

Autoimmune Disorder An Overview

Yash Arvind Hete¹ and Mr. Dipak Tonchar²

Student, Vardhaman College of Pharmacy, Karanja (Lad), Maharashtra, India¹

Guide and Assistant Professor, Vardhaman College of Pharmacy, Karanja (Lad), Maharashtra, India²

Abstract: *Autoimmune diseases are a group of disorders characterized by the immune system erroneously attacking the body's own cells, mistaking them for foreign invaders. This maladaptive immune response, driven by the production of autoantibodies, results in tissue damage and dysfunction. Autoimmune conditions may target specific organs, such as the pancreas in type 1 diabetes, or manifest systemically, as seen in systemic lupus erythematosus (SLE). Currently, over 80 distinct autoimmune diseases have been identified, with their prevalence on the rise in industrialized nations.*

The etiology of autoimmune diseases is multifactorial, involving genetic predispositions, environmental triggers, and potential infections. Common examples include rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease, though autoimmune mechanisms are also implicated in conditions like arteriosclerosis and schizophrenia. Notably, autoimmune diseases exhibit a pronounced sex disparity, disproportionately affecting females, likely due to hormonal and genetic differences. Understanding the shared pathogenesis and diverse manifestations of autoimmune diseases is critical to developing targeted treatments and addressing their growing global burden

Keywords: systemic lupus erythematosus

I. INTRODUCTION

An autoimmune disease is a condition in which your immune system attacks your body. The immune system usually guards against bacteria and viruses. When it senses these foreign invaders, it sends out an army of fighter cells to attack them. Usually, the immune system can tell the difference between foreign cells and your own cells. In autoimmune disease, the immune system mistakes part of your body, like your joints or skin, as foreign. It releases proteins called autoantibodies that attack healthy cells.

Autoimmune diseases are a range of diseases in which the immune response to self-antigens results in damage or dysfunction of tissue. It can be systemic or can affect specific organs. Autoimmune diseases represent a family of at least 80 illnesses that share a common pathogenesis, that is, an immune-mediated attack to the body's own organs. Many of the diseases are increasing in frequency in industrialized countries.

Autoimmune diseases are strongly associated with genetic, infectious, and environmental factors. Autoimmune diseases include rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and others. There are also implications of autoimmune pathology in such common heart problems as arteriosclerosis, inflammatory bowel disease, schizophrenia, etc. For most autoimmune diseases, there is a clear sex difference, whereby females are generally more frequently affected than males.

Examples:

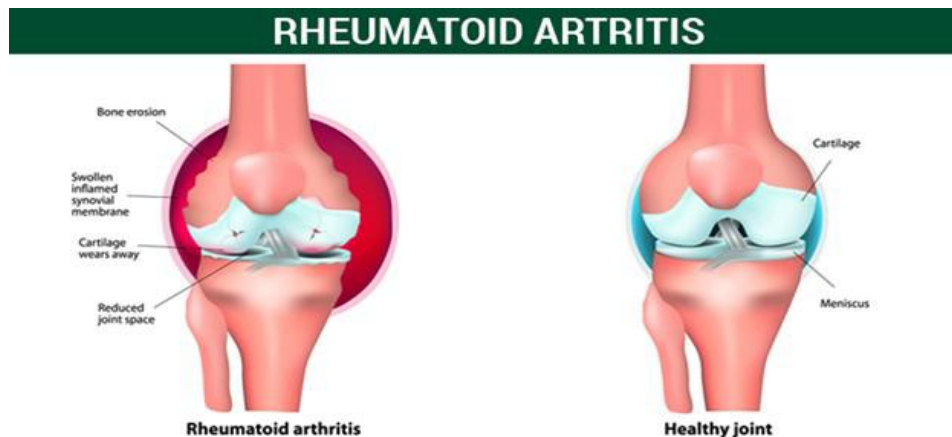
- Rheumatoid Arthritis
- Multiple Sclerosis
- Systemic Lupus Erythematosus
- Inflammatory Bowel Disease
- Addison's Disease
- Graves' Disease
- Hashimoto's Disease
- Myasthenia Gravis
- Pernicious Anemia

