# AUTOIMMUNE DISEASE

**Definition:** A disease in which the body produces antibodies that attack its own tissues, leading to the deterioration and in some cases to the destruction of such tissue.

An autoimmune disease develops when our immune system, which defends our body against disease, decides your healthy cells are foreign. As a result, your immune system attacks healthy cells. Depending on the type, an autoimmune disease can affect one or many different types of body tissue. It can also cause abnormal organ growth and changes in organ function.

There are as many as 80 types of autoimmune diseases. Many of them have similar symptoms, which makes them very difficult to diagnose. It's also possible to have more than one at the same time. Autoimmune diseases usually fluctuate between periods of remission (little or no symptoms) and flare-ups (worsening symptoms). Currently, treatment for autoimmune diseases focuses on relieving symptoms because there is no curative therapy.

Autoimmune diseases often run in families, and 75 percent of those affected are women.

**Most Common Autoimmune Diseases**

The following are some of the more common autoimmune diseases:

- rheumatoid arthritis: inflammation of joints and surrounding tissues
- systemic lupus erythematosus: affects skin, joints, kidneys, brain, and other organs
- pernicious anemia: decrease in red blood cells caused by inability to absorb vitamin B-12
- vitiligo: white patches on the skin caused by loss of pigment
- scleroderma: a connective tissue disease that causes changes in skin, blood vessels, muscles, and internal organs
- psoriasis: a skin condition that causes redness and irritation as well as thick, flaky, silver-white patches
- inflammatory bowel diseases: a group of inflammatory diseases of the colon and small intestine
- Hashimoto's disease: inflammation of the thyroid gland
- Graves' disease: overactive thyroid gland
- type 1 diabetes: destruction of insulin producing cells in the pancreas

**Causes**

The cause of autoimmune disease is unknown. There are many theories about what triggers autoimmune diseases, including:

- bacteria or virus
- drugs
- chemical irritants
- environmental irritants

**Symptoms of an Autoimmune Disease**

The symptoms vary most common symptoms are fatigue, fever, and general malaise (feeling ill). Autoimmune diseases affect many parts of the body. The most common organs and tissue affected are:

- joints
- muscles
- skin
- red blood cells
- blood vessels
- connective tissue
- endocrine glands

**Disease diagnosis**

Ordinarily, your immune system produces antibodies against harmful invaders in your body. These invaders include:

- viruses
- bacteria
- parasites
- fungi

When you have an autoimmune disease, your body produces antibodies against some of your own tissues. Diagnosing an autoimmune disease involves identifying the antibodies your body is producing.

The following tests are used to diagnose an autoimmune disease:

- autoantibody tests: any of several tests that look for specific antibodies to your own tissues
- antinuclear antibody tests: a type of autoantibody test that looks for antinuclear antibodies, which attack the nuclei of cells in your body
- complete blood count: measures the numbers of red and white cells in your blood; when your immune system is actively fighting something, these numbers will vary from the normal
- C-reactive protein (CRP): elevated CRP is an indication of inflammation throughout your body
- erythrocyte sedimentation rate: this test indirectly measures how much inflammation is in your body

**Treatment**

Autoimmune diseases are chronic conditions with no cure. Treatment involves attempts to control the process of the disease and to decrease the symptoms, especially during flare-ups. The following is a list of things you can do to alleviate the symptoms of an autoimmune disease:

- eat a balanced and healthy diet
- exercise regularly
- get plenty of rest
- take vitamin supplements
- decrease stress
- limit sun exposure

Medical interventions include:

- hormone replacement therapy
- blood transfusions
- anti-inflammatory medication
- pain medication
- immunosuppressive medication
- physical therapy

**Rheumatoid Arthritis**

An autoimmune disease is one in which the body's immune system mistakenly attacks normal cells. In autoimmune arthritis, which includes rheumatoid arthritis (RA), the immune system attacks the lining of the joints. This leads to inflammation that can affect the entire body.

