**Autoimmune Diseases and Human Health: An updated insight**

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**Running Title:** Autoimmune diseases and human health

**Abstract**

Autoimmune diseases and disorders are not the same thing. While the underlying aetiology of each illness is different, the immune system dysfunction that underpins both disorders may produce similar symptoms. One key difference is that autoimmune illnesses are characterized by an impairment of the adaptive immune system, while auto inflammatory disorders are characterized by an impairment of the innate immune system. Systemic or organ-specific inflammation that results in tissue damage is the defining feature of autoimmune/inflammatory illnesses. The prior categories for autoimmune/inflammatory conditions were auto inflammatory and autoimmune illnesses. Certain disorders, like lupus, which exhibit family aggregation and may suggest a genetic predisposition, are suggested to be the result of a complex interplay between genes and environment. There is evidence linking autoimmune diseases to clinical symptoms. Measuring auto antibodies in patients may help with diagnosis and severity analysis, which might be important for treatment. In this chapter we have focused mainly on the therapeutic interventions of different autoimmune diseases like myasthenia gravis, rheumatoid arthritis, and systemic lupus erythematosus.

**Keywords:** Autoimmune diseases, diabetes, rheumatoid arthritis, lupus erythematous, auto antigen

1. INTRODUCTION

Autoinflammatory illnesses and autoimmune disorders belong to different classes. The immune system failure that underlies both conditions might result in comparable symptoms including weariness, rash, and swelling, but the underlying etiology of each disease is distinct (Scherlinger et al., 2020). One important distinction is that autoinflammatory disorders are characterized by an impairment of the innate immune system, while autoimmune diseases are characterized by an impairment of the adaptive immune system (Leo et al., 2020). The hallmark of autoimmune/inflammatory illness is systemic or organ specific inflammation that causes tissue destruction (Evert et al., 2003). Autoinflammatory and autoimmune disorders were the previous classifications for autoimmune/inflammatory condition (Watad et al., 2017). But it soon become evident that the world is far more complicated than that, with autoimmune and autoinflammatory conditions essentially acting as extremes at either end (Tang et al., 2012).Conversely, autoimmune diseases were defined as those that are caused by the adaptive immune system and hence typified by the existence and pathophysiological engagement of autoantibodies and/or populations of self-reactive lymphocytes(Fig. 1) (Satoh et al., 2016).



**Figure 1:** Different autoimmune diseases and their target organs.

There is a spectrum of systemic autoimmune/inflammatory disorders, with ‘classical’ autoimmune conditions at one end of the spectrum and monogenic autoinflammatory conditions at the other(Croft et al., 2019).

The molecular pathophysiology of autoimmune/inflammatory conditions is complex and only partially understood, reflecting the constantly growing number of known autoimmune/inflammatory conditions, the previously mentioned inter-individual variability in phenotypes and outcomes (sometimes even between patients with the same diagnosis and/or between family members), and the observation that initially distinct disorders may move along the inflammatory spectrum from, for example, a primarily auto inflammatory to an autoimmune phenotype (this can happen over time in adult Still's disease and systemic JIA, for example) (Swinkels et al., 2018). According to what is now known, the causes of autoimmune and inflammatory illnesses are either complex genetic predispositions (more prevalent) or monogenic disease causes (rare), which are both subject to individual and environmental factors that determine the expression of the disease and/or individual phenotypes and outcomes (Wang et al., 2015).

The precise etiology of autoimmune illnesses is yet unknown, but it is most likely complex, incorporating both environmental and genetic factors (Fallah et al., 2014). A complicated interaction between genes and environment is implied in the etiology of some diseases, such as lupus, which show familial aggregation and may indicate a hereditary predisposition(Hainer et al., 2019). However, other cases have been linked to viral triggers or environmental variables.Gene regulatory mechanisms known as epigenetic events regulate chromatin's accessibility to transcriptional regulatory factors, which modifies gene expression without altering the underlying DNA sequence (Meers et al., 2019). Even while all diploid cells have the same genotype, epigenetic processes can be impacted by the environment, are dynamic but also heritable, and ultimately account for considerable diversity between cells and tissues within an organism (Simeonov et al., 2019). Histone protein post-translational modifications, non-coding RNA expression, and DNA methylation are examples of epigenetic processes (West etal., 2018).

2. HISTORICAL BACKGROUND OF AUTOIMMUNE DISEASES

Medical microbiology saw the emergence of immunology as a new specialty. A crucial question is raised by Robert Koch's research on the aetiology of infectious diseases, particularly tuberculosis, and Louis Pasteur's discoveries, which confirmed the germ hypothesis of infectious diseases. Is the host defenceless against harmful bacteria or does it have an effective defence mechanism (Lo et al., 2020).

Metchnikoff, who had worked at the Pasteur Institute in Paris since 1888, discovered the critical role of phagocytosis and intracellular killing in host defence, while Behring and Ehrlich, working at Koch’s Institute for Infectious Diseases in Berlin, identified antibodies as critical counterparts to bacterial toxins (Conigliaro et al., 2019).

Medical historians regard the mid-twentieth century as the point at which the scientific and medical societies recognized the presence of autoimmune illness (Ling et al., 2019). Several illnesses, including sympathetic ophthalmia andendophthalmitis phacoanaphylactica, were previously identified as autoimmune disorders (Kumagai et al., 2020). During the first part of the century, autoimmune illness was considered biologically improbable (Schreiber et al.,2019). Paul Ehrlich used the term horror autotoxicus to stress how autoimmunity would go against nature's reluctance to self-injury(Khan et al.,2020).

