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A Comprehensive Review on Autoimmune Diseases

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Abstract: ***Immunity refers to the inbuilt ability of the organism to resist a particular disease or to be able to protect itself from disease causing microorganisms by preventing its development. Immune system includes WBCs which includes all the neutrophils, lymphocytes including the T-cells, the B-cells & the natural killer cells, all together make up the lymphatic system, antibodies, the spleen, the thymus, the bone marrow; our skin, mucous glands, hair, tears etc. also protect our body. By autoimmunity we understand that it is misallocated response of our immune system when it releases autoantibodies to attack the healthy cells of the body. Scientists have studied a lot about autoimmunity and its disorders. By the end of the 19th century, it was first believed that our immune system has the inability to react against its own body tissue until in 20th century the concept of "horror autotoxicus" was proposed by the German immunologist Paul Ehrlich. The autoimmune disease occurs when the immune system reacts and attacks its own cells in the body as a result of breakdown of immunologic tolerance to auto reactive immune cells. Many times, genetic as well as environmental factors are the key reason for autoimmune diseases. Many kinds of research are going through as to find out the actual cause of autoimmunity; till now no actual or exact cause is known. There are at least 80 types of autoimmune diseases recognized by our scientists; some of the commonly known autoimmune diseases are: type 1 diabetes, systemic lupus erythematosus, scleroderma, thyroiditis, multiple sclerosis, autoimmune vasculitis, rheumatoid arthritis, and many more. With unusual autoimmune diseases, diagnosis may not be done instantly; the patients may suffer years before getting diagnosed properly. Most of the diseases don't have any cure; some even need lifelong treatment to ease the symptoms. The diseases will be discussed in detail in the further sections.***
Keywords: autoimmunity, immune system, cells, disease, disorder, diabetes, arthritis, lupus, ITP

I. INTRODUCTION

A. *Overview*

Our body comprises many kind of complex mechanisms and one of the major mechanism that it exhibits is immunity. The branch of study of biology and medicine related to immunity is called immunology. Our immune system comprises of many kind of or rather a complex set of organs, cells, proteins and other various substances that prevents our body from infections. Parts of the immune system include:

1) *White Blood Cells:* Includes lymphocytes (T-cells, B-cells and natural killer cells), neutrophils, basophils, monocytes, eosinophils ; these together are also known as immune cells.
2) *Antibodies:* They recognise substances called antigen which mark the microbe to be alien, then these antibodies go for destruction.
3) *Complement System:* Includes proteins and they compliment the work done by antibodies
4) *Lymphatic System:* Includes lymph nodes which trap microbes, lymph vessels - carry the colourless fluid and the lymphocytes. Its major function is to:

a) Manage the fluid level
b) React to microbes
c) Deal with cancer cells & faulty cell products
d) Absorption of fat from our intestine

5) *Spleen:* Destroys and removes microbes and damaged red blood cells; also helps in making antibodies and lymphocytes
6) *Thymus:* Produces T-lymphocytes as well as filters and checks the blood content
7) *Bone Marrow:* Found inside the big bones, it produces the most essential cells of our body including RBCs, WBCs and platelets.

Many other defence mechanisms exhibited by our body are:

a) *Skin & Hair:* It is a waterproof barrier which secretes oil that doesn't allow the microbes to enter our body. Hair along with the skin acts as a tough barrier.

b) *Lungs:* Mucous within it (plegm) traps alien particles and little tiny hair (cilia) moves this mucous upwards so it can be coughed out

c) *Digestive Tract:* The whole lining of the digestive tract is filled with mucous which contains antibodies within and the acid in the stomach helps to kill microbes

d) *Supplementary Defences:* Saliva, and tears contain anti-microbial enzymes that significantly reduces the risk of infection.

A healthy immune system works be recognising and differentiating into body's cells and alien cells, destroying the alien harmful cells and protecting our body. Many times, defects within the immune system that cause primary immunodeficiency disease additionally leads to complications in immune functioning which is a kind of response that cannot be controlled. This can lead to autoimmunity in which the response is directed against normal healthy parts of the body such as cells, tissues, organs that produce proteins known as auto-antigens. In other words, it is when the immune system attacks the body in which it resides. Antibodies made by a normal immune system recognise and prevent alien organisms from causing infections. But in autoimmunity, the antibodies are produced against the normal cells by our confused immune system, these are the kinds known as auto-antibodies. Sometimes the auto-antibodies are harmless yet they surely imply the presence of a disease. In some other autoimmune diseases, our immune system may simply react against the body's auto-antigens. Like every other immune response, this is also focussed on some particular antigens of T-cell receptor and B-cell receptor.

B. Understanding Autoimmune Diseases

In autoimmune disease the confused immune response acts in such a way that the self antigens becomes the goal/target of the adaptive immune system instead of attacking the infections. These self antigen then may drive a method or a process which is localised on a selected organ, like the ductless- thyroid gland (Grave's disease, Hashimoto's thyroiditis) or brain (multiple sclerosis); or the other responses that may also lead to a lot of general inflammatory condition (for example- Systemic Lupus Erythematosus). Following the commencement and trafficking, a small native damage can amplify the disease. In human diseases there is a proof that a small infection leads to autoimmunity, but the initiation of the disease occur as a result of multiple infections. But in contrast to the infections, the recognised antigens are processed from proteins within the target organ; this may also lead to chronic inflammatory processes that hinders the basic functioning of the tissue. In human autoimmune diseases the trigger of this process is not found out. Apart from the infections various other environmental factors also show great influence though it may not be well defined but the are relavant.