- Celiac Disease
- Vitiligo
- Autoimmune Orchitis
- Psoriasis
- Dermatomyositis
- Linear Morphea
- Acquired Hemophilia A
- Goodpasture Syndrome
- Narcolepsy
- Sympathetic Ophthalmia

There are more than 80 types of autoimmune diseases that affect a wide range of body parts. The most common diseases are listed above

Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune disease that results in a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks **synovial joints**. An autoimmune disorder, rheumatoid arthritis occurs when your immune system mistakenly attacks your own body's tissues. Unlike the wear-and-tear damage of osteoarthritis, rheumatoid arthritis affects the lining of your joints, causing a painful swelling that can eventually result in bone erosion and joint deformity.



Symptoms of Rheumatoid Arthritis:

Joint inflammation is a hallmark of rheumatoid arthritis.

Stiffness:

The joint becomes harder to use and may have a limited range of movement. "Morning stiffness" is one of the primary symptoms of rheumatoid arthritis.

Swelling:

Fluid enters the joint, making it puffy, which also contributes to stiffness.

Pain:

Inflammation inside a joint makes it sensitive and tender. Prolonged inflammation can cause damage that contributes to pain.

Redness and Warmth:

The joints may appear warmer and more pink/red compared to the neighboring skin

Other Symptoms:

Rheumatoid arthritis can affect various areas of the body, causing:

- Fatigue

- Malaise
- Loss of appetite
- Muscle aches

Causes of Rheumatoid Arthritis:

Immunologic Factors:

It occurs when the immune system attacks the synovium, the lining of the membrane that surrounds the joints.

Genetic Factors:

Approximately half of the risk for rheumatoid arthritis is believed to be genetic.

Infectious Agents:

Numerous infectious agents, including mycoplasma organisms, have been suggested as potential causes of RA over the decades.

Other Factors:

- **Smoking:** The most significant non-genetic risk factor, with RA being up to three times more common in smokers than in non-smokers, particularly in men.
- **Vitamin D Deficiency:** More common in patients with rheumatoid arthritis than in the general population. Vitamin D is essential for calcium absorption in the gut, maintaining serum calcium and phosphorus concentrations, and enabling normal bone mineralization.

Pathophysiology

The pathogenesis of rheumatoid arthritis is not completely understood. An external trigger (e.g., cigarette smoking, infection, or trauma) can initiate an autoimmune reaction, leading to synovial hypertrophy and chronic joint inflammation. Early events in the pathological process include synovial cell hyperplasia and endothelial cell activation, which progress to uncontrolled inflammation, cartilage and bone destruction, and damage to ligaments, tendons, and blood vessels. Genetic factors and immune system abnormalities propagate the disease.

Complications of Rheumatoid Arthritis:

Skin Problems:

Rheumatoid arthritis primarily affects joints, but the disease and medications used to treat it can also cause skin issues like sun sensitivity, rashes, and nodules.

Heart Involvement:

- Can cause inflammation in the lining around the heart (pericarditis).
- Increased risk of clogged arteries, leading to chest pain and heart attacks.

Eye Involvement:

- Affects less than 5% of RA patients.
- Symptoms include red, painful, or dry eyes.

Joint Impact Progression

- Progresses to larger joints like knees, ankles, elbows, hips, and shoulders.
- Symptoms typically occur symmetrically.

Tests and Diagnosis of Rheumatoid Arthritis:

Physical Exam:

To check joints for swelling, redness, and warmth, and to assess reflexes and muscle strength.

X-Rays:

Used to track the progression of rheumatoid arthritis over time, particularly in the hands and feet.

Advanced Imaging Techniques:

MRI and ultrasound may also be utilized.

