IMMUNE DEFICIENCY SYNDROME

Immunodeficiency Disorder

Immunodeficiency disorders prevent our body from adequately fighting infections and diseases. An immunodeficiency disorder also makes it easier for you to catch viruses and bacterial infections in the first place. Immunodeficiency disorders as either congenital or acquired. A congenital, or primary, disorder is one you were born with. Acquired, or secondary, disorders are disorders you get later in life. Acquired disorders are more common than congenital disorders.
Immune system includes the following organs:

- spleen
- tonsils
- bone marrow
- lymph nodes

These organs make and release lymphocytes. Lymphocytes are white blood cells classified as B cells and T cells. B and T cells fight invaders called antigens. B cells release antibodies specific to the disease your body detects. T cells kill off cells that are under attack by disease.
Examples of antigens

- bacteria, viruses, cancer cells, parasites

An immunodeficiency disorder disrupts our body's ability to defend itself against these antigens.

Types of Immunodeficiency Disorders

Primary immunodeficiency disorders are immune disorders you are born with. Primary disorders include:

- X-linked agammaglobulinemia (XLA)
- common variable immunodeficiency (CVID)
- severe combined immunodeficiency (SCID)
- alymphocytosis

Secondary disorders happen when an outside source, such as a toxic chemical or infection, attacks your body. Severe burns and radiation also can cause secondary disorders. Secondary disorders include:

- AIDS
- cancers of the immune system, such as leukemia
- immune-complex diseases, such as viral hepatitis
- multiple myeloma

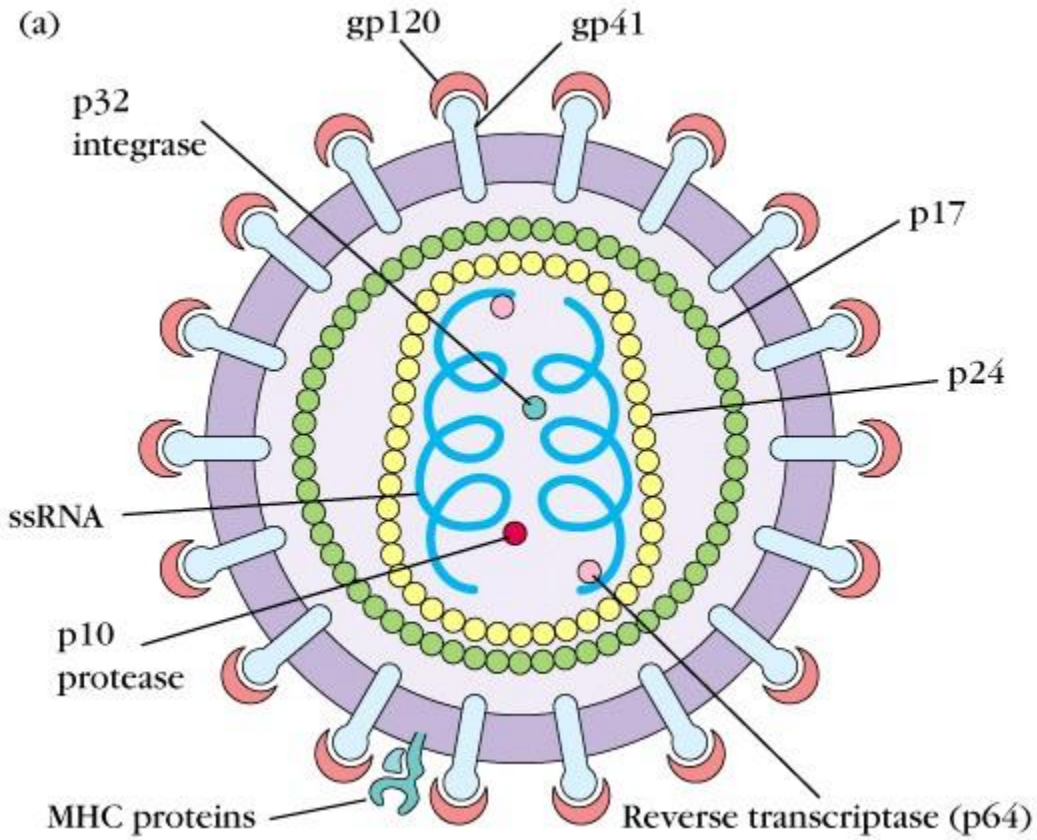
Secondary immunodeficiencies, also known as acquired immunodeficiencies, can result from various immunosuppressive agents, for example, malnutrition, aging and particular medications (e.g. chemotherapy, disease-modifying antirheumatic drugs, immunosuppressive drugs after organ transplants, glucocorticoids). For medications, the term immunosuppression generally refers to both beneficial and potential adverse effects of decreasing the function of the immune system, while the term *immunodeficiency* generally refers solely to the adverse effect of increased risk for infection.

Many specific diseases directly or indirectly cause immunosuppression. This includes many types of cancer, particularly those of the bone marrow and blood cells (leukemia, lymphoma, multiple myeloma), and certain chronic infections. Immunodeficiency is also the hallmark of acquired immunodeficiency syndrome (AIDS),[6] caused by the human immunodeficiency virus

(HIV). HIV directly infects a small number of T helper cells, and also impairs other immune system responses indirectly.

Structure of HIV

HIV is different in structure from other retroviruses. It is around 120 nm in diameter and roughly spherical. HIV-1 is composed of two copies of noncovalently linked, unspliced, single-stranded RNA enclosed by a conical capsid composed of the viral protein p24. The RNA component is 9749 nucleotides long and bears a 5' cap (Gppp), a 3' poly(A) tail, and many open reading frames (ORFs). Viral structural proteins are encoded by long ORFs, whereas smaller ORFs encode regulators of the viral life cycle: attachment, membrane fusion, replication, and assembly.



Structure of HIV

The single-strand RNA is tightly bound to p7 nucleocapsid proteins, late assembly protein p6, and enzymes essential to the development of the virion, such as reverse transcriptase and integrase. Lysine tRNA is the primer of the magnesium-dependent reverse transcriptase. The nucleocapsid associates with the genomic RNA (one molecule per hexamer) and protects the RNA from digestion by nucleases. Also enclosed within the virion particle are Vif, Vpr, Nef, and

viral protease. A matrix composed of an association of the viral protein p17 surrounds the capsid, ensuring the integrity of the virion particle. This is in turn surrounded by an envelope of host-cell origin. The envelope is formed when the capsid buds from the host cell, taking some of the host-cell membrane with it. The envelope includes the glycoproteins gp120 and gp41.

As a result of its role in virus-cell attachment, the structure of the virus envelope spike, consisting of gp120 and gp41, is of particular importance. Determining the envelope spike's structure will contribute to understanding the HIV replication cycle, and may help in the creation of a cure. The first model of its structure was compiled in 2006 using cryo-electron tomography and suggested that each spike consists of a trimer of three gp120–gp41 heterodimers. However, published shortly after was evidence for a single-stalk "mushroom" model, with a head consisting of a trimer gp120s and a gp41 stem, which appears as a compact structure with no obvious separation between the three monomers, anchoring it to the envelope. There are various possibilities as to the source of this difference, as it is unlikely that the viruses imaged by the two groups were structurally different. More recently, further evidence backing up the heterodimer trimer-based model has been found.

Pathology of AIDS

Acquired immune deficiency syndrome (AIDS) is caused by the HIV or human immunodeficiency virus. The infection causes progressive destruction of the cell-mediated immune (CMI) system, primarily by eliminating CD4+ T-helper lymphocytes.

Decreased immunity leads to opportunistic infections and certain cancers. Opportunistic infections are caused by organisms that do not cause infections in healthy individuals. HIV also directly damages certain organs like the brain.

AIDS indicates advanced HIV disease and has no cure and is considered fatal. The time from HIV infection to death however depends on the management with anti-HIV medications instituted on time and continued over long term.

The time period usually ranges from 6 months (rarely) to 15+ years. In the United Kingdom the average time is around 12 years.

HIV infection passes through a series of steps or stages before it turns into AIDS. These stages of infection as outlined in 1993 by the Centers for Disease Control and prevention are:

1. **Seroconversion illness** – this occurs in 1 to 6 weeks after acquiring the infection. The feeling is similar to a bout of flu.
2. **Asymptomatic infection** – After seroconversion, virus levels are low and replication continues slowly. CD4 and CD8 lymphocyte levels are normal. This stage has no symptoms and may persist for years together.
3. **Persistent generalised lymphadenopathy (PGL)** – The lymph nodes in these patients are swollen for three months or longer and not due to any other cause.
4. **Symptomatic infection** – This stage manifests with symptoms. In addition, there may be opportunistic infections. This collection of symptoms and signs is referred to as the AIDS-related complex (ARC) and is regarded as a prodrome or precursor to AIDS.
5. **AIDS** – this stage is characterized by severe immunodeficiency. There are signs of life-threatening infections and unusual tumors. This stage is characterized by CD4 T-cell count below 200 cells/mm3.
6. There is a small group of patients who develop AIDS very slowly, or never at all. These patients are called non-progressors.