The discovery of allergies and anaphylaxis provided the first evidence that the immune system was capable of self-harm (Fässler et al., 2019). Understanding the etiology of autoimmunity was hampered by a significant stumbling block: how the immune system discriminates between foreign and self, a mechanism that was finally identified as immunological tolerance(Fig. 2) (Finkel et al., 2021).Investigators of sympathetic ophthalmia and endophthalmitis phacoanaphylactica were positioned to disprove horror autotoxicus, but there was insufficient convincing experimental and clinical data to do so (Zhou et al., 2020). In the 1950s, autoimmune illness gained widespread recognition following seminal investigations of chronic thyroiditis and a succession of clinical laboratory advances(Rendeiro et al., 2020).

The difficulties experienced by ophthalmology scientists provide insights into how medical concepts develop (Hajishengalis et al., 2019). We examine how ocular immunology had a role in developing the notion of autoimmune illness and why it took time to gain popularity (Chua et al., 2020).

**Figure 2:**background of autoimmune diseases. Cross reaction, mutation and intolerant are the main hallmarks.

According to Paul R. Ehrlich (1901), an immune response directed toward the "self" might result in the production of antibodies that are detrimental to the individual (Schulte-Schrepping et al., 2020). His well-known "horror autotoxicus" demonstrated that the body required a method to defend itself against the risks of self-antibodies (van der Made et al., 2020).

 Paul Ehrlich (1900), considered one of the ancestors of modern immunology, created the side-chain theory, which stated that infections interact with side chain receptors on cells (Combes et al., 2021).He was the first to suggest a model for a branching antibody molecule with several binding sites for antigen and complement activation (Shin et al., 2019). In 1948, Astrid Fagraeus identified plasma B cells as predominantly engaged in antibody synthesis, and in 1957, Frank Burnet and David Talmage developed the concept of clonal selection (Defendi et al., 2020).

The discovery of two kinds of antibodies (ANAs and RF), serum factors that bind to the nuclear antigen and immunoglobulin G, dates back to the 1940s. Autoimmune illnesses have been connected to clinical symptoms, and calculating autoantibodies in patients may assist in the diagnosis and analysis of the disease's severity, which might be crucial for therapy (Bekkeringet al., 2018).It argued that cells produce a single antibody molecule that is determined before they meet an antigen, incontrast to Pauling's instructional theory of 1940, which believed that the antigen acts as a template for the antibodies (van der Meer et al., 2016). Donath and Landsteiner were the first to identify an autoimmune disorder called Donath-Landsteiner haemolytic anaemia (Wrap et al., 2020). A blood component (antibody) that binds and lyses self-red blood cells was found in a patient whosuffered paroxysmal cold haemoglobinuria after being exposed to cold in the arms or legs (Hoey et al., 2019). August Wassermann observed in Berlin that syphilis patients' sera reacted with extracts of both sick and normal tissues, allowing autoantibodies to be identified (Lung et al., 2019).

3. CLASSIFICATION OF AUTOIMMUNE DISEASES

Numerous factors can be used to categorize autoimmune disorders. The site of the autoimmune attack is one of them, this criterion is used to differentiate between systemic and organ-specific autoimmune disorders (Bettacchioly et al., 2021). This artificial classification structure serves a practical purpose in helping patients and primary care providers find the right expert (Table 1) (Abu-Rumeileh et al., 2020).

**Table 1:**Autoimmune diseases with target organ and auto stimulate antigens.

|  |  |  |
| --- | --- | --- |
| Disease | Target Organ | Known auto antigens |
| Thyroiditis (autoimmune) | Thyroid | ThyroglobulinThyroperoxidase |
| Grave’s disease | Thyroid | Thyroid-stimulating hormone receptor |
| Type 1 diabetes | Pancreatic Beta cells | Insulin, GAD, IA-2 |
| Addison’s disease | Adrenal | 21OH hydroxylase |
| Gastritis | Stomach | 17OH hydroxylase |
| Celiac disease | Small bowel | H+/K+ ATPaseIntrinsic Factor |
| Vitiligo | Melanocytes | Transglutaminase |
| Multiple sclerosis | Brain, spinal cord | TyrosinTyrosinase-related protein-2 |
| Pemphigus | Skin | Myelin basic proteinProteolipid protein |
| Hepatitis (autoimmune) | Liver | Hepatocyte antigensCytochrome; p450-1 A2 |
| Myasthenia gravis | Muscle | Acethylcholine receptor |
| Primary biliary cirrhosis | Liver bile ducts | 2-Oxoacid dehydrogenase complexes |

3.1. Systemic Specific

When autoantigens are present in nearly every kind of cell in the body, such as DNA-protein complexes, the condition isreferred to as systemic autoimmune disease(EASL et al., 2017).Consequently, a wide variety of organs and tissues are affected by the pathological damage.Rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and dermatomyositis are examples of common systemic autoimmune illnesses (Nydegger et al., 2016).

3.2. Organ Specific

Immune system attacks that target a single organ or tissue preferentially are known as organ- specific autoimmune disorders.The skin in individuals with vitiligo, the beta cells of the endocrinefew examples.

### 3.3. Graves' disease

### The production of autoantibodies against thyroid stimulating hormone(TSH) receptors (TRAb) is a characteristic of Graves’ illness. Uncontrolled thyroid hormone production and release brought on by the binding of TRAb autoantibodies to the TSH receptor can produce stimulatory effects such a fast heartbeat, weight loss, anxiety, and irritability (Arulraj et al., 2021).

### 3.4. Inflammatory bowel disease

### Crohn's disease and ulcerative colitis are two illness that fall under the umbrella term of inflammatory bowl disease (IBD), which is defined by persistent inflammation of the digestive tract (Annett et al.,2020).

