIZEMEN.O

MATRIC NO: 17/MHS02/075

COURSE CODE: NSC306

LECTURE: DR AKPOR O.A

 PRIMARY IMMUNODEFICIENCY DISORDERS

. **CGD Chronic granulomatous disease:** This is an inherited primary immunodeficiency disease (PIDD) which increases the body’s susceptibility to infections caused by certain bacteria and fungi. Granulomas are masses of immune cells that form at sites of infection or inflammation. People with CGD are unable to fight off common germs and get very sick from infections that would be mild in healthy people. This is because the presence of CGD makes it difficult for cells called the neutrophils to produce hydrogen peroxide and the immune system requires hydrogen peroxide to fight specific kinds of bacteria and fungi. These kinds of infections include, skin or bone infections and abscesses in internal organs such as the lungs, liver or the brain.

Causes: A mutation in one of the five genes can cause CGD, people with this disease inherit the mutation from a parent. The genes normally produce proteins that form an enzyme that helps the immune system work properly. When there are mutations to one of these genes, the protective proteins are not produced or they will be produced but will not function properly.

Signs and symptoms associated with infections include: the signs and symptoms associated with the infections of the skin, liver, stomach, the intestine, brain and eyes include; fever, persistent runny nose, swollen and sore lymph glands, chest pain when inhaling or exhaling, swelling and redness in the mouth, skin irritation that may include a rash and GIT problems including, vomiting, diarrhoea, stomach pain, bloody stool.

Treatment: Therapeutic options for CGD include;

* Prophylactic antibiotics and antifungal medications
* Interferon-gamma injections
* Aggressive management of acute infections
* A bone marrow transplant can cure CGD but transplant candidate and donors must be carefully selected weighing the risks and benefits carefully.

**. Common variable immunodeficiency (CVID):** This is an antibody deficiency that leaves the immune system unable to defend against bacteria and viruses resulting in the recurrent and often severe infections primarily affecting the ears, sinuses and respiratory tract. Permanent damage to the respiratory tract (bronchiectasis) may occur due to severe and repeated infections. CVID is one of the most common form of primary immunodeficiency disease, it can also be associated with autoimmune disorders that affect other blood cells causing low numbers of white cells and platelets, anaemia, arthritis and other conditions such as endocrine disorders. People with CVID are also at an increased risk for certain cancers like lymphoid and gastrointestinal cancers.

Causes: A genetic mutation causes CVID in most cases, this genetic mutation results from defects in the genes involved with the immune system and these defects cause the body to produce abnormally low amounts of a protein called immunoglobulin G (igG). Low levels of igG in the blood makes it difficult for the body to fight infections.

Signs and symptoms: symptoms of this disease vary widely from person to person and can range from mild to severe which include; breathing problems, chronic cough, diarrhoea that causes weight loss, ear infections, frequent sinus infections, recurring lung infections, including pneumonia.

Treatment: CVID is treated with immunoglobulin replacement therapy (IRT), which most often relieves symptoms and must be given regularly, it is life-long.

* Antibiotics are used to treat most infections that result from CVID though patients may need treatment for a longer duration than in healthy people
* Another form of treatment involves immunoglobulin replacement.

**. Severe combined immunodeficiency disease (SCID):** This is an inherited primary immunodeficiency disease (PIDD) that typically presents in infancy resulting in profound immune deficiency condition resulting in a weak immune system that is unable to fight off even mild infections. It is considered to be the most serious PIDD, there are several forms of SCID but the most common type is linked to a problem in a gene on the X chromosomes, affecting males. Females could also have this condition but they also inherit a normal chromosome. Other forms of SCID are caused by a deficiency of the enzyme adenosine deaminase (ADA) and a variety of other genetic defects.

Causes: SCID is caused by genetic defects that affects the function of T cells, depending on the type of SCID, B cells and NK cells can also be affected. These cells play important roles in helping the immune system battle bacteria, viruses, fungi that cause infections.