Treatment of Rheumatoid Arthritis:

There is no cure for rheumatoid arthritis. Treatments aim to reduce inflammation, relieve pain, and prevent or slow joint damage.

Medications:

NSAIDs:

Nonsteroidal anti-inflammatory drugs relieve pain and reduce inflammation (e.g., aspirin, ketoprofen, piroxicam).

Steroids:

Corticosteroids like prednisone reduce inflammation and slow joint damage. Side effects include bone thinning, cataracts, weight gain, and diabetes.

DMARDs (Disease-Modifying Antirheumatic Drugs):

Slow the progression of the disease and prevent joint damage. Examples include gold compounds, methotrexate, and sulfasalazine.

Immunosuppressants:

Suppress the immune system to control disease progression (e.g., cyclosporine, azathioprine).

Other Drugs:

Examples include anakinra, abatacept, rituximab, tocilizumab, and tofacitinib.

Therapy:

Physical or occupational therapy to maintain joint flexibility and suggest ergonomic modifications for daily tasks.

Surgery:

- Total joint replacement
- Tendon repair
- Joint fusion

Graves' Disease:

Graves' disease is an autoimmune disorder in which the immune system attacks the thyroid gland, causing it to overproduce hormones that regulate metabolism.

Symptoms of Graves' Disease:

- Anxiety and irritability
- Fine tremor of hands or fingers
- Heat sensitivity and increased sweating
- Weight loss despite normal eating habits
- Enlarged thyroid gland (goiter)
- Sleep disturbances
- Increased or irregular heartbeats
- Bulging eyes and vision problems
- Reddened or inflamed eyes

Causes of Graves' Disease:

Genetics:

Likely a genetic predisposition that increases susceptibility.

Gender:

Risk is about eight times higher in women than men.

Age:

Typically develops before age 40.

Pregnancy:

Risk increases with pregnancy or recent childbirth, especially in women with genetic susceptibility.

Smoking:

Smokers have an increased risk of Graves' disease and Graves' ophthalmopathy.

Stress:

Emotional or physical stress can trigger the onset of Graves' disease in genetically susceptible individuals

Complications of Graves' Disease:

1. Pregnancy Issues:

o Possible complications during pregnancy include miscarriage, preterm birth, fetal thyroid dysfunction, poor fetal growth, maternal heart failure, and preeclampsia. Preeclampsia is a serious condition marked by high blood pressure and other symptoms that can affect both the mother and baby.

2. Heart Disorders:

o If untreated, Graves' disease can lead to heart rhythm disorders, changes in the structure and function of the heart muscles, and heart failure, where the heart cannot pump enough blood to meet the body's needs.

Thyroid Storm:

A rare but life-threatening complication, thyroid storm (also known as accelerated hyperthyroidism or thyrotoxic crisis) occurs when hyperthyroidism becomes severe or inadequately treated. Symptoms include fever, sweating, vomiting, diarrhea, delirium, weakness, seizures, irregular heartbeat, jaundice (yellow skin and eyes), severe low blood pressure, and coma. Immediate emergency care is required.

Brittle Bones (Osteoporosis):

Untreated hyperthyroidism can lead to weak, brittle bones due to the interference of excessive thyroid hormone with calcium incorporation into bones, making them more fragile.

Pathophysiology of Graves' Disease:

Immune Mechanism:

In Graves' disease, the body produces IgG autoantibodies that target the **thyrotropin receptor** on thyroid cells. These antibodies bind to and activate the receptor, leading to the uncontrolled production of thyroid hormones. This autoimmune response is central to the manifestation of hyperthyroidism in Graves' disease.

Tests and Diagnosis:

Physical Examination:

An enlarged thyroid (goiter), bulging eyes (exophthalmos), and signs of increased metabolism such as rapid pulse and high blood pressure can be observed.

Blood Tests:

Elevated levels of **T4** (thyroxine) and suppressed levels of **TSH** (thyroid-stimulating hormone) are typical indicators of Graves' disease.