### 3.5. Multiple sclerosis

### Myelin, the protective sheath that surrounds nerve fibers in the central nervous system, is attacked by the immune systemin multiple sclerosis (MS), a neurodegenerative disease that impairs communication between the brain and the body (Soltani et al., 2019).

### 3.6. Rheumatoid arthritis

### The main target of rheumatoid arthritis (RA) is the joint, where it causes chronic inflammation that leads to discomfort and damage to the joints (Levine et al., 2018). It frequently has symmetry, so if one hand or knee has it, the other one also does.

### 3.7. Systemic lupus erythematosus

### Lupus, or systemic lupus erythematosus, is a type of autoimmune illness that affects several organs, including the kidneys, skin, joints, and nervous system(Stojan et al., 2016). A generalized lack of immunological tolerance is one of its defining features.

### 3.8. Type 1 diabetes

### The illness known as type 1 diabetes is brought on by the immune system attacking the pancreatic beta cells that produce insulin, which raises blood sugar level (Lu et al., 2019). Increased thirst, frequent urination, and inexplicable weight loss are some of the symptoms.

### 3.9. Coeliac disease

### Coeliac illness is an immunological response to gluten, a protein present in wheat, barley, and rye. Consuming gluten can include an immunological reaction in the small intestine, ca using damage to the villi, which line the gut and aid in food absorption (Zhang et al., 2017). Gluten consumption can raise the risk of gastrointestinal cancer due to its passage through the gastrointestinal system, which includes the esophagus, stomach, small and large intestine, rectum, and anus (Alpert et al., 2019).

### 3.10. Psoriasis and Psoriatic arthritis:

### Psoriasis is a skin disorder characterized by rapid cell growth, resulting in scaling on the skin surface.Inflammation and redness surrounding the scales are prevalent (Mamoshina et al., 2019). Some people with psorias is may develop psoriatic arthritis, which causes joint discomfort, stiffness, and oedema.

### 3.11. Sjögren's syndrome

### Sjögren syndrome (SjS, SS) is a chronic autoimmune illness that affects the body's moisture-producing glands (lacrimal and salivary) and frequently has major consequences for other organ systems such as the lungs, kidneys, and nervous system.

### 3.12. Undifferentiated Connective Tissue Disease

### Undifferentiated Connective Tissue Diseases arises when individuals exhibit symptoms of connective tissue disease, including blood test results and outward traits, but do not meet diagnostic criteria for any specific connective tissue disease (Rockwood et al., 2011). Some 30-40% develop a particular connective tissue disorder throughout time.

### 3.13. Multiple Sclerosis (MS)

### MS is an autoimmune illness that damages the insulating coverings of nerve cells in the brain and spine.Damage to the nervous system can impair signal transmission and cause physical, mental, and psychiatric symptoms.Symptoms may include double vision, visual loss, eye discomfort, muscular weakness, and loss of sensation/coordination (Lehallier et al., 2019).The reason is unknown;

###  however, it is likely due to immune system damage or myelin-producing cell failure,there is currently no recognized cure for multiple sclerosis.Current therapies include disease-modifying drugs to reduce inflammation and the symptoms that accompany acute flares, as well as to prevent future episodes.Physical and occupational therapy, as well as patient-centered symptom management, can improve functional capacity.

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### Figure 3:Pathophysiology and different factors of autoimmune diseases.

4. MYASTHENIA GRAVIS

Myasthenia gravis is a fast and voluntary controllable muscle weakening and weariness.Antibodies that create a breakdown in nerve-muscle communication are the cause of the disorder. One of the most prevalent conditions affecting neuromuscular transmission is myasthenia gravis. It is one of the autoimmune illnesses that is now most understood and defined. Due to an immunological response to the postsynaptic membrane of the neuromuscular junction, it is characterised by cyclical weakness and tiredness affecting a variety of ocular muscles, bulbar functions, limb, and respiratory muscles (Cohen Tervaert et al., 2018). Myasthenia gravis is diagnosed usinga combination of clinical and serological testing. With the help of the available treatment options, the illness can be successfully managed and even completely remitted.

5.1. Epidemiology

Myasthenia Gravis (MG), a chronic, uncommon autoimmune illness, the body's immune system targets neuromuscular junction components, impairing nerve to muscle signal transmission(Imbach et al., 1981). The symptoms of myasthenia gravis include weakness and exhaustion in the voluntary skeletal muscles, especially the jaw, eyes, neck, face, and limbs.

5.2 Incidence

The incidence rate of MG ranged from 1.7 to 21.3 in 55 studies undertaken between 1950 and 2007, yielding a global pooled incidence rate of 5.3 per 1,000,000 individuals annually. Between 2007 and 2019, 29 additional studies found that the incidence rate of MG ranged from 0.15 to 61.33 per 1,000,000 people annually (Sultan et al., 1984).According to a 2021 study, there are 4.1 to 30 cases of MG for per 1,000,000 people year.

5.3 Prevalence

Over the past 50 years, there has been an increase in the reported prevalence of MG, which varies by area. The prevalence rates in the world vary from 150 to 200 cases per million individuals.

* 1. Pathophysiology

 The most well-understood autoimmune condition is myasthenia gravis (MG), and research on the condition has contributed to a fundamental understanding of the mechanics behind neuromuscular transmission. Antibodies directed against the acetylcholine receptor (AChR) are the cause of myopathy (MG). These antibodies lead to a reduction in the safety factor for efficient synaptic transmission by compromising the end-plate potential (Tian et al., 2021). It is evident that complement activation is necessary for the postsynaptic surface to be destroyed by AChR antibodies.Patients with MG who do not have antibodies against the AChR have been identified to have an antigenic target that is specific to muscle kinase. T-cells are necessary for the formation of autoantibodies in MG, yet it is unclear how tolerance breaks down. There is an intriguing variation in the participation of muscle groups in MG, with the extraocular muscles being particularly involved. This article examines the processes underlying the autoimmune process of myasthenia gravis (MG), normal neuromuscular transmission, and the varying susceptibilities of the ocular muscles to MG.