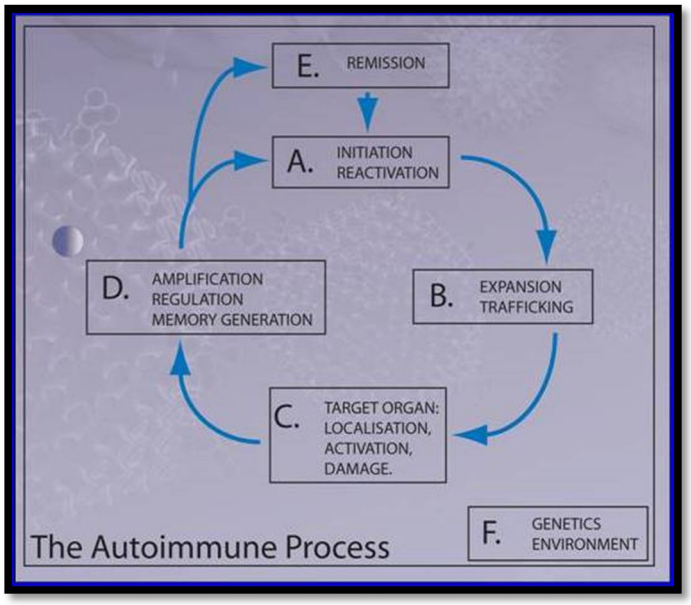

Figure 1. The Autoimmune Process

A lot of research is going on in to understand the influence of inheritance in the cause of autoimmune disease. A major study was that vulnerablity to autoimmune disease is effected by a number of polymorphic genes. Many inflammatory responses are associated with the genes that encode the proteins of these diseases, like antigen presentation, type I interferon, toll-like receptor and NF-κB signaling, B-cell and T-cell function, apoptosis, and removal of cellular debris and immune complexes. Moreover it is also found out that the same genetic modifications are often linked to different types of autoimmune diseases this suggests that there is a shared genetic pathway to lossed tolerance and for the induction of autoimmunity. An interplay of both genetic as well as environmental factors suggests the cause of autoimmunity and hence the disease occurs. Although the exact cause of the disease is unknown Most of the autoimmune diseases are chronic and last long, but many of them can be controlled with proper treatment. Sometimes the symptoms associated with these diseases may come and go but when the symptoms get worse, then that condition is known as flare-up. The complications which may come while treating the disease largely depends on the medicine, as they help to suppress the immune system which may cause side effects, which may lead to higher risk of getting infections. Also autoimmune diseases have no prevention.

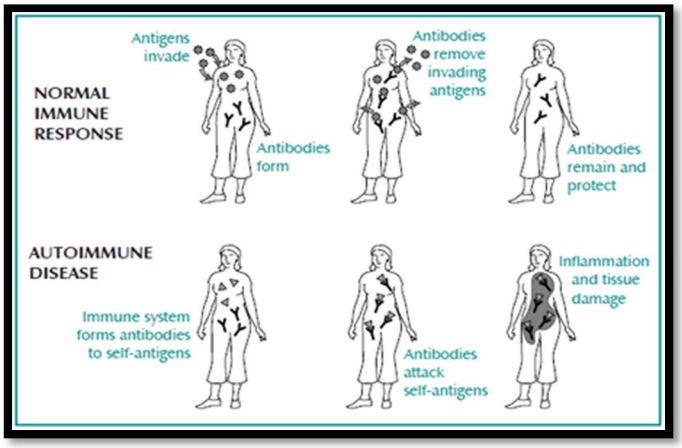

Figure 2. Normal immune system response vs. autoimmune response leading to disease

Autoimmune diseases including rheumatoid arthritis, hashimoto thyroiditis, diabetes mellitus, addison disease, celiac disease, pernacious anemia and graves' disease to name a few; are believed to effect more than one tissue or organ type. They may effect our blood vessels which may inturn result in a damage in the production of RBCs, WBCs and platelets, it may effect our connective tissues like muscles and ligaments including the joints. Skin along with endocrine glands such as thyroid and pancreas are also often effected. These effects result in disfigurement of body tissues and in the abnormal growth of the organs which changes the whole organ functioning. Even the person's appearance changes drastically. Overall, a person's life comes to a halt.

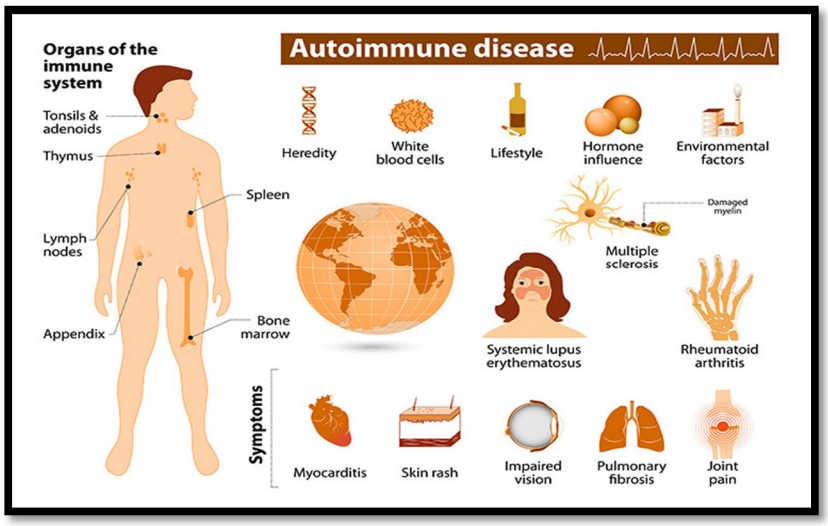

Figure 3. Autoimmune diseases: its symptoms and causes along with the organs of the immune system

A person may also have more than one autoimmune disease but their symptoms maybe somewhat similar. Though the symptoms may sometimes differ based on the type and location of the faulty immune response.

The general signs and symptoms which may tell that a person may suffer from autoimmune disease include:

- Fatigue along with malaise
- Fever
- Joint pain
- Rash

In consideration of the symptoms seen, the tests conducted by the health care provider to diagnose these diseases are:

- Antinuclear antibody tests
- Autoantibody tests
- Complete blood count (CBC)
- Comprehensive metabolic panel
- C-reactive protien (CRP)
- Erythrocyte sedimentation rate (ESR)
- Urinalysis

The main goals of the treatment are:

- Controlling the autoimmune mechanism
- Maintenance of the body's inbuilt ability to fight infections
- Overall reduction of he symptoms

Types of treatments used to cure such diseases include:

- Providing with the deficient supplements that body needs while dealing with the disease like thyroid hormone, vitamin B complex, or insulin. Medications are included too which may increase the production of these supplements in the body naturally
- Surgery to remove a damaged tissue or organ like splenectomy
- Blood transfusion if blood is affected
- If the connectives like the joints, muscles and even bones are effected which hinders with the patient' ability to move then physiotherapy is suggested to assist with the movement.