Symptoms vary greatly from person to person, as does the rate of progression. While there's no cure for this chronic condition, there are a variety of treatments that can help improve your quality of life.

likelihood of developing RA can be affected by risk factors such as:

- **gender:** women develop RA at a higher rate than men
- **age**: RA can develop at any age, but most people begin to notice symptoms between the ages of 49 and 60 years
- **family history**: you're at increased risk of having RA if other family members have it

- smoking: cigarette smoking can increase your chances of developing RA; quitting can lower your risk

**Symptoms**

Symptoms generally begin slowly and can come and go. Joint pain and inflammation affect both sides of the body equally, and can be marked by these signs:

- deformed joints
- hard bumps of tissue under the skin on your arms (nodules)
- reduced range of motion
- dry mouth
- difficulty sleeping, fatigue
- weight loss
- eye inflammation, dry eyes, itchy eyes, eye discharge
- fever
- anemia
- chest pain when you breathe

**Diagnosis**

Autoimmune diseases tend to share symptoms with other conditions, so diagnosis can be difficult, particularly in the early stages. There's no one test that can specifically diagnose RA. Instead, diagnosis involves clinical examination, patient-reported symptoms, and medical tests, including:

- rheumatoid factor test
- anti-cyclic citrullinated peptide antibody test
- blood count
- erythrocyte sedimentation rate and/or c-reactive protein
- X-rays, ultrasound, MRI

You can help with diagnosis by giving your doctor your complete medical history and keeping a record of symptoms. Don't hesitate to seek a second opinion from a specialist (rheumatologist).

**Systemic lupus erythematosus (SLE)**

Systemic lupus erythematosus (SLE) is an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue. It can affect the skin, joints, kidneys, brain, and other organs.

**Causes**

The underlying cause of autoimmune diseases is not fully known.

SLE is much more common in women than men. It may occur at any age, but appears most often in people between the ages of 10 and 50. African Americans and Asians are affected more often than people from other races.

SLE may also be caused by certain drugs.

**Symptoms**

Symptoms vary from person to person, and may come and go. Almost everyone with SLE has joint pain and swelling. Some develop arthritis. The joints of the fingers, hands, wrists, and knees are often affected.

Other common symptoms include:

- Chest pain when taking a deep breath

- Fatigue
- Fever with no other cause
- General discomfort, uneasiness, or ill feeling (malaise)
- Hair loss
- Mouth sores
- Sensitivity to sunlight
- Skin rash. A "butterfly" rash in about half people with SLE. The rash is most often seen over the cheeks and bridge of the nose, but can be widespread. It gets worse in sunlight.
- Swollen lymph nodes

Other symptoms depend on which part of the body is affected:

- Brain and nervous system: headaches, numbness, tingling, seizures, vision problems, personality changes
- Digestive tract: abdominal pain, nausea, and vomiting
- Heart: abnormal heart rhythms (arrhythmias)
- Lung: coughing up blood and difficulty breathing
- Skin: patchy skin color, fingers that change color when cold (Raynaud phenomenon)
- Kidney: swelling in the legs, weight gain

Some people have only skin symptoms. This is called discoid lupus.

**Exams and Tests**

To be diagnosed with lupus, you must have 4 out of 11 common signs of the disease. Nearly all people with lupus have a positive test for antinuclear antibody (ANA). However, having a positive ANA alone does not mean you have lupus in most cases.

The health care provider will do a physical exam and listen to your chest. An abnormal sound called a heart friction rub or pleural friction rub may be heard. A nervous system exam will also be done.

Tests used to diagnose SLE may include:

- Antinuclear antibody (ANA)
- CBC with differential
- Chest x-ray
- Serum creatinine
- Urinalysis

**Treatment**

There is no cure for SLE. The goal of treatment is to control symptoms. Severe symptoms that involve the heart, lungs, kidneys, and other organs often need treatment from specialists.