Classification and congenital myasthenic syndromes in dogs and cats

Myasthenia is a syndrome characterized by decreased neuromuscular transmission that can be inherited or acquired. Congenital myasthenic syndromes (CMSs) are a clinically heterogeneous collection of hereditary illnesses affecting the neuromuscular junction (NMJ) of skeletal muscle with an early onset. Myasthenia gravis (MG) is an acquired autoimmune disorder with autoantibodies targeting the NMJ. Regarding treatment and result, it is critical to recognise both illnesses as diseases.Examining the published research on MG and CMSs in dogs and cats, and then suggest a categorization scheme for MG and CMSs in dogs and cats based on a comparison with published human classifications (Signore et al., 2018). First, the appearance of myasthenia gravis is characterized as focal, generalized, or acute fulminating. Subclassification is based on seronegativity or the mechanism of autoimmune illness. The mechanism of autoimmune disease is related to the administration of thiourylene medicine to cats or the existence or absence of a thymoma. The impacted NMJ component, the mechanism of the neuromuscular transmission failure, the affected protein, and finally the mutant gene responsible are used to categorise congenital myasthenic disorders. Intending to facilitate identification of the disease categories for both illnesses by presenting this classification of MG and CMSs as well as direct care, improve prognosis, and offer a foundation for more research on these disorders.

Causes

In order to communicate with your muscles, your nerves release chemicals known as neurotransmitters that attach to receptor sites on your muscle cells. This process is known as the nerve-muscle junction.The immune system produces antibodies in myasthenia gravis that obstruct or damage a large number of your muscles' acetylcholine (as-uh-teel-KOH-leen) receptor sites. Your muscles get fewer nerve messages when there are fewer accessible receptor sites. Weakness results from this.Moreover, antibodies have the ability to inhibit a protein known as muscle-specific receptor tyrosine kinase, or MuSK (TIE-roh-seen KIE-nays). The nerve-muscle junction is formed in part by this protein (Ding et al., 2021). Myasthenia gravis may result from antibodies directed against this protein.This illness may be exacerbated by antibodies directed against lipoprotein-related protein 4 (LRP4). Additional antibodies have been discovered via research studies, and this number of antibodies will probably increase over time.

Myasthenia gravis in certain individuals is not brought on by antibodies that obstruct LRP4, MuSK, or acetylcholine (Vulto et al., 2017). Seronegative myasthenia gravis, sometimes referred to as antibody-negative myasthenia gravis, is the name given to this kind of the disease. Generally speaking, scientists still think that autoimmunity plays a role in this kind of myasthenia gravis; the antibodies that are responsible have just not been identified yet.

Thymus gland

One component of your immune system is the thymus gland. This gland is situated beneath the breastbone in the upper chest. The antibodies that obstruct acetylcholine are thought to be produced by the thymus gland or to have assisted in their production.In healthy adults, the thymus gland is small, but in newborns it is enormous. However, the thymus gland is larger than normal in some adults with myasthenia gravis. Thymomas, or tumours of the thymus gland, are another condition that some myasthenia gravis patients develop. Thymomas, also called malignant, are rarely cancerous. However, thymomas can develop into malignancy.

Among the things that can exacerbate myasthenia gravis are:

• Weary

• Disease or illness.

• Surgery.

• Tension.

• Certain medications, including beta blockers, antibiotics, quinidine gluconate, quinidine sulphate, quinine (Qualaquin), phenytoin (Dilantin), and several anaesthetics.

• Maternity.

• Menstrual cycles.

Symptoms

Myasthenia gravis causes muscular weakness that deteriorates with use of the affected muscle. Muscle weakness can come and go because the majority of the time the symptoms improve with rest (Rajewsky et al., 2019). But with time, the symptoms usually worsen. Usually, a few years after the sickness starts, they get the worst of it.

You could have myasthenia gravis and it could damage any muscle you can control. Affected muscle groups vary in frequency of occurrence.

Muscles in the eyes

The early signs of myasthenia gravis usually affect the eyes in over half of cases. Among the symptoms are

• Ptosis is the term for drooping of one or both eyelids

• Diplopia is the term for double vision, which can be either vertical or horizontal and gets better or goes away when one eye is closed.

Muscles of the face and throat

Face and throat muscles are involved in the initial symptoms of myasthenia gravis in around 15% of cases. These signs and symptoms may:

* Difficulty in speaking.
* Difficulty in swallowing
* Impact the chewing process, halfway through a meal, the chewing muscles may start to ache. This is particularly valid if you've been consuming tough foods like steak (Weinreichet al., 2020).
* Alter your facial expressions.
* Muscles in the neck and limbs:

Additionally, myasthenia gravis can result in weakness in the arms, legs, and neck. Leg weakness can have an impact on gait. It is difficult to hold up the head when neck muscles are weak.

Diagnosis

Neurological test

Testing could be one way your doctor examines your neurological health

• Adaptations.

• Strength of muscles.

• Tone of muscles.

• Touch and visual senses.

• Sync.

• Equilibrium.

The following tests could be performed to support a myasthenia gravis diagnosis

Test with an ice pack

Your healthcare professional may apply an ice bag to your eyelid if it is drooping. Your healthcare practitioner takes out the bag after two minutes and assesses your drooping eyelid for potential improvement.