Most of the patients prefer drugs (immunosuppressive medicines) to reduce the abnormal response of the immune system. These medicines include steroids such as - prednisone and non-steroid drugs such as - azathioprine, cyclophosphamide, mycophenolate, sirolimus, or tacrolimus. Targeted drugs such as tumor necrosis factor (TNF) blockers and Interleukin inhibitors can also be used as medicines for some diseases.

II. REVIEW OF LITERATURE

A. History of Autoimmunity

The discovery or the knowledge of autoimmunity infact of immunology as a whole dates back to the 1900s because in the late 19th century everyone believed that the immune system is simply unable to attack its own cells until in the 20th when Ehrlich brought up the term "horror autotoxicus", then interpreted as 'autoimmunity cannot happen'. He then re-adjusted the previous theories and finally recognized the tissue attacks because of autoimmunity. In 1904, the nature of the antibody autohemolysin was described and confirmed, but still autoimmunization was not stated as the main cause of the disease hemoglobinuria. Years 1915-1945 was of total eclipse yet the researches were going on related to many organs in our body including the brain, the kidney, the lungs and many others. In 1945, when the theoretical concept was appearing feasible after taking concepts from several research undertakings: the use of adjuvants; the Coombes anti-globulin reaction; the Waaler-Rose rheumatoid factor; Hargraves' LE cell; the Witebsky-Rose experimental induction of thyroiditis with autologous thyroid gland, and others; this was marked as the 'awakening' period. By the starting of the 1960s resistance to the concept of autoimmunization had weakened, due to the publishing of a monograph on autoimmune disease in 1963, and by the 1965 the consensus published reached at a larger international conference. Thus by 1965 the conspectus arbitrary completes and from then the research on autoimmunity and on autoimmunization is constantly going on and hence different types of autoimmune diseases are getting discovered along with their different factors and causes.

B. What Causes Autoimmune Diseases?

As we all know that when our immune system confuses and begins to attack the normal cells and body's own tissues and organs, it results in serious complications known as autoimmune diseases. But what actually triggers our immune system to act like this? There are many theories and many researches going on to find out its actual cause as till now the exact cause is unknown. Many theories suggest that this immune system malfunctioning happens because of many genetic and environmental factors. Prolonged use of some drugs may trigger our immune system and may cause autoimmune disorders. Many times, its seen that virus and bacterias and drugs can also trigger some changes in the body and may confuse our immune system to work properly. As the scientists first efforts were to find out about the triggering factors, it lead them to study the animal models and in some of them it clearly showed that the infections might also trigger autoimmune diseases; as in the instance of Coxsackie B4 virus in diabetes mellitus and encephalomyocarditis virus in autoimmune myositis. In these two models the virus is considered to work on increasing immunogenicity of autoantigen subordinate to local inflammation.

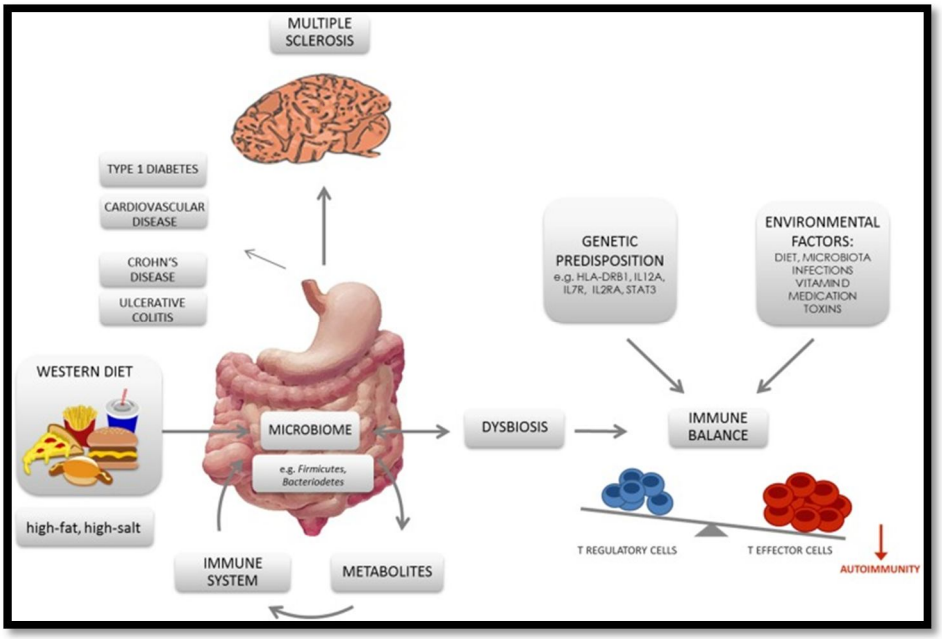

Figure 4. Schematic diagram displaying the nexus between 'Western diet', gut microbiota, T cells, and autoimmunity

It is believed that genes play an important role in determining the risk of acquiring autoimmune disease. Many times people are born with certain genes that may increase their risk of having some particular disease. Sometimes, having a close relative with an autoimmune disease also increases the chances. However, they account for only a fraction of chance. Familial predisposition of having RA and SLE is usually identified like in a family the mother may have RA but her child may have SLE. Hence genetic factor play a major role. Environmental and lifestyle factors like stress, infections, climate, occupation, pollution, chemical irritants have a huge effect as studies shows that people living in the urban environment as more susceptible to be effected by these factors therefore, are also susceptible to having the disease. The 'Western diet' as we say or the diet containing high amout of sugar, fat and having processed food is thought to be linked to inflammation and hence may increase the risk of developing the disease. Alcoholism and cigarette smoking is a major factor contributing to a person's weak health.

C. Types of Autoimmune Diseases

Many of the clinicians tend to divide the autoimmune diseases in two categories – systemic (as in systemic lupus erythomatosus) and organ-specific (as in pernacious anemia). This classification is helpful to the medical professionals but it doesn't distinguish or tells about the causative differences among the diseases. A helpful division distinguishes among diseases during which there's an overall alteration within the selection, regulation and killing process of the T-cells or the B-cells and the individuals during which the response is anomalous to a specific antigen, self or foreign, causes autoimmunity. This classification is beneficial for the medical professionals on deciding the therapy to be carried out, which may contrast according to the pathogenic mechanism.