Mild forms of the disease may be treated with:

- NSAIDs for joint symptoms and pleurisy (Talk to your provider before taking these drugs.),
- Low doses of corticosteroids such as prednisone
- Corticosteroid creams for skin rashes
- A drug also used to treat malaria (hydroxychloroquine) and low-dose corticosteroids for skin and arthritis symptoms
- A biologic drug named belimumab may be helpful in some people.

## Severe Combined Immune Deficiency (SCID)

Severe Combined Immune Deficiency (SCID, pronounced "skid") is a potentially fatal primary immunodeficiency in which there is combined absence of T-lymphocyte and B-lymphocyte function. There are at least 13 different genetic defects that can cause SCID. These defects lead to extreme susceptibility to very serious infections. This condition is generally considered to be the most serious of the primary immunodeficiencies.

### Definition of SCID

SCID is a rare, potentially fatal syndrome of diverse genetic causes in which there is combined absence of T-lymphocyte and B-lymphocyte function.

### Deficiency of the Common Gamma Chain of the T-Cell Receptor (X-SCID)

The most common form of SCID, affecting nearly 45% of all cases, is due to a mutation in a gene on the X chromosome that encodes a component shared by the T-cell growth factor receptor and other growth factor receptors. This component is referred to as γc, for common gamma chain. Mutations in this gene result in very low T-lymphocyte and NK-lymphocyte counts, but the B-lymphocyte count is high. Despite the high number of B-lymphocytes, there is no B-lymphocyte function since the B-cells have abnormal receptors for growth factors on their cell surfaces.

This deficiency is inherited as an X-linked recessive trait. Only males have this type of SCID, but females may carry the gene and have a 1 in 2 chance (50%) of passing it on to each son as well as a 1 in 2 chance of passing the carrier state on to each daughter.

### Adenosine Deaminase Deficiency

Another type of SCID is caused by mutations in a gene that encodes an enzyme called adenosine deaminase (ADA). ADA is essential for the metabolic function of a variety of body cells but especially T-cells. The absence of this enzyme leads to an accumulation of toxic metabolic by-products within lymphocytes that cause the cells to die. ADA deficiency is the second most common cause of SCID, accounting for 15% of cases. Babies with this type of SCID have the lowest total lymphocyte counts of all, and T, B and NK-lymphocyte counts are all very low. This form of SCID is inherited as an autosomal recessive trait. Both boys and girls can be affected. Lack of the ADA enzyme also leads to neurological problems such as cognitive impairment, hearing and visual impairment, and low muscle tone and movement disorders. The neurological problems are not fully curable by bone marrow transplantation.

### Deficiency of the Alpha Chain of the IL-7 Receptor

Another form of SCID is due to mutations in a gene that encodes another growth factor receptor component, the alpha chain of the IL-7 receptor (IL-7Rα). When T, B and NK-cell counts are done, infants with this type have B- and NK-cells, but no T-cells. However, the B-cells do not work because of the lack of T-cells. IL-7Rα deficiency is the third most common cause of SCID accounting for 11% of SCID cases. It is inherited as an autosomal recessive trait. Both boys and girls can be affected.

### Deficiency of Janus Kinase 3

Another type of SCID is caused by a mutation in a gene that encodes an enzyme found in lymphocytes called Janus kinase 3 (Jak3). This enzyme is necessary for function of the above-mentioned γc. Thus, when T, B and NK-lymphocyte counts are done, infants with this type look

very similar to those with X-linked SCID. Snce this form of SCID is inherited as an autosomal recessive trait both boys and girls can be affected. Jak3 deficiency accounts for less than 10% of cases of SCID.