Blood examination:

Unusual antibodies that block the receptor sites where nerves instruct your muscles to contract may be detected by a blood test.

Stimulating nerves repeatedly

In this nerve conduction study, the testing muscles' skin is covered with electrodes that the physicians place there. Electricity is applied in tiny pulses across the electrodes (Kohler et al.,2019). These pulses gauge the nerve's ability to communicate with the muscle.The nerve is put through multiple tests during this examination to see whether weariness impairs the nerve's capacity to convey impulses. The test's results aid in the diagnosis of myasthenia gravis.

EMG, or single-fiber electromyography

This test examines the electrical activity going between your brain and your muscle. To test a single muscle fibre, a thin wire electrode must be inserted through your skin and into a muscle.

Visualising

prescribe an MRI or CT scan.

Tests for pulmonary function

These tests determine whether breathing is being affected by your disease.

Treatment

Medications

* Antagonists of cholinesterase

Medication like pyridostigmine (Mestinon, Regonal)enhances the nerve-muscle transmission. While these medications don't cure anything, they can help some people's muscles contract more forcefully and stronger.Intense salivation and perspiration, diarrhoea, nausea, and upset stomach are possible adverse effects.

* Corticosteroids

Prednisolone (Rayos), a corticosteroid, inhibits the immune system and reduces its capacity to create antibodies (Adamson et al., 2019). On the other hand, prolonged use of corticosteroids might have major adverse consequences. These include diabetes, weight gain, deteriorating bones, and an increased risk of some infections.

* Immunosuppressive medicines

It is also possible for your doctor to recommend additional medications that alter your immune system. These medications may consist of mycophenolate mofetil (Cellcept), cyclosporine (Sandimmune, Gengraf, and others), methotrexate (Trexall), azathioprine (Azasan, Imuran), or tacrolimus (Astagraf XL, Prograf, and others). Corticosteroids and these medications, which have a months-long half-life, may be combined.Immunosuppressant side effects can include increased infection risk as well as liver or renal damage (Terwiel et al., 2019).

 Intravenous treatment

 The following treatments are typically administered briefly to address symptoms that worsen out of the blue or prior to surgery or other treatments

* Plasmapheresis (plaz-muh-fuh-REE-sis)

This technique involves a dialysis-like filtering process. Your blood is run through a machine that eliminates the antibodies preventing messages from reaching your muscles from your nerve terminals. Nevertheless, the benefits of this surgery typically wear off within a few weeks (Llanos et al., 2019). Finding veins for therapy can become difficult after multiple surgeries.

Plasmapheresis carries some risks, such as bleeding, cramping in the muscles, irregular heartbeat, and blood pressure decline. An allergic reaction to the liquids used to replace the plasma occurs in certain individuals.

* Intravenous immunoglobulin (IVIg)

Your body receives normal antibodies from this therapy, which modifies the reaction of your immune system. Benefits can last three to six weeks and are typically noticeable in less than a week. Chills, headaches, vertigo, and fluid retention are among the moderate side effects that are occasionally experienced.

* Antibody that is monoclonal

Myasthenia gravis patients are administered eculizumab (Soliris) and rituximab (Rituxan) intravenously. These drugs are typically utilised in cases where no other therapy is effective. They may cause major adverse consequences.

Operation

There are some myasthenia gravis sufferers who have thymus gland tumours. A thymectomy—the removal of the thymus gland—is required if you have a tumour known as a thymoma.Eliminating the thymus gland may help alleviate symptoms even in the absence of a tumour. It may take years for this operation to start showing results, though.

There are two types of thymectomy procedures: minimally invasive and open. To access the chest and remove the thymus gland, an open surgical procedure involves the physician splitting the sternum, the middle portion of the breastbone.Tiny incisions are used in minimally invasive surgery to remove the thymus gland.

6. RHEUMATOID ARTHRITIS

The term" Arthritis" means joint inflammation, joints are places where two bones meet. There are various types of arthritis present, Rheumatoid arthritis is one of them. Rheumatoid arthritis is a disease which causes irreversible joint damage and disability (Starshinova et al., 2018). Generally diagnosis is done by combination of both clinical and laboratory features. Patient's suffering from polyarthritis ofjoints of the hands and feet generally faces problems like early morning stiffness and sometimes constitutional symptoms.Proteins prepared by our immune system can attack healthy tissue in our body, those are known as rheumatoid factors. Elevated levels of rheumatoid factor in blood are common in autoimmune diseases such as rheumatoid arthritis and Sjogren syndrome. Normal range of Rheumatoid factor level is 0-20 units per mililiter of blood.

Risk factor

Factors influencing high risk of rheumatoid arthritis

1. Gender

 Women are mostly affected to Rheumatoid arthritis as compared to men.

1. Age

Generally, occurs in middle age.

1. Smoking

Smoking cigarettes increase high risk of rheumatoid arthritis,if one havea genetic disposition for the development of the disease.

1. Overweight

People with excess obesity may face high risk of developing rheumatoid arthritis.

Pathophysiology

* Antigen presentation to T cells.
* T and B cell Multiplicity in the synovial lining angiogenesis.
* Build up of neutrophils in synovial fluid.
* Initial formation of Pannus ( a sheet of granulation tissue containing inflammation, known as the Pannus, proliferates from the synovial membrane and invades the joint
* Erosion of subchondral bone.
* Invasion of cartilage by Pannus proliferation of chondrocytes.
* Ligament laxity.
* Reduced range of motion, contractures, joint instability and systemic problems.