The pathological spectrum of HIV infection is changing as the infection spreads into new communities with different potential opportunistic diseases, and as medical science devises drugs against HIV replication.

Geographical pathology of HIV/AIDS

Genetics and geographical location has a role in the pattern of opportunistic infections. A second determinant is the speed of decline in the immune system. Many of the opportunistic infections are of low virulence and are only encountered if patients survive with low CMI.

Genetics and earlier site of stay also plays a role. For example, African HIV-infected patients reside in the UK have high rates of tuberculosis and this is usually a reactivation of latent infection acquired in the country of origin.

Some opportunistic infections include;

Viral infections

- Cytomegalovirus (CMV)
- Herpes simplex
- Herpes zoster
- Measles
- Human papilloma virus (HPV)
- Human herpes virus 8 (HV8)
- Epstein-Barr virus (EBV)

Bacterial infections

- Recurrent bacterial pneumonia (commonly Streptococcus pneumoniae)
- Mycobacterium tuberculosis
- Non-tuberculosis mycobacteriosis
- Systemic non-typhoid Salmonella infections
- *Pseudomonas spp*. septicaemia and `vasculitis'

Fungal infections

- Candida severe infection
- *Pneumocystis jiroveci pneumonia*
- *Cryptococcus neoformans*
- *Histoplasma capsulatum*
- *Coccidioides immitis*
- *Aspergillus spp.*
- *Penicillium marneffei*

Protozoal infections

- *Toxoplasma gondii*
- *Cryptosporidium parvum*
- *Isospora belli*
- *Leishmania spp.*
- *Microsporidia spp.*
- *Acanthamoeba spp.*
- *Trypanosoma cruzi*

Tumours

- Kaposi's sarcoma
- Primary cerebral lymphoma
- High-grade non-Hodgkin lymphoma
- Carcinoma (invasive) of the cervix

- Carcinoma of the conjunctiva
- Carcinoma of the anus
- T-cell lymphoma
- Hodgkin's disease
- Lympho proliferative disease, pre-lymphomatous

Risk for Immunodeficiency Disorders

People who have a family history of primary disorders have a higher-than-normal risk for developing primary disorders.

Impaired immune system can lead to a secondary immunodeficiency disorder. For example, exposure to bodily fluids infected with HIV can cause AIDS.

Proteins are important for your immunity. An insufficient amount of protein in the diet can reduce the strength of your immune system. Our body also produces proteins when you sleep that help your immune system fight infection. For this reason, lack of sleep reduces your immune defenses.

Cancers and chemotherapy drugs can also reduce your immunity.

Signs of an Immunodeficiency Disorder

Each disorder has unique symptoms. One symptom of a weakened immune system is frequent or chronic illnesses, including pinkeye, sinus infections, colds, or diarrhea. If these problems don't respond to treatment or you don't completely get better over time, your doctor might test you for an immunodeficiency disorder. Recurrent pneumonia and yeast infections could also suggest you have a disorder.

Diagnosis

- ask about patients medical history
- perform a physical exam
- determine patients T cell count
- determine patients white blood cell count

Vaccines can test our immune system response in what is called an antibody test. Doctor will give you a vaccine and then test your blood for its response to the vaccine a few days or weeks later. If you don't have an immunodeficiency disorder, your immune system will produce antibodies to fight the organisms in the vaccine. You might have a disorder if your blood test doesn't show antibodies.

Treatment

The treatment for each immunodeficiency disorder will be tailored to its specific conditions. For example, AIDS causes several different infections. Your doctor will prescribe medications that are appropriate for each infection.

Treatment for immunodeficiency disorders commonly includes antibiotics and antibody replacement. A drug called interferon is a common treatment for the viral infections caused by a disorder.

If your bone marrow isn't producing enough lymphocytes, your doctor might order a bone marrow transplant.

Prevention

Primary disorders can be controlled and treated, but they cannot be prevented.

Secondary disorders can be prevented in a number of ways. For example, it's possible to prevent yourself from getting AIDS by not having unprotected sex with someone who carries HIV.

Sleep is very important for a healthy immune system. According to the Mayo Clinic, adults need about eight hours of sleep per night. It's important that you stay away from people who are sick if your immune system isn't working properly.
If you have a contagious immunodeficiency disorder like AIDS, you can keep others healthy by practicing safe sex and not sharing bodily fluids with people who don't have the condition.

Molecular Basis of Diabetes

Definition:

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects of insulin secretion, insulin action, or both

Diabetes classification:

There are two main types of diabetes: type-1 and type-2. Type-1 diabetes is due to the autoimmune-mediated destruction of pancreatic beta cells, resulting in insulin deficiency. Patients with type-1-diabetes require exogenous insulin for survival. Its frequency amounts to nearly 10% of all diabetes cases. There is marked geographical variation in its prevalence, Scandinavian countries showing the highest rate of this illness. Type-2 diabetes accounts for approximately 90% of diabetes cases, and is characterized by impaired insulin action and/or abnormal insulin secretion. The worldwide diabetes epidemic relates particularly to type-2 diabetes. Besides type-1 and type-2 diabetes, there are other specific types of diabetes as described on Table 1. To understand the metabolic and molecular mechanisms responsible for type-2 diabetes, it is necessary to understand the regulation of fuel metabolism in the human body.

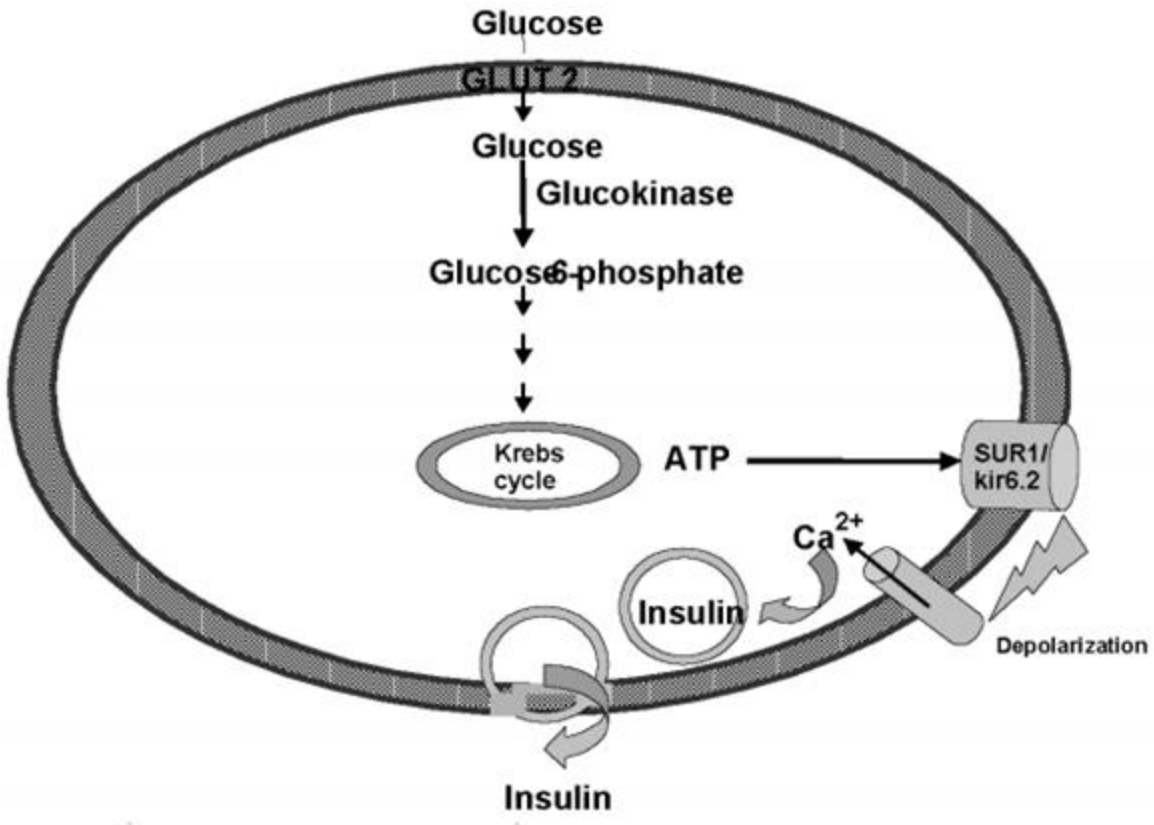
Basic principles of metabolism:

In the fed state, fuels in excess are stored as glycogen and triglycerides. During the fasting state these reservoirs are broken down to provide fuels. Energy reservoirs are built up and broken down in response of hormonal messages. In the fed state, coordination of insulin secretion by the pancreatic beta cells along with the responsiveness to insulin of major glucose metabolic tissues such as muscle, liver and fat, control plasma glucose. Insulin promotes glucose uptake, glycogen synthesis in the liver and muscle, lipid formation to be stored in the adipose tissue, and protein synthesis in most cells. The rate limit step in whole body glucose uptake is the transport of glucose into skeletal muscle cells, this accounts for more that 75% of glucose uptake. Alongside the insulin stimulatory effect on fuel reservoir synthesis, in the fed state, the hormone has restrained functions on glucose output and lipolysis. In the fasting state, decreased plasma insulin

concentration and increased counterinsulin hormones, such as glucagons, glucocorticoids, and catecholamines, contribute to glucose output via glycogen breakdown and gluconeogenesis, and via lipolysis as well as decreased synthesis and increased protein degradation. Beside the classical regulating hormones, a considerable piece of evidence indicates that adipose tissue hormones, adipokines, as well as free fatty acids, influence metabolism and fuel expenditure. Below, we describe the basic knowledge of the molecular mechanisms involved in insulin secretion and of responsiveness to insulin in normal conditions. We also describe the role of adipose tissue in fuel metabolism.

Molecular mechanisms of insulin secretion

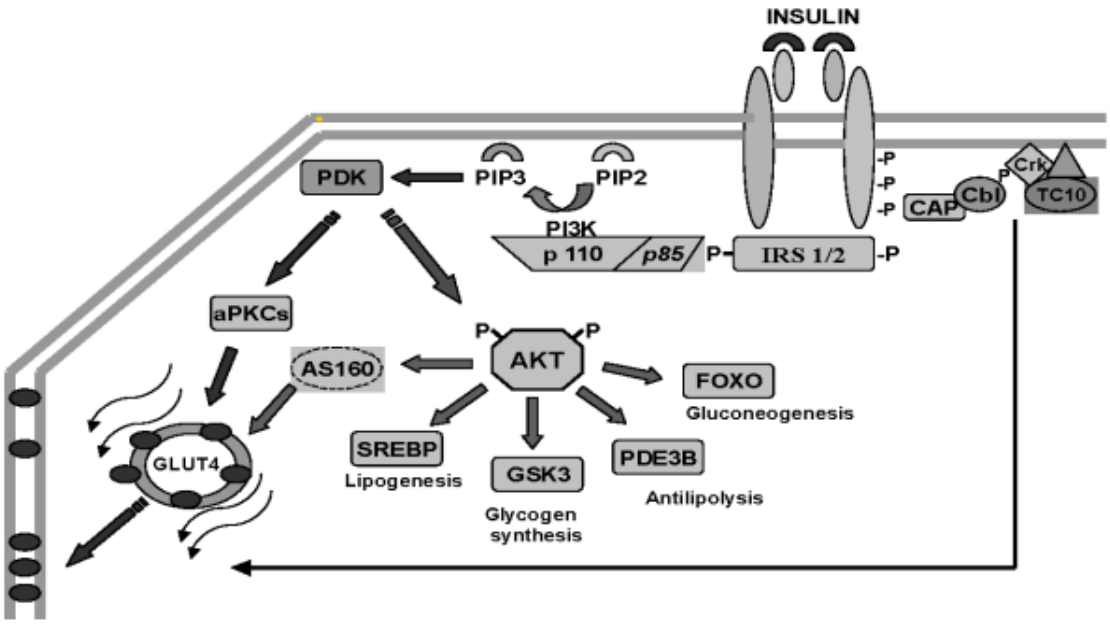
Insulin secretion in response to glucose is a complex, multistep process that requires transport and oxidation of glucose, electrophysiological changes and fusion of insulin-containing secretory granules with the beta-cell plasma membrane. Glucose enters the cell by facilitated diffusion mediated by a group of structurally related glucose transport proteins (GLUT), characterized by 12 hydrophobic helical domains. To date, at least 12 GLUTs have been described [8]. In the pancreatic beta cell, glucose is transported by the glucose transporter 2 isoform (GLUT2). Glucose is phosphorylated to form glucose-6-phosphate by glucokinase. This enzyme plays a critical role in glucose-induced insulin secretion and is considered the glucosensor of the pancreatic beta cell. Due to its kinetic characteristics, glucokinase is a determining factor for glucose phosphorylation and hence for its metabolism through glycolysis and oxidation.



Insulin secretion in response to glucose: Glucose enters the cell by facilitated diffusion mediated the glucose transporter 2 isoform (GLUT2) and it is phosphorylated to form glucose-6-phosphate by glucokinase. The generation of ATP by glucose oxidation leads to closure of the ATP-sensitive K+ channel, a hetero-octamer comprised of four subunits of the sulphonylurea 1 receptor (SUR1) and four subunits of the inwardly rectifying K+ channel Kir6.2. The closing of the ATP-sensitive K+ channel leads to depolarization of the plasma membrane and influx of extracellular calcium. This leads to fusion of insulin-containing secretory granules with the plasma membrane and the release of insulin into the circulation.

Molecular mechanisms of insulin signaling

Insulin starts its action by binding to the insulin receptor; this leads to a cascade of events that involves protein and membrane phospholipid phosphorylation, scaffold and docking proteins, and cytoeskeleton activity.



Molecular mechanisms of insulin signaling. The insulin interaction with its receptor promotes insulin receptor autophosphorylation, and catalyses the phosphorylation of cellular proteins such as members of the IRS family and Cbl. Upon tyrosine phosphorylation, these proteins interact with signalling molecules, resulting in a diverse series of signalling pathways, including activation of PI3K and the activation of TC10. These pathways act in a concerted fashion to coordinate the regulation of glucose transporter 4 (GLUT4) vesicle trafficking, protein synthesis, enzyme activation and inactivation, and gene expression, which results in the regulation of glucose, lipid and protein metabolism.

Metabolism in type-2 diabetes

Insulin secretion:

Type-2 diabetes arises when pancreatic beta cells fail to secrete sufficient insulin to andle with the insulin resistance demand, because of acquired betacell secretory dysfunction and/or decreased beta-cell mass. Recent studies have presented evidence that the beta-cell mass plays a pivotal role in determining whether an individual will progress to type-2 diabetes. These defects may be caused by primary beta-cell defects, such as seen in the monogenic diabetes forms of MODY, or by secondary beta-cell defects, caused by glucotoxicity, increased free fatty acids, cytokines, mitochondrial dysfunction and/or metabolic stress.

Type-2 diabetes is characterized by impaired insulin action and/or abnormal insulin secretion. An early abnormality in the disease is insulin resistance; a defective state in which insulin is unable to exert its biological effects at circulation concentrations that are effective in

normal subjects. Insulin resistance has been proposed as the key linking factor for the metabolic syndrome disease cluster of glucose intolerance, hypertension and dyslipidemia. Insulin resistance leads to profound decreases in glucose uptake and glycogen synthesis in peripheral tissues. Impaired hepatic glycogen stores and glycogen synthase activity are also observed in insulin resistance. Insulin resistance yields to defective suppression of hepatic glucose output, under the fasting as well as the fed state. Resistance to the antilipolytic action of insulin also favors triglyceride breakdown in adipose tissue and the generation of free fatty acids, which inhibit insulin-stimulated glucose uptake and metabolism in skeletal muscle, stimulate hepatic gluconeogenesis and interfere with insulin receptor signals. Changes in serum adipokine concentrations are also part of the insulin resistant state. At the pre-onset of type-2 diabetes, resistance to the glucose-lowering action of insulin tends to lead a slight increase of blood glucose concentration, which stimulates insulin secretion and causes hyperinsulinemia. Initially hyperinsulinemia is able to overcome insulin resistance. The diabetic state develops when insulin secretion cannot longer be sustained to compensate insulin resistance, and it is at this stage that fasting and post-prandrial hyperglycemia is apparent.

Genetic factors:

After the elucidation of Mendelian disorders with diabetes as a major phenotypic feature it has become clear that type-2 diabetes is heterogeneous and may result from defects in one or more molecular pathways. Genetic defects of the beta cell, usually referred to as maturity-onset diabetes of the young (MODY), can result from mutations in any of at least six different genes. Most of the MODY subtypes are caused by mutations in transcription factors, which are involved in the tissue-specific regulation of gene expression in the liver and in pancreatic beta-cells. Other related genetic factors are due to insulin receptor mutations.