Though this kind of mechanistic clasification is usually used for animal models, we often are not able to determine whether the disease in human body arises either because of an overall abnormality in the functioning of the lymphocyte or due to an antigen-specific abnormality. Organ-specific autoimmune diseases are those diseases in which a particular tissue or an organ is targeted by the individual's system. Examples include: the thyroid gland in patients with Grave's disease, the beta cells of the endocrine pancreas in patients with type 1 diabetes, or the skin in patients with vitiligo. Whereas in systemic autoimmune diseases the autoantigens can be found in almost any type of cell in the body. For example: the DNA protein complexes. Subsequently, many different tissues and organs are involved in the pathalogical damage.

Table 1. Human systemic autoimmune diseases

Autoimmune disease	Self-antigens	Cause of autoimmunity
1. Systemic lupus erythomatosus (SLE)	DNA, nuclear proteins, cytoplasmic proteins, RBCs & platelet membranes	Autoantibodies, Immune complexes
2. Rheumatoid arthritis	Joints	Autoantibodies, Immune complexes
3. Scleroderma	Heart, lungs, kidneys, gastrointestinal tract	Autoantibodies
4. Sjögren syndrome	Salivary gland, liver, kidney, thyroid	Autoantibodies
5. Multiple sclerosis	Brain	Autoantibodies, T-cells

Table 2. Human organ-specific autoimmune diseases

Autoimmune disease	Affected organ	Self-antigen	Cause of autoimmunity	Effect of autoimmune response
1. Autoimmune hemolytic anemia	RBCs	RBC membrane proteins	Autoantibodies	Hemolysis
2. Pernacious anemia	RBCs	a)Intrinsic factor in gastric secretions b)Gastric parietal cells	Autoantibodies	Interfere with absorption of vitamin B_{12} (anemia)
3. Idiopathic thrombocytopenic purpura	Platelets	Platelet membrane proteins	Autoantibodies	Platelet destruction
4. Goodpasture's syndrome	Kidney & Lung	Basement membrane antigens of kidney and lung	Autoantibodies	Damage of the basement membrane of kidney and lungs
5. Bullous pemphigoid	Skin	Basement membrane zone of skin	Autoantibodies	Tense blister formation
6. Pemphigous vulgaris	Skin	Desmoglin-3	Autoantibodies	Blister formation in the mucous membrane
7. Hashimoto's thyroiditis	Thyroid	Thyroid protein and thyroid cells	T-cells, Autoantibodies	Destruction of thyroid (hypothyroidism)
8. Insulin dependent diabetes mellitus (IDDM)	Pancreas	Beta-cells of islets of Langherhans in pancreas	T-cells, Autoantibodies	Destruction of beta cells (diabetes)
9. Grave's disease	Thyroid	Thyroid-stimulating hormone receptors	Autoantibodies	Stimulates thyroid (hyperthyroidism)
10. Myasthenia gravis	Muscle	Acetylcholine receptors	Autoantibodies	Destruction and blocking of acetylcholine receptors

D. Understanding Diseases in Detail

In order to understand what are actually autoimmune diseases and how they effect our body, we shall take some examples.

1) Systemic Lupus Erythomatosus (SLE)

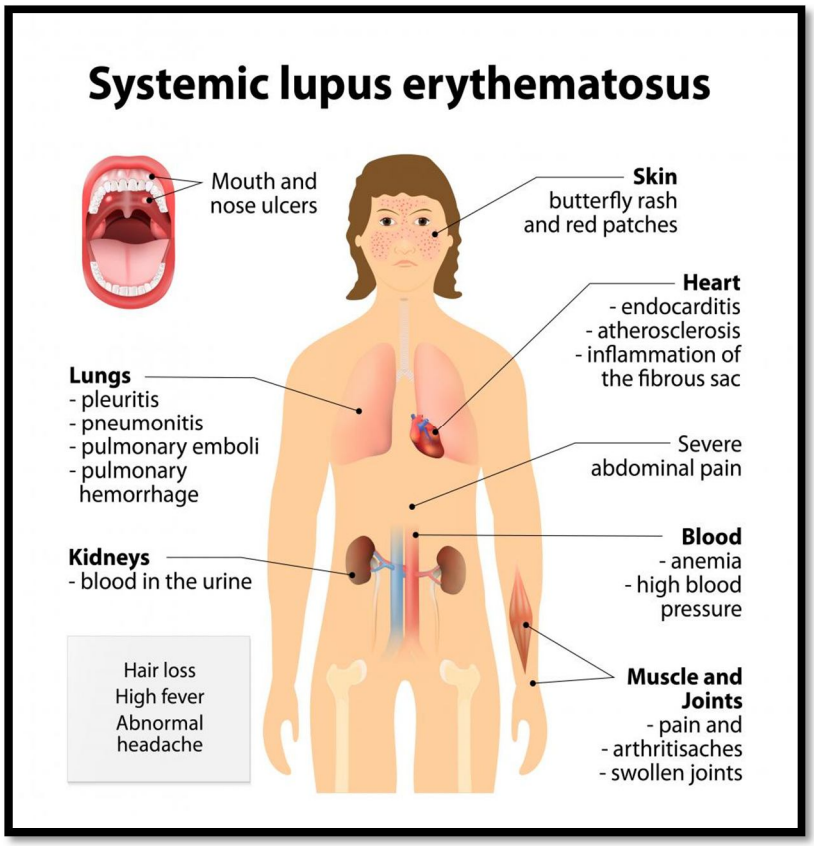

Figure 5. Symptoms of systemic lupus erythomatosus

Systemic lupus erythematosus (SLE) is honestly a heterogeneous autoimmune disease. It is not a contagious disease. The Hippocrates recorded the first known case of lupus back in the year 400 BC. It's generally a long-term condition which causes swelling and rashes (called butterfly-rashes) in the skin. There are mainly two types of lupus - Discoid lupus in which rashes appear only in some small areas of skin or it may be widespread, the second type is the SLE in which many body parts are effected. Lupus effects many different parts of the body including the internal organs and when the symptoms begin to occur in the internal parts then it is a serious case. As the internal organs of the patient are damaged then it may be life threatening too. All the symptoms associated with lupus can be seen in the figure. Mental health is also effected somewhat in which the patient may suffer from anxiety and depression.