Complications

* Rheumatoid arthritis including medications increases the risk of osteoporosis (weakening of bones that increases the risk of fracture).
* Nodules of rheumatism - These hard lumps of tissue most often develop in the area of pressure points,like the elbows. But there nodules can develop anywhere in the body, even in lungs and heart.
* The immune system can be weakened by rheumatoid arthritis and many of the drugs used to treat it,which increases the risk of infections. Vaccination yourself against diseases including COVID-19, shingles, pneumonia,and influenza to protect yourself.
* Carpal tunnel syndrome - The nerve that supplies the majority of our hand and fingers may be compressed if rheumatoid arthritis affect our wrists.
* Lung condition - Breathlessness that worsens over time is a possible consequence of lung tissue inflammation and scaring in rheumatoid arthritis patients.
* Thyroid cancer - An increase risk of lymphomas, a class of blood malignancies that originate in the lymphatic system, is associated with rheumatoid arthritis.

Sign and symptoms

Rheumatoid arthritis symptoms and signs can include:

* swelling, warm, and sensitive joints
* stiffness in the joints that normally gets worse in the mornings and after sitting still
* weariness, fever, and appetite loss
* Smaller joints, especially those connecting your toes and fingers to your feet, are typically the first to be affected by early-stage rheumatoid arthritis.Symptoms frequently extend to the wrists, knees, ankles, elbows, hips, and shoulders as the illness worsens. Most of the time, the same joints on both sides of your body experience problems.

Rheumatoid arthritis patients also experience non-joint signs and symptoms in about 40% of cases. Potentially impacted areas include:

* Eyes
* Lungs
* Skin
* Heart
* Salivary glands
* Nerve tissue
* Bone marrow
* Blood vessels

The signs and symptoms of rheumatoid arthritis can vary widely in intensity and sometimes appear and go, times of relative remission, during which the pain and swelling subside or vanish, alternate with times of heightened disease activity, known as flares. Rheumatoid arthritis can cause joints to move and distort over time.

Diagnosis

The most frequent systemic inflammatory arthritis to be diagnosed is rheumatoid arthritis. The most common groups afflicted are women, smokers, and anyone with a family history of the condition. Having at least one joint with noticeable swelling that cannot be attributed to another illness is a requirement for diagnosis. The more minor joints impacted, the higher the chance ofbeing diagnosed with rheumatoid arthritis. Rheumatoid factor or anti-citrullinated protein antibody, as well as an increased C-reactive protein level or erythrocyte sedimentation rate, all point to a diagnosis of rheumatoid arthritis in an inflammatory arthritis patient. Renal and hepatic function tests, as well as a complete blood count with differential, should be part of the first laboratory evaluation. Testing for tuberculosis, hepatitis B, and hepatitis C is recommended for patients receiving biologic drugs. Early treatment with disease-modifying antirheumatic medications is possible with an earlier diagnosis of rheumatoid arthritis.

Treatment

To manage the disease, drug combinations are frequently employed. The first-line treatment for rheumatoid arthritis is usually methotrexate. Tumour necrosis factor inhibitors, for example, are considered biologic medicines and can be combined for dual therapy. Reduction of joint discomfort and swelling, avoidance of radiographic damage and apparent deformity, and maintenance of job and personal activities are the objectives of treatment (Starshinova et al.,2020). For patients with significant joint deterioration whose symptoms are not well controlled with medicine, joint replacement is indicated.

1. SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE), another name for lupus, is a chronic (long-term) inflammatory illness that can affect nearly every area of the body, with the skin,joints, kidneys, heart, lungs, bones, blood, and brain being the most commonly affected. An individual with systemic lupus erythematosus has an autoimmune illness, which means that their own immune system targets and damages their own healthy cells and tissues. No two persons with lupus have the same exact form of the disease because it can affect any organ system. Nonetheless, the majority of individuals suffering from lupus or systemic lupus erythematosus (SLE) report experiencing remissions or times when their symptoms appear tobe minimal or nonexistent, and flare-ups or relapses, which are marked by increased inflammation (Table 2).

**Table 2:**Various antigens their nature, prevalence and association with systemic lupus erythematosus

|  |  |  |  |
| --- | --- | --- | --- |
| Antigen | Nature | Prevalence in SLE | Association |
| Hep-2 cell nuclei | ANA | > 95% | Numerous autoimmune diseases |
| dsDNA | Native, double-stranded DNA | 40%-60% | High specificity for lupus, titers correlate with disease activity |
| Histones |  | 50%-70% | Drug-induced lupus |
| Sm | Small nuclear RNAs complexed with protein | 20% - 30% | High specificity for lupus |
| Nuclear RNP (U1 RNP) | Small nuclear RNAs complexes with protein | 30% -40% | $$MCTD$$ |
| SS-A (Ro) | Protein associated with RNA | 30% -50% | $Sjögren sy$ndrome, subacute cutaneous lupus, neonatal lupus with heart block, SLE with interstitial pneumonia |
| SS-B(La) | Protein bound to small RNA | 10% -15% | $Sjögren sy$ndrome |
| Ku | DNA binding proteins | 10% -39% | MCTD, scleroderma, primary pulmonary hypertension |
| Ki | Nuclear protein | 8%- 31% | Arthritis, pericarditis, and pulmonary hypertension in patients with SLE |
| PCNA/cyclin | Cell cycle protein | 3% |  |
| Hsp90 | Heat shock protein | 50% | Polymyositis |
| p ribosomal protein, rRNP | Ribosomal phosphoprotein | 10% | Neuropsychiatric SLE |
| ssDNA | Single-stranded DNA | 70% |  |
| β2-glycoprotein1 | Anionic proteins, cardiolipin | 25% | Lupus anticoagulant, arterial and venous thromboses, neurologic disease |

The following are risk factors for systemic lupus

genetic predisposition, -DR3 haplotype among others, including HLA-B8ultraviolet (UV) radiation from sunlightinfection by viruses, especially Epstein-Barr virus hormones, toxins, such smoke from cigarettes. Smokers have higher rates of both milder and more severe SLE. Moreover, smoking reduces the efficiency of other treatments like antimalarial medications.