RESPIRATORY DISORDER

Respiratory disease is a medical term that encompasses pathological conditions affecting the organs and tissues that make gas exchange possible in higher organisms, and includes conditions of the upper respiratory tract, trachea,bronchi, bronchioles, alveoli, pleura and pleural cavity, and the nerves and muscles of breathing.

The study of respiratory disease is known as pulmonology.

Common Respiratory Disorders Include:

Chronic Obstructive Pulmonary Disease (COPD) - Irritation of the lungs can lead to asthma, emphysema, and chronic bronchitis and people can develop two or three of these together.

Chronic Bronchitis - Any irritant reaching the bronchi and bronchioles will stimulate an increased secretion of mucus. In chronic bronchitis the air passages become clogged with mucus, and this leads to a persistent cough.

Emphysema - The delicate walls of the alveoli break down, reducing the gas exchange area of the lungs. The condition develops slowly and is seldom a direct cause of death.

Asthma - Periodic constriction of the bronchi and bronchioles makes it more difficult to breathe.

Pneumonia - An infection of the alveoli. It can be caused by many kinds of both bacteria and viruses. Tissue fluids accumulate in the alveoli reducing the surface area exposed to air. If enough alveoli are affected, the patient may need supplemental oxygen.

Disorders of the respiratory system are usually treated internally by a pulmonologist or respiratory physician.

CYSTIC FIBROSIS

Cystic fibrosis is a hereditary disorder affecting the exocrine glands. It causes the production of abnormally thick mucus, leading to the blockage of the pancreatic ducts, intestines, and bronchi and often resulting in respiratory infection.

Cystic fibrosis causes various effects on the body, but mainly affects the digestive system and lungs. The degree of cystic fibrosis involvement differs from person to person. However, the persistence and ongoing infection in the lungs, with destruction of lungs and loss of lung function, eventually causes death in the majority of people who have cystic fibrosis.

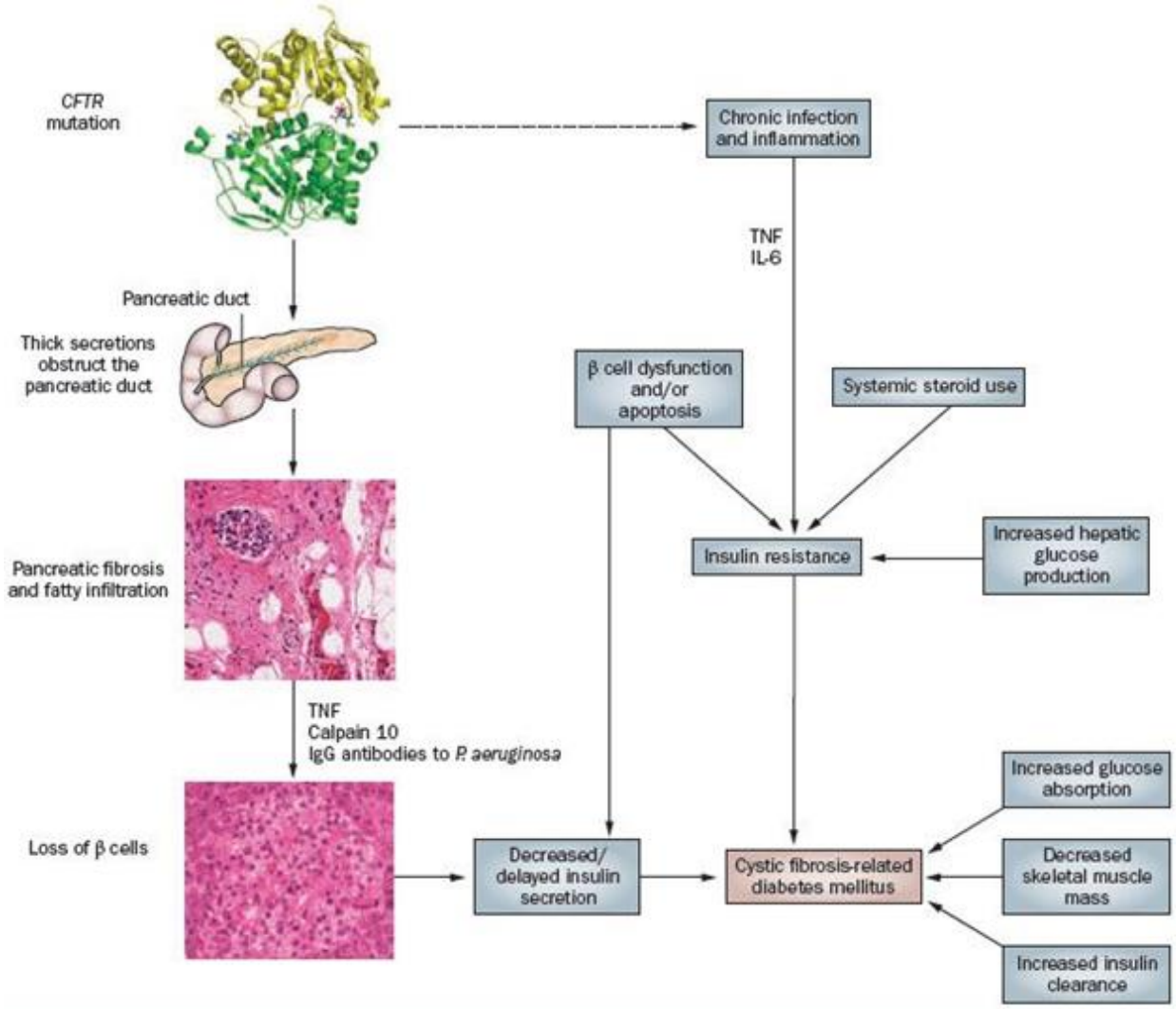
Typical complications caused by cystic fibrosis are difficulty in digesting fats and proteins; vitamin deficiencies due to loss of pancreatic enzymes; and progressive loss of lung function.

Causes of Cystic Fibrosis

Cystic fibrosis is a genetic disease that occurs when a child inherits two abnormal genes, one from each parent. Approximately, one in 25 Canadians carry an abnormal version of the gene responsible for cystic fibrosis. Carriers do not have cystic fibrosis, nor do they exhibit any of the symptoms of the disease.

When two parents who are carriers have a child, there is a 25 percent chance that the child will be born with cystic fibrosis. There is also a 50 percent chance that the child will be a carrier; and a 25 percent chance that the child will neither be a carrier nor have cystic fibrosis.

Pathophysiology of Cystic fibrosis



Symptoms of cystic fibrosis

Cystic fibrosis is a multi-system disorder that produces a variety of symptoms including:

- Persistent cough with productive thick mucous
- Wheezing and shortness of breath
- Frequent chest infections, which may include pneumonia
- Bowel disturbances, such as intestinal obstruction or frequent, oily stools
- Weight loss or failure to gain weight despite possible increased appetite
- Salty tasting sweat
- Infertility (men) and decreased fertility (women)

DIAGNOSING CYSTIC FIBROSIS

If a doctor suspects a patient has cystic fibrosis, a ‘sweat test’ may be administered. This simple and painless test measures the amount of salt content present in sweat. If the test comes back positive, it means the sweat content collected contains more salt than usual and validates a diagnosis of cystic fibrosis. In addition, a test for the presence of enzymes in the intestine can be performed.

TUBERCULOSIS

What is Tuberculosis?

Tuberculosis, commonly known as TB, is a bacterial infection that can spread through the lymph nodes and bloodstream to any organ in your body. It is most often found in the lungs. Most people who are exposed to TB never develop symptoms because the bacteria can live in an inactive form in the body. TB bacteria cause death of tissue in the organs they infect. Active TB disease can be fatal if left untreated.

Because the bacteria that cause tuberculosis are transmitted through the air, the disease can be contagious. Infection is most likely to occur if you are exposed to someone with TB on a day-to-day basis, such as by living or working in close quarters with someone who has the active disease. Even then, because the bacteria generally stay latent (inactive) after they invade the body, only a small number of people infected with TB will ever have the active disease. The remaining will have what's called latent TB infection -- they show no signs of infection and won't be able to spread the disease to others, unless their disease becomes active.

TB was once a widespread disease. It was virtually wiped out with the help of antibiotics developed in the 1950s, but the disease has resurfaced in potent new forms -- multidrug-resistant TB and extensively drug-resistant TB. Today, these new and dangerous forms of the disease -- resistant to some of the commonly used drug treatments -- have created a public health crisis in many large cities worldwide. If you have TB -- in its active or latent state -- you must seek medical treatment.