Signs and symptoms: these include, severe respiratory infections, other symptoms in infants include, poor growth, rashes that look like eczema, chronic diarrhoea, recurrent thrush in the mouth. Although all these symptoms may not present, often SCID is associated with recurrent viral infections and causes several hospitalizations before it is discovered.

Treatment: the only cure for SCID is bone marrow transplant which provides a new immune system to the patient. Affected infants will often die within the first year of life without treatment with this hematopoietic stem cell transplantation (HSCT). Gene therapy treatment for SCID has also been successful in clinical trials but not without complications.

**. Inflammatory bowel disease (IBD):** Is an umbrella term used to describe disorders that involve chronic inflammation of the digestive tract, types of IBD include;

 **. Ulcerative colitis:** this conditioncauses long-lasting inflammation and sores (ulcers) in the innermost lining of your large intestine (colon) and rectum.

**. Crohn’s disease:** it is characterized by inflammation of the lining of the digestive tract, which often spreads deep into affected tissues.

Causes of IBD: The exact cause of inflammatory bowel disease is unknown but a possible cause is due to an immune system malfunction, when the immune system tries to fight off an invading virus or bacterium, an abnormal immune response causes the immune system to attack the cells in the digestive tract. Heredity also plays a partial role and is more common in people who have family members with the disease, however most people with IBD don’t have this family history.

Signs and symptoms: Both ulcerative colitis and crohn’s disease usually involve severe diarrhoea, fatigue, unintended weight loss, abdominal pain and cramping, fever, reduced appetite, and blood in the stool.

Treatment: Anti-inflammatory drugs which include corticosteroids and aminosalicylates (e.g. delzicol, colazal, dipentum).

* Immune system suppressors e.g. azathioprine (azasan, Imuran), mercaptopurine (purinethol, purixan) etc.
* Tumor necrosis factor (TNF)- alpha inhibitors e.g. infliximab (remicade), adalimumab (humira) etc.
* Antibiotics may be used in addition to other medications or when the infection is a concern, in most cases of perianal crohn’s disease. Examples of antibiotics include, ciprofloxacin and metronidazole.
* Other medications which could be given include; anti-diarrhoeal, pain relievers, iron supplements, calcium and vitamin D supplements.

**. X-linked agammaglobulinemia (XLA):** this is an inherited disorder due to the inability to produce B cells or the immunoglobulins (antibodies) that the B cells make. XLA is also called bruton type agammaglobulinemia, X-linked infantile agammaglobulinemia and congenital agammaglobulinemia. People with XLA have extremely low numbers of B cells, and blood tests will show extremely low levels of all types of immunoglobulins. People with XLA fail to develop antibodies to specific germs and will not produce protective antibodies to specific germs after immunizations.

Causes: the mutated gene responsible for XLA codes for protein bruton tyrosine kinase, or BTK, and is located on the X chromosome, it is an X-linked recessive disease. Because males only have one X chromosome, they are affected if they inherit an X chromosome containing mutated BTK genes.

Signs and symptoms: infants with XLA develop frequent infections of the ears, throat, sinuses and lungs. Serious infections develop in the bloodstream, central nervous system, skin and the internal organs. These children tend to cope well with most short-term viral infections but are very susceptible to chronic viral infections such as hepatitis, they usually lack or have very small tonsils.

Treatment: people with XLA receive intravenous or subcutaneous immunoglobulin regularly

* Antibiotics are also used to treat infections.
* Immunoglobulin replacement therapy (IRT)

 SECONDARY IMMUNODEFICIENCY DISORDERS

**. AIDS (Acquired immunodeficiency syndrome):** AIDS is a disease that can develop in people with HIV, it’s the most advanced stage of HIV. But just because a person has HIV does not mean they will develop AIDS. HIV kills CD4 cells and healthy adults have a CD4 count of 500 to 1500 per cubic millimeter. A person with HIV whose CD4 count falls below 200 per cubic millimeter will be diagnosed with AIDS. If AIDS does develop, it means that the immune system is severely compromised. It is weakened to the point where it can no longer fight off most diseases and infections and that makes the person more vulnerable to a wide range of illnesses such as, tuberculosis, oral thrush, cryptococcal meningitis, pneumonia etc.