Radioactive Iodine Uptake Test:

This test measures how quickly the thyroid gland takes up iodine. A high uptake of iodine is consistent with Graves' disease

Treatment of Graves' Disease

Beta-Blockers:

Used to control symptoms like rapid heart rate, anxiety, and sweating.

Antithyroid Medications:

Medications like **Methimazole** or **Propylthiouracil** are used to inhibit thyroid hormone production.

Radioactive Iodine:

This treatment involves destroying all or part of the thyroid gland, effectively controlling hormone overproduction.

Surgery:

If medications or radioactive iodine are not tolerated or effective, thyroidectomy (removal of the thyroid gland) may be necessary. This is a permanent option but often results in hypothyroidism, requiring lifelong hormone replacement therapy

Monitoring:

After treatment, most patients develop hypothyroidism, which needs management through thyroid hormone replacement.

Inflammatory Bowel Disease (IBD):

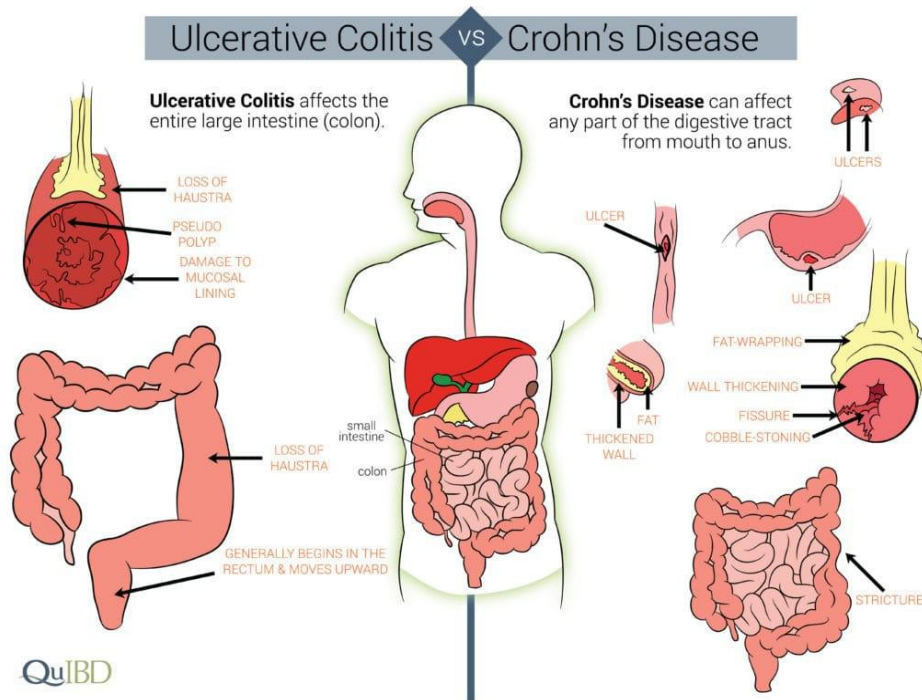
IBD refers to chronic conditions causing inflammation of the gastrointestinal (GI) tract. The two most common forms are **ulcerative colitis** and **Crohn's disease**.

Ulcerative Colitis (UC):

UC causes long-lasting inflammation and ulcers in the innermost lining of the large intestine (colon) and rectum. The inflammation typically starts in the rectum and may extend upwards into the sigmoid colon, descending colon, transverse colon, and in some cases, the entire colon.

Crohn's Disease:

Crohn's disease can affect any part of the gastrointestinal tract but most commonly involves the terminal ileum and caecum. It may extend into the ascending colon. Both UC and Crohn's disease share symptoms like diarrhea, abdominal pain, fatigue, and weight loss



Symptoms of IBD:

Ulcerative Colitis:

Stool urgency, fatigue, increased bowel movements, mucus in stool, abdominal pain, and blood in stool are common symptoms.