Causes

The main cause of TB is *Mycobacterium tuberculosis*, a small, aerobic, nonmotile bacillus. The high lipid content of this pathogen accounts for many of its unique clinical characteristics. It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than an hour. Mycobacteria have an outer membranelipid bilayer. If a Gram stain is performed, MTB either stains very weakly "Gram-positive" or does not retain

dye as a result of the high lipid and mycolic acid content of its cell wall. MTB can withstand weak disinfectants and survive in a dry statefor weeks. In nature, the bacterium can grow only within the cells of a host organism, but *M. tuberculosis* can be cultured in the laboratory.

The *M. tuberculosis* complex (MTBC) includes four other TB-causing mycobacteria: *M. bovis*, *M. africanum*, *M. canetti*, and*M. microti*. *M. africanum* is not widespread, but it is a significant cause of tuberculosis in parts of Africa. *M. bovis* was once a common cause of tuberculosis.

Risk of TB

People with compromised immune systems are most at risk of developing active tuberculosis.

HIV suppresses the immune system, making it harder for the body to control TB bacteria. People who are infected with both HIV and TB are around 20-30% more likely to develop active TB than those who do not have HIV.

Tobacco use has also been found to increase the risk of developing active TB. Over 20% of TB cases worldwide are related to smoking.

Symptoms of tuberculosis

While latent TB is symptomless, the symptoms of active TB include the following:

- Coughing, sometimes with mucus or blood
- Chills
- Fatigue
- Fever
- Loss of weight
- Loss of appetite
- Night sweats.

Tuberculosis usually affects the lungs, but can also affect other parts of the body. When TB occurs outside of the lungs, the symptoms can vary accordingly. Without treatment, TB can spread to other parts of the body through the bloodstream:

- TB infecting the bones can lead to spinal pain and joint destruction
- TB infecting the brain can cause meningitis
- TB infecting the liver and kidneys can impair their waste filtration functions and lead to blood in the urine

- TB infecting the heart can impair the heart's ability to pump blood, resulting in a condition called cardiac tamponade that can be fatal.

Diagnosis of tuberculosis

To check for TB, a health care provider will use a stethoscope to listen to the lungs and will check for swelling in the lymph nodes. They will also ask about symptoms and medical history as well as assessing a person's risk of exposure to TB.

The most common diagnostic test for TB is a skin test where a small injection of PPD tuberculin, an extract of the TB bacterium, is made just below the inside forearm.

The injection site should be checked after 2-3 days, and if a hard, red bump has swollen up then it is likely that TB is present.

There are other tests that are available to diagnose TB. Blood tests, chest X-rays and sputum tests can all be used to test for the presence of TB bacteria, and may be used alongside a skin test.

MDR-TB is more difficult to diagnose than regular TB. It is also difficult to diagnose regular TB in children

Treatments for tuberculosis

The majority of TB cases can be cured when the right medication is available and administered correctly.

The precise type and length of antibiotic treatment depends on a person's age, overall health, potential resistance to drugs, whether the TB is latent or active, and the location of infection (i.e. the lungs, brain, kidneys).

People with latent TB may need just one kind of TB antibiotics, whereas people with active TB (particularly MDR-TB) will often require a prescription of multiple drugs.

Antibiotics are usually required to be taken for a relatively long time. The standard length of time for a course of TB antibiotics is about 6 months.

All TB medication is toxic to the liver, and although side effects are uncommon, when they do occur, they can be quite serious. Potential side effects should be reported to a health care provider and include:

- Fever
- Jaundice
- Loss of appetite
- Nausea and vomiting.

It is important for any course of treatment to be completed fully, even if the TB symptoms have gone away. Any bacteria that have survived the treatment could become resistant to the medication that has been prescribed, and could lead to developing MDR-TB in the future.

Directly observed therapy (DOT) can be recommended. It involves a health care worker administering the TB medication to ensure that the course of treatment is completed.

Prevention of tuberculosis

Avoiding other people by not going to school or work, or sleeping in the same room as someone, will help to minimize the risk of germs from reaching anyone else. Wearing a mask, covering the mouth and ventilating rooms can also limit the spread of bacteria.

In some countries, BCG injections are given to children in order to vaccinate them against tuberculosis. It is not recommended for general use in the US because it is not effective in adults, and it can adversely influence the results of skin testing diagnoses.

The most important thing to do is to finish entire courses of medication when they are prescribed. MDR-TB bacteria are far deadlier than regular TB bacteria. Some cases of MDR-TB require extensive courses of chemotherapy, which can be expensive and cause severe adverse drug reactions in patients.

BRONCHITIS

What is Bronchitis?

Bronchitis is a respiratory disease in which the mucus membrane in the lungs' bronchial passages becomes inflamed.

As the irritated membrane swells and grows thicker, it narrows or shuts off the tiny airways in the lungs, resulting in coughing spells that may be accompanied by phlegm and breathlessness.

The disease comes in two forms: acute (lasting from one to three weeks) and chronic (lasting at least 3 months of the year for two years in a row).

People with asthma may also have asthmatic bronchitis, inflammation of the lining of the bronchial tubes.

Acute bronchitis may be responsible for the hacking cough and phlegm production that sometime accompany an upper respiratory infection. In most cases, the infection is viral in origin, but sometimes it's caused by bacteria.

If you are otherwise in good health, the mucus membrane should return to normal after you've recovered from the initial lung infection, which usually lasts for several days.

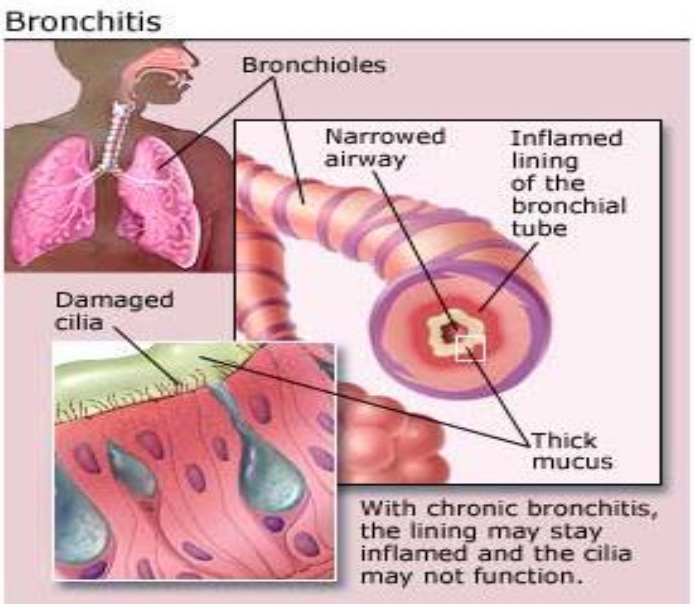
If you continue smoking, the damage to these cilia prevent them from functioning properly, thus increasing your chances of developingchronic bronchitis. In some heavy smokers, the mucus membrane lining the airways stays inflamed and the cilia eventually stop functioning altogether. Clogged with mucus, the lungs are then vulnerable to viral and bacterial infections, which over time distort and permanently damage the lungs' airways. This permanent condition is called COPD (chronic obstructive pulmonary disease). Your doctor can perform a breathing test, called spirometry, to see if you have developed COPD. WebMD has many resources to help you to successfully quit smoking.

Acute bronchitis is very common. The disorder often can be treated effectively without professional medical assistance. However, if you have severe or persistent symptoms or high fever, or if you cough up blood, you should see your doctor right away.

Seek emergency medical help if you have trouble breathing or have chest pain.

Acute bronchitis is inflammation of the bronchial tubes. The most common cause of acute bronchitis is a viral or bacterial infection, but other causes may include irritants like tobacco smoke, air pollution, or chemicals. The primary symptom of acute bronchitis is a cough.

Chronic bronchitis is a serious long-term disorder that often requires regular medical treatment. If you suffer from chronic bronchitis, you are at risk for developing heart problems, as well as more serious lung diseases and infections, so you should be monitored by a doctor.



Chronic bronchitis is one of two main types of a COPD. The other main form of COPD is emphysema. Both forms of COPD make it difficult to breathe.

What Causes Bronchitis?

Acute bronchitis is generally caused by lung infections, 90% of which are viral in origin. Repeated attacks of acute bronchitis which weaken and irritate bronchial airways over time can result in chronic bronchitis.

Industrial pollution is another culprit. Chronic bronchitis is found in higher-than-normal rates among coal miners, grain handlers, metal molders, and other people who are continually exposed to dust and fumes. But the chief cause is heavy, long-term cigarette smoking, which irritates the bronchial tubes and causes them to produce excess mucus. The symptoms of chronic bronchitis are also worsened by high concentrations of sulfur dioxide and other pollutants in the atmosphere.