Although the main cause of getting lupus is unclear, still it is believed genetic, hormonal and environmental factors play a major role. It doesn't pass from parents to children directly, but yes if one has a relative with lupus then the person is surely at the risk of developing it. Lupus is much more common among women than men. Women of Chinese origin, African or Caribbean origin are more likely to be effected; children below the age of five are generally not affected by this disease. In this, the body starts to make autoantibodies which attacks the body's own tissues only, the reason to this is unknown still some factors are believed to cause this.

Those factors are:

a) Illness or infection
b) Strong sunlight
c) Changes in the hormones
d) Cigerette smoking
e) Some medications – causes drug-induced lupus

Diagnosis of lupus is difficult as it differs from patient to patient; in order to control it's conditions, it should be diagnosed as soon as possible. Diagnosis is based on the symptoms, physical examination, blood tests as well as many other tests. Name of some tests are:

- *Anti-nuclear Antibody (ANA) Test:* It doesn't confirm lupus as many times patients who don't have lupus are also tested positive. Yet about 95% of the effected individuals are tested positive with the help of this test.
- *Anti-double-stranded DNA (anti-dsDNA) Antibody Test:* About 70% of the patients with lupus have these antibodies. If the test results are positive then the patient is likely to have lupus as it doesn't show a positive result for the ones who don't have it
- *Anti-Ro Antibody Test:* If tested positive for this antibody, the individuals are likely to have skin rashes and suffer from dry eyes and dry mouth, which can detect some other disease known as Sjögren's syndrome**.**
- *Anti-phospholipid Antibody Test:* A positive result on this antibody means developing blood clot and an increased risk miscarriage. The tests may be repeated many times as these antibodies may come and go.
- *Kidney and Liver Function Tests:* Includes urine and blood tests, helps doctor to diagnose the functioning of the kidney and the liver and if any organ is affected or not.
- *Blood cell Counts:* It helps the doctors to know whether the bone marrow is affected or not due to the patient's condition or drugs.
- *Scans and X-Rays:* To check the overall performance and functioning of the organs such as lungs, heart, liver etc.

As for the treatment, there is no permanent cure for lupus at present; however, the condition can be improved by drugs. The earlier the treatment starts the better it is. Drugs used to treat lupus are non-steroidal anti-inflammatory drugs - NSAIDs (like aspirin, ibuprofen, naprosyn, or indomethacin) these can reduce inflammation and pain in the joints; if used for a long time may cause thinning of the lining of stomach and may also cause problems with kidneys, corticosteroids (like prednisone and prednisolone) used to reduce inflammation and as creams to treat rashes, disease-modifying anti-rheumatic drugs - DMARDs (such as azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil) it may reduce the effects of overactive immune response, antimalarials (like hydroxychloroquine) used to reduce inflammation and help control cholesterol levels and kidney functions; useful for fatigue and joint pain too, though it may also effect the eyes and benlysta, it may also include statins, diuretics, anticoagulants, antibiotics, stimulants. Biological therapies (like rituximab and belimumab) have a very specific consequence on some cells of the immune system; they can disrupt or lessen the activity of B-cells which in lupus make autoantibodies that attack the body's tissues. Apart from taking the medications, must keep a healthy diet, exercise frequently and avoid smoking to maintain a healthy lifestyle and avoid risks of further complications.

2) *Rheumatoid Arthritis (RA):* It is a complex disease, the early symptoms include joint pain, joint swelling and stiffness of the joint; the symptoms start to become worse with time, it starts developing in the small joints of fingers of hands and toes. Many people develop fleshy swellings known as rheumatoid nodules under the skin of the joint which may or may not cause the pain. It is believed that the first case of arthritis was observed back in the 4500 BC, yet the term "rheumatoid arthritis" was given in the year 1859 by a British man named Dr. Alfred Baring Garrod. If left untreated it could become more worse and may cause complications in organs such as the heart, salivary glands, bone marrow and the lungs, it may also affect the nerves causing long-term disability.

Apart from the stiffness, pain and swelling of joints, it shows some more symptoms like:

a) Redness along the joint
b) Fatigue
c) Poor appetite
d) Weight loss
e) Fever
f) Sweating
g) Dry eyes
h) Chest pain

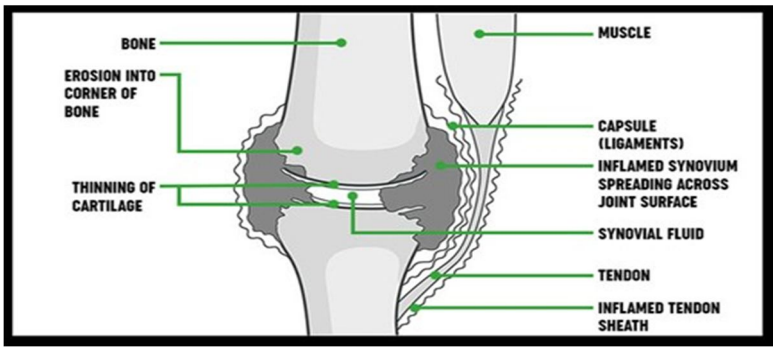

Figure 6. The front view of a badly affected joint in rheumatoid arthritis

According to a data, it affects around 40000 individuals of the age 16 and above. In rheumatoid arthritis the immune systems attack synovial fluid in the joints of our body causing inflammation; it permits our body to send the extra fluid and blood to a part of the body which is attacked by some kind of infection. Though the inflammation is seen on the outside, what happens in the inside is that the capsule around the joint is now unable to hold the joint properly around the stretched synovium; this causes the joint to be unstable and thus the deformation occurs as it can now move to unusual places. It occurs in 4 stages:

- *Stage 1:* It is the early stage in this only the pain, stiffness and swelling is observed, the tissue and the synovium swells up; no damage to bones
- *Stage 2:* It is the moderate stage where the joint cartilage is damaged. Motion of the joints becomes restricted
- *Stage 3:* This is the critical stage where the damage leads to the bones as well. Bone becomes damaged (eroded), deformity occurs, patients can feel muscle weakness, motion is lost and pain severs.
- *Stage 4:* This is the end stage, no inflammation occurs any further, here people experience pain, stiffness, swelling and mobility loss, muscle strength is lost as well as the joints fuse causing ankylosis.