Crohn's Disease:

Symptoms include abdominal pain, diarrhea, weight loss, fatigue, and in some cases, blood in the stool. Severe Crohn's disease may also involve symptoms outside the intestines, such as kidney stones and iron deficiency

Causes of Inflammatory Bowel Disease (IBD):

Immunological Factors:

The exact cause of IBD is unknown, but it is believed to involve a dysregulated immune response. A functioning immune system usually protects the body from harmful pathogens and foreign organisms. However, in IBD, the immune system responds incorrectly to environmental triggers such as viruses and bacteria, causing inflammation in the gastrointestinal tract.

Inflammatory Bowel Disease (IBD):

Inflammatory Bowel Disease (IBD) is an idiopathic disorder caused by a dysregulated immune response to host intestinal microflora. The term **IBD** commonly refers to two distinct conditions: **ulcerative colitis** and **Crohn's disease**. While these diseases share some similarities, they also have distinct morphological appearances and manifestations.

Types of IBD:

Ulcerative Colitis

Ulcerative colitis causes long-lasting inflammation and sores (ulcers) in the innermost lining of the large intestine (colon) and rectum. Classically, it begins in the rectum and extends upward in a continuous manner, affecting the sigmoid colon, descending colon, transverse colon, and sometimes the entire colon.

Crohn's Disease

Crohn's disease can involve any part of the gastrointestinal (GI) tract but most commonly affects the terminal ileum (last 15–25 cm) and may extend into the caecum and sometimes into the ascending colon. Unlike ulcerative colitis, Crohn's disease may present with patchy inflammation.

Symptoms:

Ulcerative Colitis

- Stool urgency
- Fatigue
- Increased bowel movements
- Mucus in stool
- Abdominal pain
- Blood in stool

Crohn's Disease

- Abdominal pain
- Diarrhea
- Weight loss
- Fatigue
- May present with bloody stool
- Fever
- Severe cases may include symptoms outside the intestinal tract, such as kidney stones or iron deficiency.

Causes of Inflammatory Bowel Disease:

The exact cause of IBD remains unknown, but it is believed to result from a combination of genetic, environmental, and immunological factors.

Immunological Factors

IBD is associated with a defective immune system.

Normally, the immune system attacks harmful organisms (e.g., viruses and bacteria) to protect the body.

In IBD, the immune system responds abnormally to environmental triggers, causing inflammation in the gastrointestinal tract.

Exogenous Factors:

Microbial Factors

Evidently, several pathogens may be associated with IBD, such as:

Bacteria: *Mycobacterium avium* subspecies *paratuberculosis*, *Clostridium difficile*, *Escherichia coli*, *Listeria monocytogenes*, and *Campylobacter concisus*.

Viruses: Cytomegalovirus, Epstein-Barr virus, and measles virus.

Parasites: Various pathogenic parasites may also contribute to the development and progression of the disease.

Smoking

Smoking has been implicated in the causation of Crohn's disease, with studies showing a significant association

Oral Contraceptives

Long-term use of oral contraceptives has been linked to an increased risk of developing Crohn's disease in some studies. However, no conclusive evidence suggests an increased risk for ulcerative colitis.

Psychological Factors:

i) Stress

ii) Emotional or Physical Trauma

Nonsteroidal Anti-inflammatory Medications (NSAIDs):

Medications such as ibuprofen (*Advil*, *Motrin IB*), naproxen sodium (*Aleve*), and diclofenac sodium may increase the risk of developing IBD or exacerbate symptoms in those already diagnosed with the disease.

Family History:

Having a close relative, such as a parent or sibling, with IBD increases the likelihood of developing the disease.

Complications:

Complications of Crohn's Disease

- **Bowel Obstruction:** Chronic inflammation can cause the bowel wall to thicken and narrow, potentially leading to obstruction and requiring surgical intervention.
- **Malnutrition:** Reduced ability of the intestine to absorb nutrients, potentially causing anemia due to low iron or vitamin B12 levels.
- **Fistulas:** Inflammation may create an atypical connection between different body parts, such as a perianal fistula, which may lead to infection or abscess formation.
- **Anal Fissure:** Small tears in the tissue lining the anus, often associated with painful bowel movements and the potential development of perianal fistulas.