NEUROPSYCHIATRIC DISORDER

Psychiatry is the branch of psychiatry science that investigates the links between mental illness and organic disease of the brain. Neuropsychiatry is the branch of medicine dealing with diseases affecting the brain and the nervous system.

Parkinson's disease

Parkinson's disease (PD) is a progressive disease of the nervous system marked by tremor, muscular rigidity, and slow, imprecise movement, chiefly affecting middle-aged and elderly people. It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine.

Parkinson's disease (PD) is a chronic and progressive movement disorder, meaning that symptoms continue and worsen over time. Parkinson’s involves the malfunction and death of vital nerve cells in the brain, called neurons. Parkinson's primarily affects neurons in an area of the brain called the substantia nigra.

Parkinson's disease affects the way you move. It happens when there is a problem with certain nerve cells in the brain.

Normally, these nerve cells make an important chemical called dopamine. Dopamine sends signals to the part of your brain that controls movement. It lets your muscles move smoothly and

do what you want them to do. When you have Parkinson's, these nerve cells break down. Then you no longer have enough dopamine, and you have trouble moving the way you want to.

Parkinson's is progressive, which means it gets worse over time. But usually this happens slowly, over many years. And there are good treatments that can help you live a full life.

No one knows for sure what makes these nerve cells break down. But scientists are doing a lot of research to look for the answer. They are studying many possible causes, including aging and poisons in the environment.

Abnormal genes seem to lead to Parkinson's disease in some people. But so far, there is not enough proof to show that it is always inherited.

The four main symptoms of Parkinson's are:

- Tremor, which means shaking or trembling. Tremor may affect your hands, arms, or legs.
- Stiff muscles.
- Slow movement.
- Problems with balance or walking.

Tremor may be the first symptom you notice. It's one of the most common signs of the disease, although not everyone has it.

More importantly, not everyone with a tremor has Parkinson's disease.

Tremor often starts in just one arm or leg or on only one side of the body. It may be worse when you are awake but not moving the affected arm or leg. It may get better when you move the limb or you are asleep.

In time, Parkinson's affects muscles all through your body, so it can lead to problems like trouble swallowing or constipation.

In the later stages of the disease, a person with Parkinson's may have a fixed or blank expression, trouble speaking, and other problems. Some people also lose mental skills (dementia).

People usually start to have symptoms between the ages of 50 and 60. But sometimes symptoms start earlier.

Who gets Parkinson's disease?

As stated previously, men are about 1.5 times more likely to develop Parkinson's disease than women; however, although the majority of all patients that get the disease are over 60, the total chance of getting the disease is about 2% to 4% in this age group. Consequently, the disease is not rare but the chances of someone age 60 or over developing the disease is not high.

Parkinson's disease Causes?

Cells in the substantia nigra, a part of the brainstem that controls movement, slow down and then stop producing dopamine as the cells die. Dopamine helps nerve cells communicate about movement; without the dopamine, body commands about normal movement are disrupted resulting in Parkinson's disease because the brain does not receive the necessary messages about how and when to move. Unfortunately, the ultimate cause of Parkinson's disease, the reason that the cells in the brainstem become altered and die, is not known but researchers suggest that a combination of both genetic and environmental factors cause about 90% of all Parkinson's disease.

Pathophysiology of Parkinson's Disease

Although we are learning more each day about the pathophysiology of Parkinson's disease, it is still considered largely idiopathic (of unknown cause). It likely involves the interaction of host susceptibility and environmental factors. A small percentage of cases are genetically linked and genetic factors are being intensely studied.

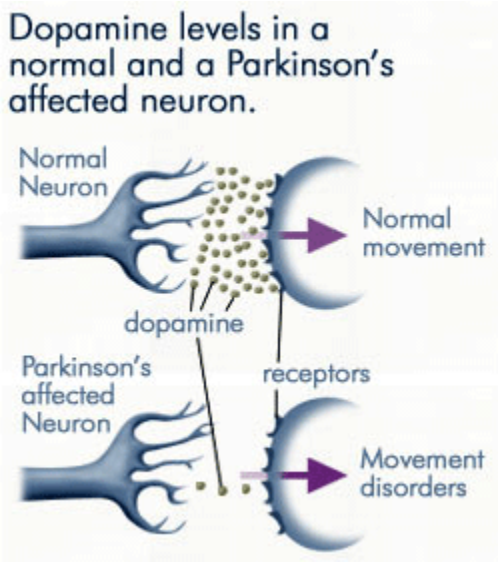
Physiologically, the symptoms associated with Parkinson's disease are the result of the loss of a number of neurotransmitters, most notably dopamine. Symptoms worsen over time as more and more of the cells affected by the disease are lost. The course of the disease is highly variable, with some patients exhibiting very few symptoms as they age and others whose symptoms progress rapidly.

Parkinson's is increasingly seen as a complex neurodegenerative disease with a sequence of progression. There is strong evidence that it first affects the dorsal motor nucleus of the vagus nerve and the olfactory bulbs and nucleus, then the locus coeruleus, and eventually the substantia nigra. Cortical areas of the brain are affected at a later stage. Damage to these various neuronal systems account for the multi-faceted pathophysiologic changes that cause impairments not just to the motor system but also to the cognitive and neuropsychological systems.

Progressive Loss of Dopamine

Although dopamine cell loss cannot be measured directly, measurements in neurologically normal people and in nonhuman primates reveal a slow progressive loss of dopamine with age. In Parkinson's disease the loss occurs at a much greater rate and both biochemical measures and imaging studies suggest there is a significant decrease in dopamine by the time motor symptoms appear. In this view, Parkinson's disease is an accelerated version of the cell death seen with

normal aging (Cookson, 2009). This is illustrated in the graph below, which shows the decline of dopaminergic neurons during normal aging, in idiopathic PD, in PD caused by environmental or genetic factors, and in early-onset PD.



As less and less dopamine is produced by the neurons affected by Parkinson's disease, far less dopamine is available to bind to the dopamine receptors on the post-synaptic membrane

ALZHEIMER'S DISEASE

Definition: **Alzheimer's disease** is a progressive, degenerative **disorder** that attacks the brain's nerve cells, or neurons, resulting in loss of memory, thinking and language skills, and behavioral changes.

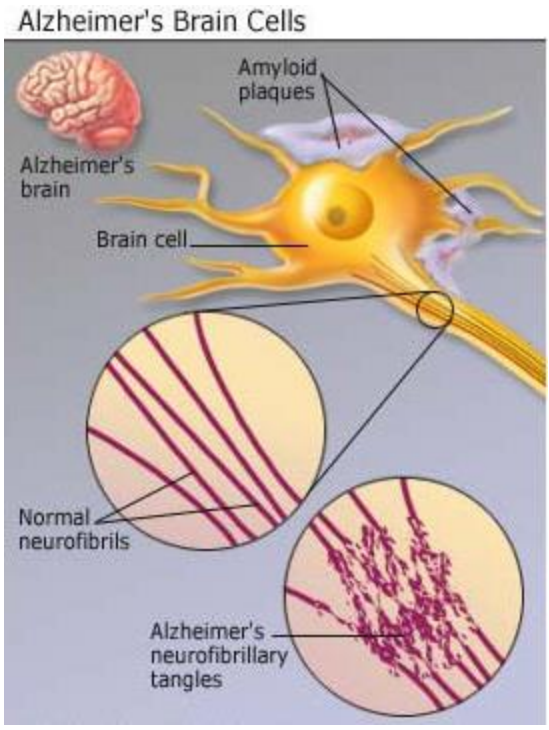
The disease makes brain tissue break down over time. It usually happens to people over age 65.

A person can live with Alzheimer's disease for just a few years or for a few decades. More often, however, people live with it for about 9 years. About 1 in 8 people age 65 and over has the disease. Women are more likely to have it than men.

What Causes Alzheimer's disease?

People who get Alzheimer's disease are usually older, but the disease isn't a normal part of aging. Scientists aren't sure why some people get it and others don't. But they do know that the symptoms it causes seem to come from two main types of nerve damage:

- Nerve cells get tangles, called neurofibrillary tangles.
- Protein deposits called beta-amyloid plaques build up in the brain.



The causes could be a protein in blood called ApoE (for apolipoprotein E), which the body uses to move cholesterol in the blood.

There are a few types of ApoE that may be linked to a higher risk of Alzheimer's. It could be that certain forms of it cause brain damage. Some scientists think it plays a role in building the plaques in the brains of people with Alzheimer’s.