Apart from the attack of our faulty immune system there are many underlying risk factors which may cause arthritis; they are:

- *Age:* It usually affects adults but the people of the age of 40 to 60 are more likely to have it.
- *Sex:* More common among women than men
- *Genetics:* Having a relative with RA can increase the risk
- *Weight:* People who are overweight are generally more prone to RA
- *Diet:* Eating much of red meat and not having much of vitamin-C in the diet may increase the risk of having rheumatoid arthritis. People who do not exercise frequently are also at risk. Also, people who smoke are also prone to it.

Diagnosis is based on the physical symptoms, x-ray scans and blood tests. Blood tests are used to see the changes occurred in our body like if the person has anemia or not as RA causes anemia amongst patients. X-Rays are used to diagnose the damage caused to the joints. There are three main means to treat arthritis:

- Surgery
- Drugs
- Physical therapies

Drugs include:

- Steroids are used to reduce pain, stiffness and inflammation; used for short term pain relief. To avoid side effects it is not prescribed for long term use.
- DMARDs which include the conventional synthetic DMARDs (like azathioprine, myocrisin, plaquenil, leflunomide, methotrexate, and sulfasalazine), biological therapies (like etanercept, infliximab, rutiximab) and targeted synthetic DMARDs (like baricitinib, tofocitinib).
- Painkillers which help to reduce pain.
- NSAIDs used to reduce pain, inflammation and stiffness; usually taken orally or in the form of a cream, or supposedly needs to be inderted inside the bum. Ibuprofen is commonly prescribed.

Apart from the medications prescribed the patient must exercise, put heated items or cold items on the joint, physiotherapy, hydrotherapy is also suggested

3) *Graves' Disease:* Robert Graves in 1835 was the first person to identify hyperthyroidism which was linked to autoimmunity and hence named it Graves' disease. The overactivity of the entire thyroid gland leads to this autoimmune disease. In Graves' disease, antibodies like the thyrotropin receptor antibodies (TRAb) or thyroid stimulating immunoglobulin (TSI) makes the thyroid cells work more. The antibodies tend to stimulate the thyroid cells by binding at the receptors, resulting in their overproduction and therefore the release of thyroid hormones; which results in overactive thyroid gland leading to hyperthyroidism. Apart from the confused antibody action, other factors also may lie for its pathogenesis including high concentrations of antibodies which act against thyroglobulin, thyroid peroxidase, and probably the sodium–iodide carrier in thyroid tissue. Sometimes these serum antibody levels are low in patients or even undetectable. It is believed to have a genetic predisposition, but no such specific gene is found till now. Though the environmental factors and endogenous facvtors also play a major role. Females are thought to be at much risk than men. All the symptoms associated with graves' disease can be seen in the image.

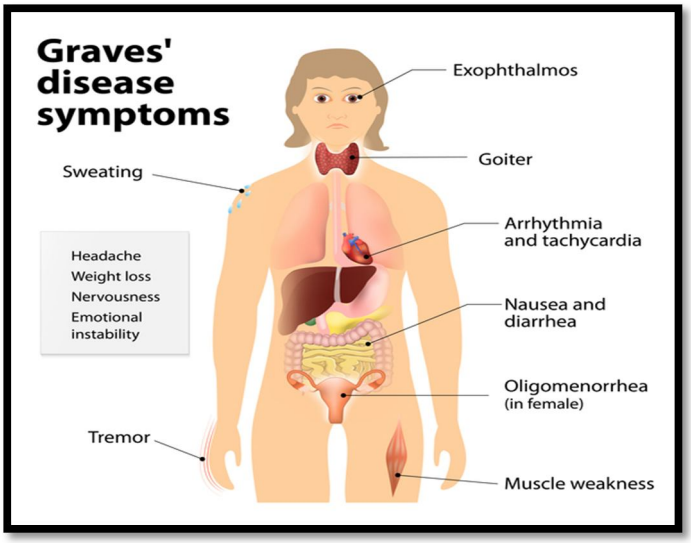

Figure 7. Symptoms of Graves' disease

The diagnosis of Graves' disease is based on clinical and biochemical examination on hyperthyroidism as well as lab tests for the confirmation of the actual cause. The physical examination which involves eye disease or the signs of dermopathy or ophthalmopathy is sufficient to confirm the cause of hyperthyroidism. It is seen that patients having pre-existing goiter often show the presence of Graves' disease too. Tests conducted are: blood tests to know the levels of thyroid hormones and their activity (thyroxine, or T4, and triiodothyronine, or T3 and thyroid-stimulating hormone – TSH); measurement of TRAb or TSI antibodies, if the test results positive then it confirms the disease, but even if it turns out to be negative then the doctor must conduct radioactive iodine uptake test (RAIU) in order to confirm the diagnosis.

Table 3. Treatment for Graves' disease

Treatment	Dosage	Side effects
Anti-thyroid drug (carbimazole or its metabolite methimazole or propylthiouracil)	Dose decreased aseuthyroidism is achieved or a single high dose together with thyroxin to prevent hyperthyroidism	Rashes, fever, lack of taste & smell, nausea, acute hepatic neurosis, vasculitis, insulin-autoimmune syndrome, agranulocytosis, etc.
Radioactive iodine	Generally based on clinical assessment, but some give doses on the basis of uptake and turnover studies	Transient or permanent hypothyroidism and worsening opthalmopathy, radiation thyroiditis, overexposure to radiation
Subtotal thyroidectomy or near-total thyroidectomy		Hypothyroidism, recurrent laryngeal-nerve damage, hemorrhage, anesthetic complications

4) *Idiopathic Thrombocytopenic Purpura (ITP):* Idiopathic Thrombocytopenic Purpura (ITP) is also known as Autoimmune Thrombocytopenic Purpura (ATP) is an autoimmune disease seen more in females than in males (ratio 3:1). After the initial reports of this disease dates back to 1556 and 1658, the German physician Paul Gottlieb Werlhof in 1735 wrote the first complete report of ITP. Earlier when the platelets were not discovered then it was considered as "Werlhof's disease". Idiopathic word is referred to the unknown cause of the disease as earlier the cause was unknown but now the cause is known that is why now it is known as ATP instead of ITP. In this the autoantibodies (7 *S* IgG) are produced against the platelets, and perhaps because of megakaryocytes, it leads to destruction of the platelets which lowers its count. The resultant destruction induces purpura and hemorrhage if the platelet count reaches a critical level (<30000/μL). It is a non-contagious disease. There are two types of ITP:

a) *Chronic ITP:* Lasts longer; commonly seen in adults.

b) *Acute ITP:* Short term; persists up to six months or even less. Commonly occurs among children.