Causes of AIDS: AIDS is caused by HIV because a person cannot get it if they have not contracted HIV. Also, if a person with HIV develops an opportunistic infection associated with HIV like pneumonia, they can still be diagnosed with AIDS even if their CD4 count is above 200.

Signs and symptoms: these include, recurrent fever, chronic swollen lymph glands especially of the armpits, neck and groin, chronic fatigue, night sweating, dark splotches under the skin or inside the mouth, nose or eyelids, sores or lesions of the mouth and tongue, genitals, or anus, bumps lesions or rashes of the skin, recurrent or chronic diarrhoea, rapid weight loss, neurologic problems such as trouble concentrating, memory loss and confusion.

Treatment: some of the medications approved for treating HIV and AIDS include;

* Nucleoside reverse transcriptase inhibitors (NRTI); they include, abacavir (ziagen, ABC), didanosine (videx, dideoxyinosine), emitricitabine (emtriva, FTC) etc.
* Protease inhibitors (PI): they include, amprenavir (agenerase, APV), atazanavir (reyataz, ATV), fosamprenavir (lexiva, FOS) etc.
* Non-nucleotide reverse transcriptase inhibitors (NNRTI): they include, delvaridine (rescriptor, DLV), efravirenz (sustiva, EFV), nevirapine (viramune, NVP).
* Fusion inhibitors: this includes, enfuvirtide also known as fuzeon or T-20.
* Highly active antiretroviral therapy (HAART): this is a combination of three or more drugs including, protease inhibitors and other anti-retroviral medications.

**. Chronic lymphocytic leukemia (CLL):** this is a type of cancer of the blood and bone marrow which is the spongy tissue inside bones where blood cells are made. The term chronic in this disorder comes from the fact that it typically progresses more slowly than other types of leukemia. While the term lymphocytic comes from the cells called the lymphocytes, which help the body fight against infection.

Causes: there is no conclusion to what starts the process that causes chronic lymphocytic leukemia, but there is a genetic mutation in the DNA of the blood producing cells which produces abnormal, ineffective lymphocytes. Beyond being ineffective, these abnormal lymphocytes continue to live and multiply when normal lymphocytes would die. The abnormal lymphocytes accumulate in the blood and certain organs, where they cause complications. They may crowd the healthy cells out of the bone marrow and interfere with normal blood cell production.

Signs and symptoms: many people with chronic lymphocytic leukemia have no early symptoms but those who develop signs and symptoms experience the following; enlarged but painless lymph nodes, fatigue, fever, pain in the upper left portion of the abdomen, which may be causes by an enlarged spleen, night sweats, weight loss, frequent infections.

Treatment: chemotherapy, the common drugs for CLL includes, bendamustine (bendeka, treanda), fludarabine most common for people with CLL who are younger and do not have a deletion in chromosome 17, pentostatin, cladribine, chlorambucil, cyclophosphamide.

* Targeted therapy: this includes, monoclonal antibodies and these drugs include (rituximab, ofatumumab, obinutuzumab, venetoclax)

Kinase inhibitors the drugs include; ibrutinib (imbruvica) which is approved for people with CLL who have received at least 1 other treatment and ibrutinib (zydelig) which is another type of kinase inhibitor given orally.

* Radiation therapy
* Bone marrow transplantation / stem cell transplantation
* Combining systemic therapies, combinations which may include fludarabine are generally used for younger patients e.g. (rituximab and fludarabine), (cyclophosphamide, fludarabine and rituximab), (pentostatin, cyclophosphamide and rituximab), etc.