Types of Systemic lupus erythematosus

1. Systemic lupus erythematosus -The most prevalent type of lupus is systemic lupus erythematosus (SLE)
2. Cutaneous lupuserythematosus (CLE)

Skin-specific lupus or cutaneous lupus erythematosus (CLE) (which includes discoid lupus erythematosus (DLE) and subacute cutaneous lupus erythematosus (SCLE) Skin lupus erythematosus (CLE) can manifest either systemically involved or not.

III) Drug-induced lupus erythematosus (DILE)

A condition similar to lupus that is brought on by some pharmaceutical medications. Characteristics of drug-induced lupus erythematosus (DILE) set it apart from typical (idiopathic) SLE. For instance, DILE appears concurrently with drug exposure and disappears after treatment is finished.

IV) Neonatal lupus erythematosus

A rare disorder known as neonatal lupus erythematosus affects newborns of lupus-affected women. Neonatal lupus refers to lupus that affects infants born to women who have the disease. Anti-Sjögren's syndrome-related antigen A (also known as anti-Ro; SSA/Ro) or anti-Sjögren's syndrome-related antigen B (also known as anti-La; SB/La) antibodies from the mother pass through the placenta and cause neonatal lupus, which is characterised by congenital heart block, photosensitivity rash, cytopenia, and abnormalities of the liver (Nydegger et al., 1974).

V) Child-onset lupus or juvenile-onset systemic lupus

Juvenile-onset systemic lupus erythematosus (JSLE) or child-onset lupus erythematosus. SLE, often known as "child-onset lupus" or "juvenile-onset systemic lupus," can also affect children. It has been separated into a distinct class because of the clinical distinctions between usual adult-onset SLE and child-onset SLE.

## Complications of Lupus:

Particularly when it is active, lupus disease may cause young women to develop accelerated atherosclerosis, or artery blockage, which may result in heart attacks, heart failure, and strokes. Therefore, it is imperative that lupus patients exercise and reduce other heart disease risk factors, such as smoking, high blood pressure, and high cholesterol, in addition to managing their condition.One of the most prevalent and dangerous symptoms of lupus is inflammation of the kidneys. Dialysis and renal failure may result if it remains undiagnosed. By obtaining treatment as soon as kidney disease manifests, you can contribute to preventing these dangerous consequences. Among these indicators are:

* High blood pressure
* Swollen feet and hands
* Puffiness around your eyes
* Changes in urination (blood or foam in the urine, going to the bathroom more often at night, or pain or trouble urinating)

Inflammation caused by systemic lupus erythematosus (SLE) can affect many areas of your body, including your:

Kidneys

Kidney failure is one of the main causes of death for lupus patients, and the disease can cause severe kidney damage (lupus nephritis).

**Brain and central nervous system:** The central nervous system and the brain. Lupus can cause brain damage that manifests as headaches, vertigo, altered behaviour, visual issues, strokes, or seizures. Many lupus sufferers struggle with memory loss and may find it difficult to articulate their ideas.

**Blood and blood vessels**

vascular and blood flow, Anaemia, or low red blood cell count, and a higher risk of bleeding or blood clotting are among the blood issues that can result from lupus. Vasculitis, or inflammation of the blood vessels, is another effect it may have.

Lungs

Breathing difficulties may result from an inflammation of the lining of the chest cavity, which is more likely in people with lupus. Pneumonia and lung bleeding are also potential outcomes.

Heart

 Inflammation of the heart muscle (myocarditis), arteries (arteritis), or cardiac membranes (pericarditis) can all be brought on by lupus. There is also a significant rise in the risk of heart attacks and cardiovascular disease.

## Lupus Causes

Your immune system defends your body against infections and cancer when it is in good health. Your body's immune system targets healthy tissue when you have lupus, an autoimmune illness. Your genetic makeup and environmental factors most likely have a combined role in your development of lupus. But neither the aetiology nor the factors influencing the disease's variable manifestation are understood. Physicians are aware that a variety of elements are necessary, such as the "correct" genetic composition, exposure to the environment, and features unique to each organ. In addition, lupus patients may have trouble getting rid of ageing and damaged cells from their bodies, which constantly stimulates the immune system and causes an aberrant reaction.

It seems that exposure to environmental triggers for lupus can cause the disease to flare up in persons who have a hereditary propensity for it. In most cases, however, the cause of lupus remains unknown. Among the possible triggers are:

* Sunlight: Exposure to the sun may bring on lupus skin lesions or trigger an internal response in susceptible people.
* Infections: Having an infection can initiate lupus or cause a relapse in some people.
* Medications: Lupus can be triggered by certain types of blood pressure medications, anti-seizure medications and antibiotics. People who have drug-induced lupus usually get better
* when they stop taking the medication. Rarely, symptoms may persist even after the drug is stopped.