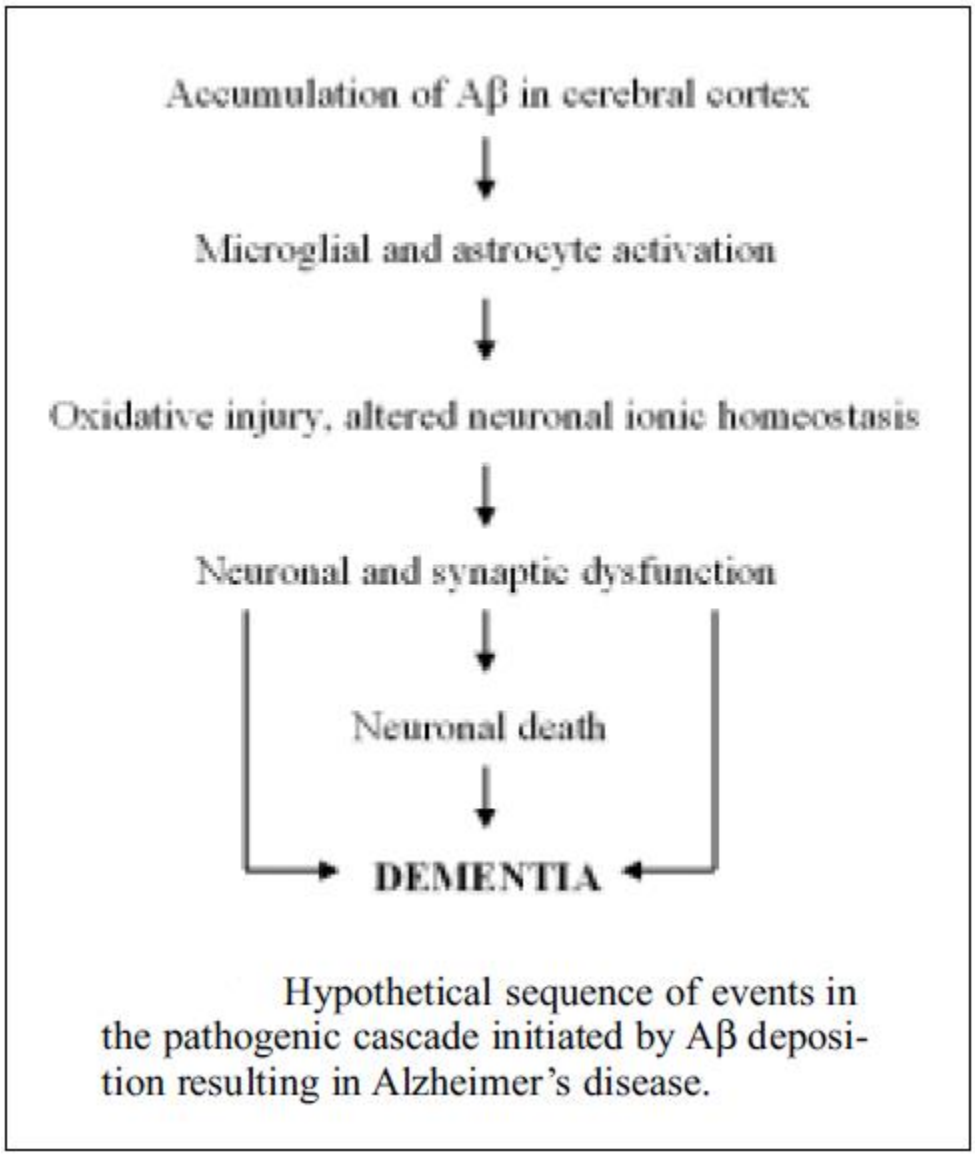
Whether or not ApoE partly causes Alzheimer's, genes almost certainly play a role in the disease. Someone with a parent who had the disease is more likely to have it, too.

There is some evidence that people with high blood pressure and high cholesterol have a greater chance of getting Alzheimer's. More rarely, head injuries may be a reason, too -- the more severe they are, the greater the risk of Alzheimer's later in life.

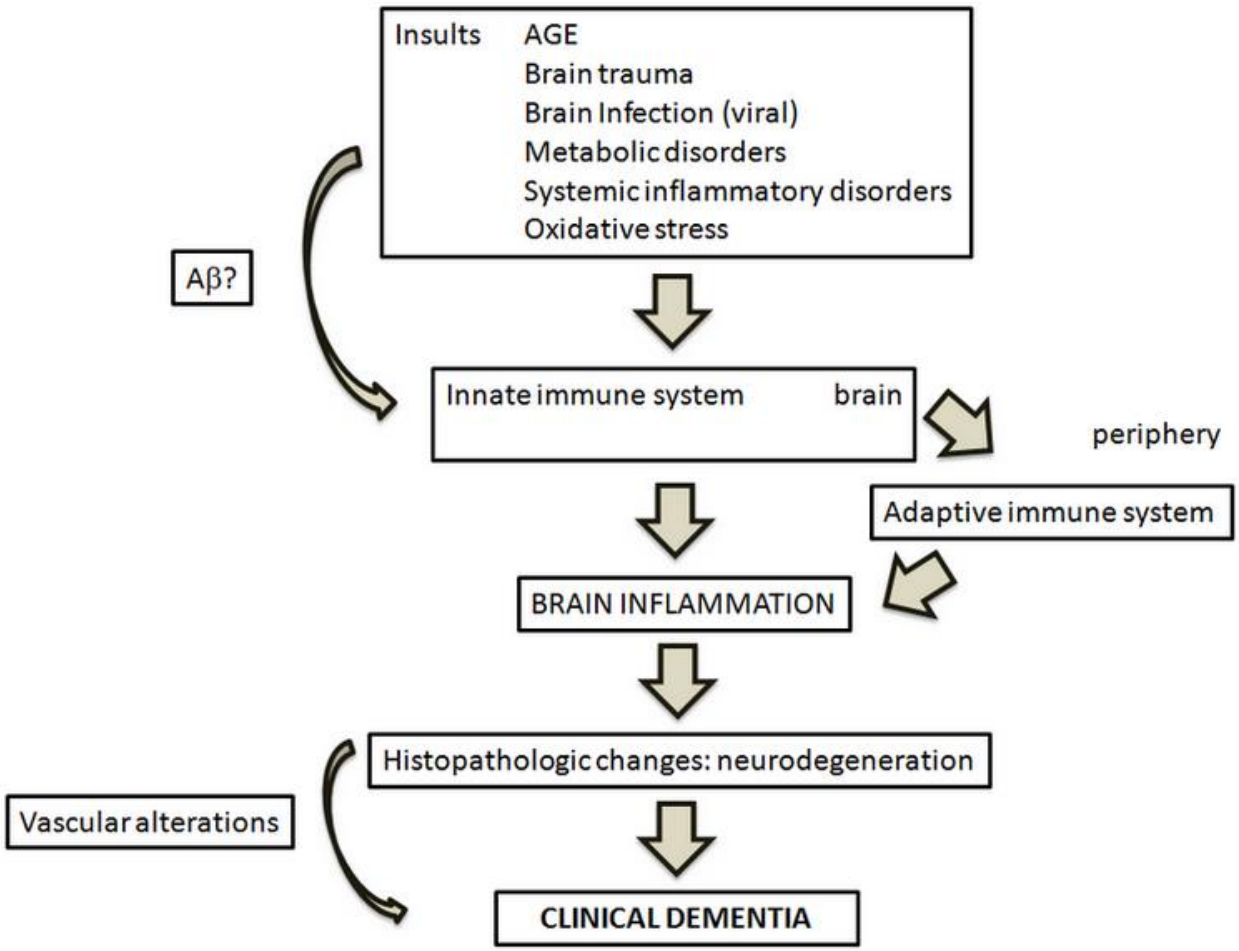
Pathophysiology of Alzheimer’s disease

Alzheimer’s disease (AD) is a progressive dementia with loss of neurons and the presence of two main microscopic neuropathological hallmarks: extracellular amyloid plaques and intracellular neurofibrillary tangles • Early onset AD, the rare familial form, is the result of a mutation in one of three genes: (amyloid precursor protein), (, presenilin 1) or (, presenilin 2). The sporadic form occurs usually after 65 years of age and accounts for most cases; it most likely results from a combination of genetic and environmental influences • The only confirmed risk factors for sporadic AD are age and the presence of the E4 allele of (apolipoprotein E) • Amyloid plaques

comprise mainly of the neurotoxic peptide amyloid (Aβ, Abeta), cleaved sequentially from a larger precursor protein (APP) by two enzymes: β-secretase (also called BACE1) and γ-secretase (comprising four proteins, one of which is presenilin). If APP is first cleaved by the enzyme α-secretase rather than β-secretase then Aβ is not formed • Neurofibrillary tangles comprise mainly of the protein tau which binds microtubules, thereby facilitating the neuronal transport system. Uncoupling of tau from microtubules and aggregation into tangles inhibits transport and results in microtubule disassembly. Phosphorylation of tau may play an important role in this • Selective vulnerability of neuronal systems such as the cholinergic, serotonergic, noradrenergic and glutamatergic systems form the basis of current rational pharmacological treatment



Hypothetical sequence of events in the pathogenic cascade initiated by Aβ deposition resulting in Alzheimer's disease.