The common symptoms of ITP are:

- Bruising easily and prolonged bleeding
- Appearance of petechiae, usually on the lower legs
- Spontaneous nosebleeds
- Bleeding gums
- Blood in the urine and stool
- Unusual heavy menstruation in women
- Abundant blood loss during surgery

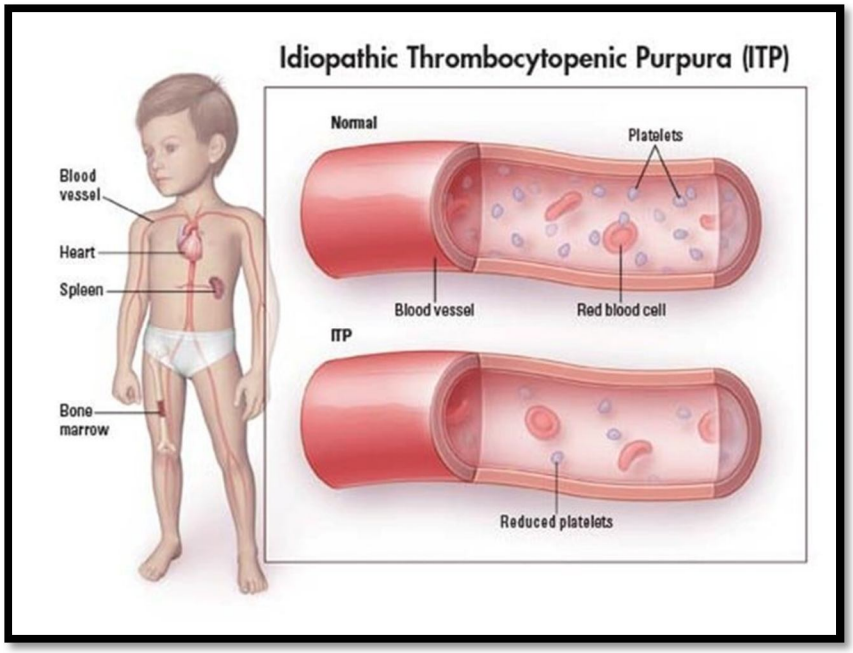

Figure 8. The difference between a normal blood vessel and an ITP affected blood vessel

The diagnosis is based on physical examinations and certain lab tests.

- *Blood Tests:* It includes the tests to evaluate the liver and kidney functions. It is also conducted to know the full blood count (can be done by taking the blood test sample or through a blood smear) and even to check for platelet antibodies.
- *Bone Marrow Test:* If the platelet count is low then the bone marrow test is conducted. If the test result comes out to be abnormal then the patient doesn't have ITP. As in ITP, the bone marrow is normal as the platelets get destroyed in the blood stream and spleen after leaving the marrow.

Treatment for acute ITP is not needed as the children usually recover from it within 6 months, though the chronic form might need some treatment based on the number of platelets in the blood or the amount of blood lost while bleeding. Low RBC count or the platelet count might indicate the risk of internal bleeding. Treatments include:

- *Medications:*

- Corticosteroids: like Prednisone helps in increasing the number of platelet by decreasing the activity of the immune system.
- Intravenous immunoglobulin (IVIg): if the platelet count is to be increased quickly then this is the best option.
- Anti-D Immunoglobulin: patients having the Rh-blood type; works like IVIg only to increase the platelet count maybe even faster. May have some side effects.
- Rituximab (Rituxan): antibody therapy which attacks the immune system; this medication binds with B-cells and destroys them which in turn is beneficial as now less protein will be produced to destroy the platelet cells.
- Thrombopoietin receptor agonist: like romiplostim (Nplate) and eltrombopag (Promacta) causes the bone marrow to produce more and more platelets in order to stop the excessive bruising and bleeding.
- General immunosuppressant: such as cyclophosphamide (Cytoxan), azathioprine (Azasan, Imuran), mycophenolate (CellCept), they tend to inhibit the whole immune system's activity. Though they may also have some side effects.
- Antibiotics: *Helicobacter pylori* are thought to be associated with ITP and causes peptic ulcers. Antibiotics help in the destruction of these microbes and hence help in the increase of platelet count.

- *Surgery:* Splenectomy or the removal of spleen would be necessary if the medications don't give the desired result.
- *Emergency Treatment:* Usually involves transfusion of concentrated platelets and intravenous administration of corticosteroids or IVIg or anti-D treatment.
- *Lifestyle Changes:* Lesser consumption of alcohol and to engage in light sport activity over the high sport activity to avoid injury.

Though, sometimes the treatment has much more adverse effect on the patient's health than the disease itself. The long-term use of steroids may cause serious side effects which may result in – osteoporosis, cataract, diabetes, loss of muscle mass and an increased risk of acquiring infections. Splenectomy also causes a high a risk of acquiring bacterial infections, which may cause the patient seriously ill.

E. Epidemiology of Autoimmune Diseases

In today's world it is believed that one of the leading causes of death of women are them acquiring autoimmune diseases. The disease usually starts during the child-bearing years of a woman (15-45 years). Hence, all the middle-aged and young women are at risk. The reason of women acquiring these diseases is unclear yet it is believed that the presence of two X chromosome may have some genetic effect which may increase their risk of acquiring them. Estimates of people getting affected from autoimmune disease ranges greatly like there would be just 1 case of sclerosis whereas there would be more than 20 cases of RA per 100000; it may also vary from 5 cases of chronic active hepatitis per 100000 cases to more than 500 diagnosed cases/incidents of graves' disease, RA or even thyroiditis. Almost 85% of the patients are females for these diseases. Some of the autoimmune diseases occur in some particular area or to some specific individuals, like African-Americans and Hispanic people are more likely to get lupus than Caucasians and that Type - 1 diabetes is more common among white people. The figure below shows that women are generally more susceptible to acquire autoimmune disease.