Complications of Ulcerative Colitis

- **Toxic Megacolon:** A severe condition where the colon rapidly widens and swells.
- **Perforated Colon:** A life-threatening complication often resulting from toxic megacolon but can occur independently.

Pathophysiology:

The location and appearance of inflammatory lesions differ significantly between Crohn's disease and ulcerative colitis, with distinct characteristics defining each condition

Crohn's Disease:

In Crohn's disease, inflammatory lesions extend through the bowel wall, often creating lesions that can simultaneously occur in separate areas. Granulomas typically form first, followed by ulceration and abscess formation. Fistulas may develop between the affected areas and the bladder, vagina, or rectum. Repeated episodes lead to a "cobblestone" appearance in the gut wall, with permanent scarring and constriction.

Ulcerative Colitis (UC):

The characteristic lesion in UC is the crypt abscess, a pus-filled, necrotic lesion that starts at the base of the tubular glands in the intestinal mucous membrane. These lesions ulcerate and bleed during flare-ups, healing with scarring and constriction. The immune mechanism that suppresses inflammation in a healthy individual is defective in IBD, resulting in uncontrolled inflammation. This is due to the activation of CD4+ T cells, which secrete cytokines that promote inflammation in the gut.

Tests and Diagnosis:

IBD is diagnosed through a combination of medical history, physical examination, imaging tests, and laboratory tests:

Physical Examination:

Tenderness in the abdomen.
Signs of anemia (e.g., paleness).
Joint swelling or skin rashes.
Mouth ulcers or tenderness in the stomach due to inflammation.

General Investigations:

Blood Tests: To detect changes in red and white blood cells:

Red Blood Cells: Reduced or smaller red blood cells may indicate anemia.

White Blood Cells: Elevated white blood cells suggest inflammation or infection.

Certain antibodies can help identify specific types of IBD (e.g., Crohn's or ulcerative colitis).

Stool Tests: Used to rule out other causes of gastrointestinal diseases.

Upper Gastrointestinal (UGI) Series: Examines the upper part of the digestive tract.

Upper Gastrointestinal Endoscopy: Looks at the interior of the esophagus, stomach, and duodenum.

Sigmoidoscopy/Colonoscopy: These tests are used to examine the colon, with colonoscopy being preferred as it allows for full examination.

Abdominal X-ray: Used to detect complications or obstructions in the abdomen.

CT Scan: Provides detailed images to diagnose complications, such as obstructions.

MRI: Uses magnetic fields to create detailed images of internal structures

Treatment:

Treatment of IBD involves medications to control symptoms, reduce inflammation, and maintain remission:

Anti-inflammatory Drugs:

Aminosalicylates (ASAs): Medications like Sulfasalazine, Mesalamine, Basaloid, and Olsalazine help reduce inflammation, particularly for ulcerative colitis.

Corticosteroids: More powerful anti-inflammatory drugs (e.g., prednisone, hydrocortisone) may be used for flare-ups, either orally or intravenously.

Immunosuppressants:

Drugs like Azathioprine, 6-Mercaptopurine, Methotrexate, and Cyclosporine help suppress the immune system, reducing inflammation and improving symptoms.

Other Medications:

Antibiotics: Used to manage infections, especially in patients with fever.

Antidiarrhoeal Medications: Caution is advised as they may worsen certain conditions like toxic megacolon.