The term kidney disease refers to any disease, disorder, or condition that affects the kidneys. Here is a list of different types of kidney diseases.

- Alport Syndrome - A genetic disorder that affects the young men and causes damage to the blood vessels in the kidney and profound hearing loss
- Diabetic Nephropathy – damage to or disease of the kidney
- Fabry Disease – A rare inherited disorder where GL3 or globotriasycleramide accumulates in the blood vessels causing damage to the kidney as well as heart and brain
- Focal Segmental Glomerulosclerosis - scarring of the glomeruli, the kidney's tiny blood vessels
- Glomerulonephritis – an inflammation of the glomeruli, the tiny filtering units of the kidney
- IgA Nephropathy (Berger's Disease) – a disease characterized by the build up of proteins IgA within the kidney leading to the inflammation of glomeruli known as berger's disease

- Kidney Stones - A solid concretion, varying in size and shape, formed in the kidneys from minerals in the urine; stones composed of calcium are the most common. A stone may stay in the kidney or pass out in the urine stream, often without notice. If a stone is large enough, it can block the flow of urine, causing great pain; a stone that obstructs the flow for a long period of time can cause damage to the kidney. A stone with jagged edges can cause scarring of the kidney.
- Minimal Change Disease - Also known as MCG, this disease is the number one cause of Nephrotic Syndrome in children; although the kidney's glomeruli do not appear scarred or changed, protein nevertheless leaks into the urine

- Nephrotic Syndrome – A nonspecific disorder that occurs when the kidney's glomeruli are damaged, causing leakage of protein into the urine and edema. The kidney ailments MCG and FSGS are causes of this syndrome. The term MCG or Minimal Change Disease is often used interchangeably with Nephrotic Syndrome.

- Polycystic Kidney Disease or PKD - Also known as PKD or PCKD, an inherited disease in which the kidneys develop many cysts and become enlarged. There are two forms of PKD – Autosomal Dominant PKD (ADPKD), in which one inherited gene causes the disease, usually affecting adults later in life, but sometimes affecting children as well; and the rarer form known as Autosomal Recessive PKD (ARPKD), in which two copies of the abnormal gene are present. ARPKD is a very serious illness that affects babies and children.

What is diabetes insipidus?

Diabetes insipidus (DI) is a rare disease that causes frequent urination. The large volume of urine is diluted, mostly water. To make up for lost water, a person with DI may feel the need to drink large amounts and is likely to urinate frequently, even at night, which can disrupt sleep and, on occasion, cause bedwetting. Because of the excretion of abnormally large volumes of dilute urine, people with DI may quickly become dehydrated if they do not drink enough water. Children with DI may be irritable or listless and may have fever, vomiting, or diarrhea. Milder forms of DI can be managed by drinking enough water, usually between 2 and 2.5 liters a day.

What is the difference between diabetes insipidus and diabetes mellitus?

DI should not be confused with diabetes mellitus (DM), which results from insulin deficiency or resistance leading to high blood glucose, also called blood sugar. DI and DM are unrelated, although they can have similar signs and symptoms, like excessive thirst and excessive urination.

Glomerular filtration rate is a test used to check how well the kidneys are working. Specifically, it estimates how much blood passes through the tiny filters in the kidneys each minute.

Osteoporosis is a progressive bone disease that is characterized by a decrease in bone mass and density which can lead to an increased risk of fracture. In osteoporosis, the bone mineral density (BMD) is reduced, bone microarchitecture deteriorates, and the amount and variety of proteins in bone are altered. Osteoporosis itself has no symptoms; its main consequence is the increased risk of bone fractures. Osteoporotic fractures occur in situations where healthy people would not normally break a bone; they are therefore regarded as fragility fractures. Typical fragility fractures occur in the vertebral column, rib, hip and wrist.

Osteomalacia is the softening of the bones caused by defective bone mineralization secondary to inadequate amounts of available phosphorus and calcium, or because of overactive resorption of calcium from the bone as a result of hyperparathyroidism (which causes hypercalcemia). Osteomalacia in children is known as rickets, and because of this, use of the term *osteomalacia* is often restricted to the milder, adult form of the disease. It may show signs as diffuse body pains, muscle weakness, and fragility of the bones. The most common cause of the disease is a deficiency in vitamin D, which is normally obtained from the diet and/or from sunlight exposure.

Periosteum is a membrane that covers the outer surface of all bones, except at the joints of long bones. Endosteum lines the inner surface of all bones. Periosteum consists of dense irregular connective tissue. Periosteum is divided into an outer "fibrous layer" and inner "osteogenic layer". The fibrous layer contains fibroblasts, while the cambium layer contains progenitor cells that develop into osteoblasts. These osteoblasts are responsible for increasing the width of a long bone and the overall size of the other bone types. After a bone fracture the progenitor cells develop into osteoblasts and chondroblasts, which are essential to the healing process.

Cartilage is a flexible connective tissue found in many areas in the bodies of humans and other animals, including the joints between bones, the rib cage, the ear, the nose, the bronchial tubes and the intervertebral discs. It is not as hard and rigid as bone but is stiffer and less flexible than muscle. Cartilage is composed of specialized cells called chondrocytes that produce a large amount of extracellular matrix composed of collagen fibers, abundant ground substance rich inproteoglycan, and elastin fibers. Cartilage is classified in three types, *elastic cartilage*, *hyaline cartilage* and *fibrocartilage.*

Lithotripsy is a medical procedure involving the physical destruction of hardened masses like kidney stones, gallstones. The term is derived from the Greek words meaning "breaking (or pulverizing) stones". Lithotripsy is a medical procedure used to treat kidney stones. It may also be used to treat stones in other organs, such as the gall bladder or the liver. Kidney stones are collections of solid minerals that sometimes form in the kidneys. Healthy kidneys do not have these stone-like formations. Most stones pass out of the body naturally during urination.
Stones may consist of small, sharp-edged crystals, or smoother, heavier formations that resemble polished river rocks. Sometimes these larger formations do not pass in the urine. These stones can cause kidney damage. People with kidney stones may experience bleeding, pain, or urinary tract infections. When stones begin to cause these types of problems, your doctor may suggest lithotripsy in order to break up the stones.

SKIN DISORDERS

Psoriasis is a long-lasting autoimmune disease which is characterized by patches of abnormal skin. These skin patches are typically red, itchy, and scaly. They may vary in severity from small and localized to complete body coverage. Injury to the skin can trigger psoriatic skin changes at that spot, which is known as the Koebner phenomenon.

There are five main types of psoriasis: plaque, guttate, inverse, pustular, and erythrodermic. Plaque psoriasis, also known as psoriasis vulgaris, makes up about 90% of cases. It typically presents with red patches with white scales on top. Areas of the body most commonly affected are the back of the forearms, shins, around the navel, and the scalp. Guttate psoriasis has drop-shaped lesions. Pustular psoriasis presents with small non-infectious pus-filled blisters. Inverse psoriasis forms red patches in skin folds. Erythrodermic psoriasis occurs when the rash becomes very widespread, and can develop from any of the other types. Fingernails and toenails are affected in most people at some point in time. This may include pits in the nails or changes in nail color.

Psoriasis is generally thought to be a genetic disease which is triggered by environmental factors. In twin studies, identical twins are three times more likely to both be affected compared to non-identical twins; this suggests that genetic factors predispose to psoriasis. Symptoms often worsen during winter and with certain medications such as beta blockers or NSAIDs. Infections and psychological stress may also play a role. Psoriasis is not contagious. The underlying mechanism involves the immune system reacting to skin cells. Diagnosis is typically based on the signs and symptoms.

There is no cure for psoriasis. However, various treatments can help control the symptoms. These treatments may include steroid creams, vitamin D3 cream, ultraviolet light, and immune system suppressing medications such as methotrexate. About 75% of cases can be managed with creams alone. The disease affects 2–4% of the population. Men and women are affected with equal frequency. The disease may begin at any age. Psoriasis is associated with an increased risk of psoriatic arthritis, lymphomas, cardiovascular disease, Crohn's disease, and depression. Psoriatic arthritis affects up to 30% of individuals with psoriasis