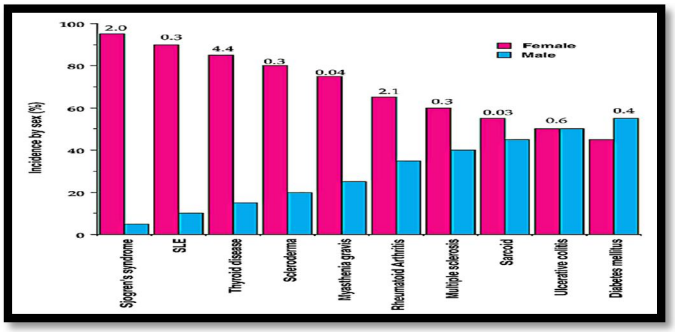

Figure 9. Sex differences in acquiring autoimmune disease

III. CONCLUSION

This term paper has presented the most simplified yet easy way to understand what is meant by autoimmune diseases. Beginning with some information about immunity and autoimmunity and then discussing about autoimmune diseases and its types. In order to understand autoimmune diseases and its effects some of the diseases were explained such as Systemic Lupus Erythomatosus (SLE), Rheumatoid arthritis (RA), Graves' disease and Idiopathic Thrombocytopenic Purpura (ITP). The report mentions all the problems associated with autoimmunity and how does it affect the humans. I would conclude these topics by sharing a small summary of it as to know what all topics were covered and what all we learnt from it.

We learnt that the immunity is the inbuilt ability of an organism to protect itself from various disease-causing infections, when this our immune system gets confused or doesn't work properly then it is ought to attack its own cells and tissues causing various diseases. The history of immunology dates back to 1900s but the researches are going on from a long time. With all the medical advances the scientists have achieved a lot in this field still the exact cause of acquiring autoimmune diseases is unknown. However, there are theories which tell us that genetic, environmental, lifestyle habits and some infecting agents including microorganisms like viruses and bacteria may trigger the immune system to behave in such a way. It is also found out that most of the diseases occur to women and that different diseases have different number of cases worldwide. In order to get a better view of how actually autoimmune diseases hinders life's overall functioning we took 4 diseases as examples 2 from systemic kind & 2 from organ-specific kind. They all had one thing in common that how they have no actual treatment. Generally, these diseases are treated either through surgeries or medications which usually include drugs like corticosteroids, immunosuppressant and various other antibody related drugs. By the epidemiology report we got to know that women are at a much higher risk than men for acquiring these diseases and that some diseases are seen to be area specific too.

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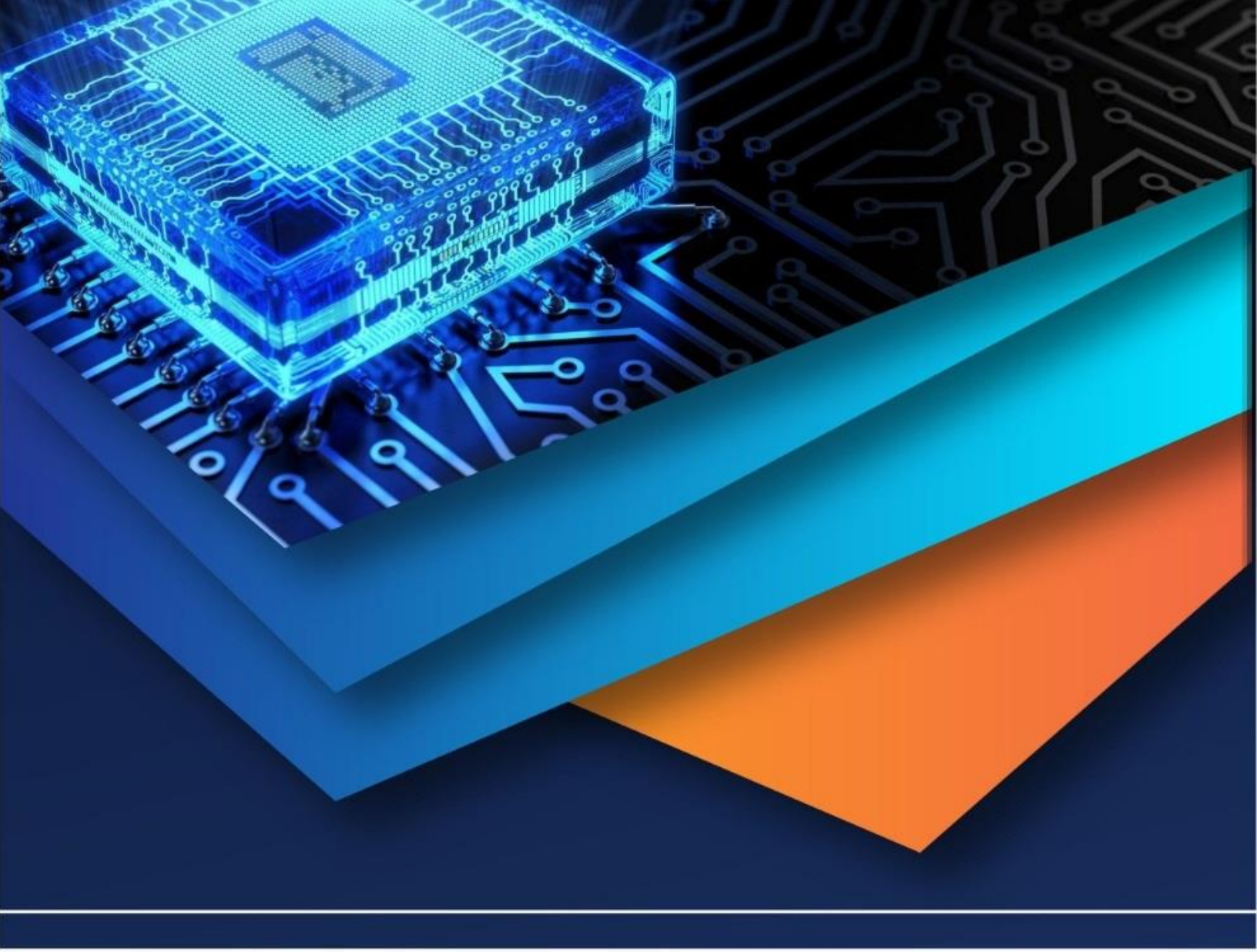

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