**Other Causes of SCID**

Five more types of SCID for which the molecular cause is known are those due to mutations in genes that encode proteins necessary for the development of the immune recognition receptors on T- and B-lymphocytes. These are: recombinase activating genes 1 and 2 (RAG1 and RAG2) deficiency, Artemis deficiency, Cernunnos deficiency, and Ligase 4 deficiency. Infants with these types of SCID lack T- and B-lymphocytes but have NK-lymphocytes. These deficiencies are all inherited as autosomal recessive traits.

**Treatment of SCID**

Until definitive treatment such as stem cell transplantation, the infant with SCID needs to be isolated from children outside the family, especially from young children. If there are siblings who attend daycare, religious school, kindergarten or grade school, the possibility of bringing infectious illnesses into the home represents the greatest danger.

Fortunately, effective treatments, such as stem cell transplantation, exist that can cure the disorder. The future holds the promise of gene therapy for several more types of SCID.

## UNIT –V GENETIC DISORDER

A **genetic disorder** is a **disease** caused by one or more abnormalities in the genome, especially a condition that is present from birth (congenital). Most **genetic disorders** are quite rare and affect one person in every several thousands or millions.

Types of genetic disorder

The following are the different types of genetic diseases:

Chromosomal abnormalities

Single gene defects

Multifactorial problems

**Chromosomal abnormalities**

Chromosomal abnormalities in the baby may be inherited from the parent or may occur with no family history. The following chromosomal problems are the most common:

- **Aneuploidy.** More or fewer chromosomes than the normal number, including:
  - **Down syndrome (trisomy 21).** Cells contain three #21 chromosomes.
  - **Turner syndrome.** One of the two sex chromosomes is not transferred, leaving a single X chromosome, or 45 total.
- **Deletion.** Part of a chromosome is missing, or part of the DNA code is missing.

- **Inversion.** When a chromosome breaks and the piece of the chromosome turns upside down and reattaches itself. Inversions may or may not cause birth defects depending on their exact structure.
- **Translocation.** A rearrangement of a chromosome segment from one location to another, either within the same chromosome or to another.
  - **Balanced translocation.** The DNA is equally exchanged between chromosomes, and none is lost or added. A parent with a balanced translocation is healthy, but he or she may be at risk for passing unbalanced chromosomes in a pregnancy.
  - **Robertsonian translocation.** A balanced translocation in which one chromosome joins the end of another.
- **Mosaicism.** The presence of two or more chromosome patterns in the cells of a person, resulting in two or more cell lines (for example, some with 46 chromosomes, others with 47).

STRUCTURAL CHROMOSOME ABNORMALITIES

The mostly seen type of the disease is the one seen once at every 500 births called balanced translocation (reciprocal or robertson translocation). If the chromosome group has normal complement of genetic knowledge, the structural re-arrangements are called balanced. Some arrangements have stability and they are conveyed without any change during cell division. To be able to accept a chromosome which is re-arranged as stabile, The chromosome have to has normal structure (only one centromere or two telomerases).

**TRANSLOCATION**

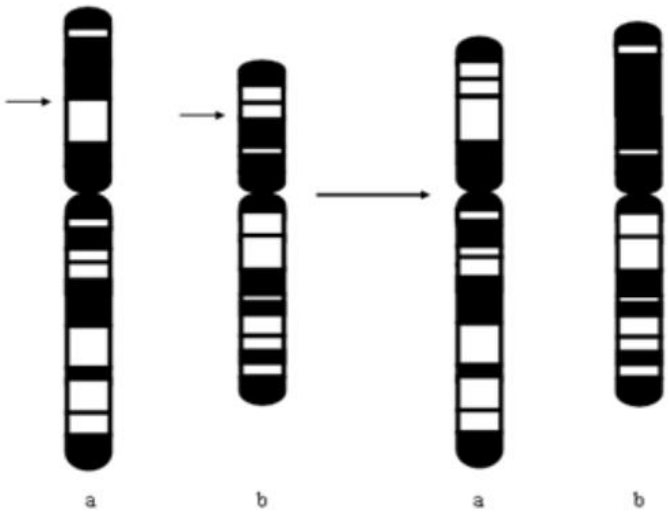
If a piece is broken off from chromosome and it locates another chromosome, a translocation event occurs. Translocations are divided into three subtitles:

- **Reciprocal translocation**
- **Rentric translocation ( robertsonian )**
- **Insertional translocation (transposition)**

**Reciprocal translocation**

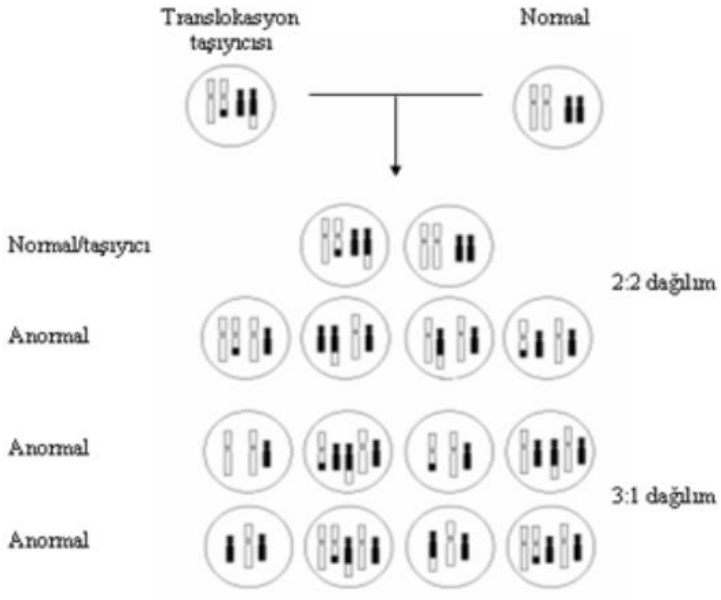
It is a break off two chromosomes and reciprocally replacements of their pieces. It is observed at the rate of 1/500.

***The mechanism of reciprocal translocations***




This rearrangement does not make a phenotype effect. But because of unbalanced gamete, at every pregnancy there is high risk (85%).

***Probable embryos at the disease carrier of reciprocal translocations***

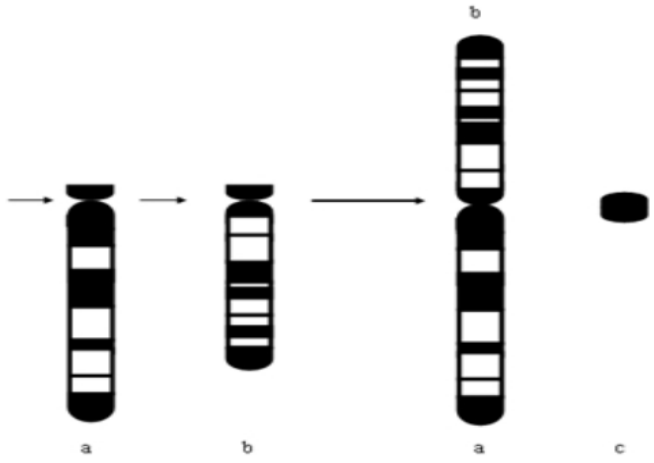



**Centric Translocation ( Robertsonian)**

That observed between two homological or non-homological 2 acrecentric chromosomes is called centric translocation. On this rearrangement long and short arms of two different

chromosomes merged with themselves. United short arms disappear and just two different long arms merged their centromeric areas are observed. These disappeared chromosome pieces of short arms do not make an effect because of having multiple copies of rRNA genes just like at acrocentric chromosomes. At this patients have 45 chromosomes. Even if there a quantitative deficiency, there is no change on genetic material.

***Robertsonian translocation mechanism***




At peoples having Robertsonian translocations, there is a high possibility to see gamete cells having unbalanced genetic structure even if it has lower percentage (66%) than that at reciprocal translocations.

***Probable embryos at Robertsonian translocations***