## Lupus Signs and Symptoms

##  Many times, lupus patients experience non-lupus-specific symptoms. Fever, exhaustion, weight loss, blood clots, and patchy or hairline-related hair loss are a few of them. In addition, they could experience impaired circulation in their fingers and toes, heartburn, and stomach ache. Miscarriages can happen to pregnant women.Nonetheless, skin symptoms are present in about 90% of patients with systemic lupus erythematosus. The following are the most typical places where systemic lupus erythematosus skin lesions occur:

* Face, especially cheeks and nose
* Sun-exposed skin on arms, backs of hands, upper chest, and upper back due to increased sensitivity to sunlight (photosensitivity)
* Fingers and fingernails
* Mouth or nose
* Scalp

A butterfly rash (malar blush) is a characteristic cutaneous feature in systemic lupus erythematosus. After being exposed to the sun, redness around the cheekbones and nose bridge may arise weeks before other symptoms do.Photo-distribution, or skin exposed to the sun, can result in a rash, particularly on the backs of the hands and fingers. The arms and trunk may also be affected by this rash, which takes the form of red, scaly areas.Tiny, painless ulcers can appear in the mouth, particularly on the roof of the mouth, or more frequently in the nose.Hair loss is a possible symptom of lupus that affects the scalp skin. Patchiness or thinning throughout the scalp, particularly at the temples, are possible

Prevention of Lupus

Nobody is aware of a preventative measure for systemic lupus erythematosus (SLE) because its cause is unclear. By minimising sun exposure (wearing hats, long sleeves, and sunscreen), getting enough sleep, and taking prescribed medicine, flares of lupus may be lessened. Taking calcium and vitamin D supplements can lower your risk of osteoporosis.

## Lupus Diagnosis

No one test can diagnose lupus. The combination of blood and urine tests, signs and symptoms, and physical examination findings leads to the diagnosis. Unusual blood tests, including:

* Low blood cell counts, such as low platelets, white blood cells, or anaemia.
* Antinuclear antibodies that are positive (ANA) result: nearly all lupus patients have specific aberrant antibodies, such as anti-double-strand DNA (also known as anti-dsDNA), anti-Smith (also known as anti-Sm), or antiphospholipid antibodies, which have the ability to trigger the body to start attacking itself.Your doctor will conduct a number of blood tests to confirm the diagnosis if they believe you have lupus based on your symptoms. The ANA blood screening test is the most significant. A negative ANA indicates the absence of lupus. If your ANA test results are positive, you may have lupus and require more testing. Antibodies specific to the diagnosis of lupus, such as anti-dsDNA and anti-Sm, are part of these blood tests.Antiphospholipid antibodies indicate an increased risk for specific problems, such as blood clots or miscarriage. Doctors also may evaluate levels of particular complement proteins (a part of the immune system) in the blood, to assist detect the disease and follow its progress (Bogdanos et al., 2017).

## Lupus Treatment

## The lupus is a long-term illness. Remission induction is the goal of treatment. The kind and severity of your symptoms will determine how you are treated. A thorough discussion of the advantages and hazards with your doctor is necessary to decide what medications to use and whether your symptoms and signs should be addressed. It’s possible that you and your doctor will need to adjust your medicine or dosage as your symptoms come on and off. The following drugs are most frequently used to treat lupus:

NSAIDs, ornonsteroidal anti-inflammatory medications

For the treatment of lupus-related pain, edoema, and fever, over-the-counter NSAIDs like ibuprofen (Advil, Motrin IB, and others) and naproxen sodium (Aleve) may be utilised. Prescriptions are available for stronger NSAIDs. Stomach bleeding, kidney issues, and an elevated risk of heart problems are among the side effects of NSAIDs. Prior to using any over-the-counter (OTC) medication for your lupus, always get your doctor's approval.

Immunosuppressive medicines

In severe lupus patients, immune-suppressive medications may be beneficial. Trexall, mycophenolate mofetil (CellCept), and azathioprine (Imuran, Azasan) are a few examples. Mycophenolate mofetil has recently been used to treat lupus nephritis, a severe kidney illness associated with the disease. An increased risk of infection, liver damage, lower fertility, and an increased risk of cancer are possible side effects.

Combination therapy

To manage lupus and avoid tissue damage, medical professionals may mix and match a few different drugs. Every therapy has advantages and disadvantages. The majority of immune-suppressive drugs have potential negative effects and need to be closely watched. A higher risk of infections, nausea, vomiting, diarrhoea, hair loss, high blood pressure, and osteoporosis (weak bones) are possible side effects of these medications. When a medication has negative effects or the disease enters a remission, rheumatologists may decide to discontinue it altogether or reduce the dosage. Because of this, it's critical to have thorough and regular physical examinations as well as laboratory testing to monitor your symptoms and adjust your care as necessary.

Steroids

Prednisone and other corticosteroids help reduce lupus-related inflammation. Steroids at high dosages, including methylprednisolone (A-Methapred, Medrol), are frequently used to treat severe renal and brain diseases. Weight gain, bruising easily, osteoporosis (thinning bones), high blood pressure, diabetes, and an elevated risk of infection are some of the side effects. Larger dosages and longer treatment regimens carry a larger risk of adverse effects (Song etal., 2020).

8. CONCLUSION

Symptoms of inflammation have been linked to autoimmune diseases, and autoantibody counts in patients may help with diagnosis and severity assessments of the condition, which may be important for treatment. Myasthenia gravis is the most well-understood autoimmune disease; studies on the disease have advanced our knowledge of the basic principles underlying neuromuscular transmission. Rheumatoid arthritis and several medications used to treat it may decrease the immune system, which raises the risk of infections. Methotrexate is often the first line of therapy for rheumatoid arthritis. Biologic medications, such as tumour necrosis factor inhibitors, may be used in combination for dual treatment. Risk factors for systemic lupus genetic predisposition, including the -DR3 haplotype, include exposure to sunlight, HLA-B8 ultraviolet (UV) radiation, viral infection, including Epstein-Barr virus hormones, toxins, and cigarette smoke. Over-the-counter NSAIDs, such as ibuprofen (Advil, Motrin IB, and others) and naproxen sodium (Aleve), may be used to treat fever, edoema, and pain associated with lupus. There is a higher chance of side effects with higher doses and longer treatment plans.

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