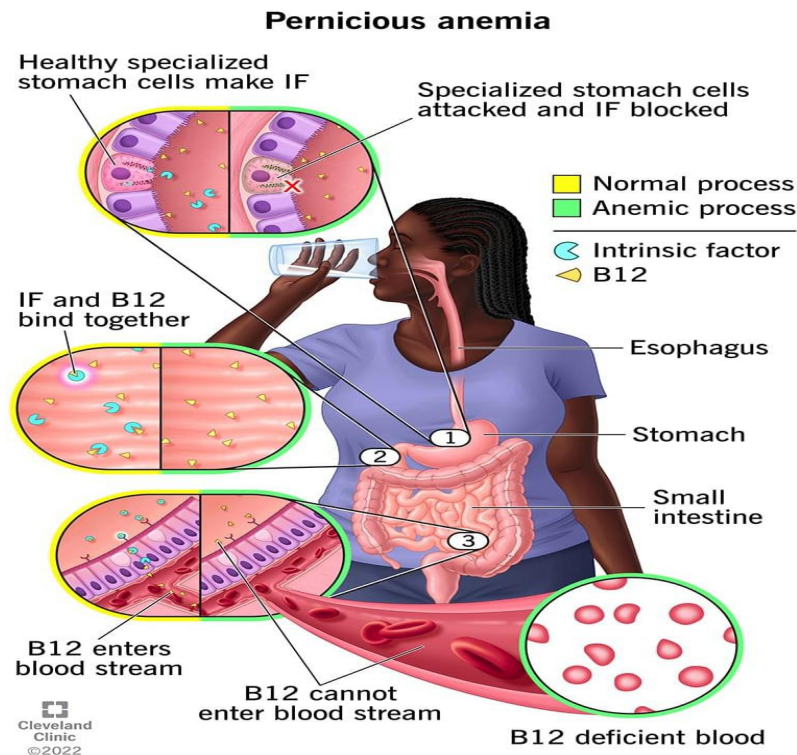
Iron Supplements: For anemia caused by chronic intestinal bleeding.

Bowel Rest: Sometimes prescribed for Crohn's disease to reduce symptoms and allow the bowel to heal.

Surgery: In cases of severe complications or ineffective medication, surgery may be necessary to remove damaged portions of the bowel. Although surgery can help manage symptoms, it does not cure Crohn's disease

Pernicious Anemia:

Pernicious anemia is a condition caused by the inability of the stomach to produce intrinsic factor (IF), which is necessary for the absorption of vitamin B12. This autoimmune disorder leads to vitamin B12 deficiency, which can cause severe damage to the nervous system if untreated.



Symptoms:

Early symptoms include diarrhea, constipation, loss of appetite, pale skin, shortness of breath (especially during exercise), and heartburn.

As the deficiency worsens, neurological symptoms like confusion, short-term memory loss, depression, numbness, tingling, balance issues, and hallucinations may occur.

Causes:

- Surgery: Removal of part of the stomach or small intestine reduces vitamin B12 absorption.
- Small Intestine Bacterial Overgrowth (SIBO): Excessive bacteria in the small intestine may consume vitamin B12.

- Medications: Some antibiotics, diabetes medications, and anticonvulsants can affect B12 levels.
- Diet: A vegan or vegetarian diet may lack sufficient vitamin B12.
- Conditions: Diseases like celiac or Crohn's disease may impair B12 absorption.

Tests and Diagnosis:

- Vitamin B12 Levels: A direct measure of B12 deficiency.
- Lactate Dehydrogenase (LDH): Elevated LDH can indicate pernicious anemia.
- Methylmalonic Acid (MMA): High levels confirm B12 deficiency.
- Homocysteine Levels: Elevated levels can suggest B12 deficiency.
- Antibody Tests: Can detect antibodies attacking the parietal cells or intrinsic factor.
- Endoscopy: To check for damage or atrophy in the stomach lining.

Treatment:

- Vitamin B12 injections that are followed closely over time.
- Following the blood level of vitamin B12 over course of therapy.
- Vitamin B12 injections can be given daily/weekly until the B12 levels return to a healthy range.

II. CONCLUSION

Autoimmune diseases are a diverse group of conditions caused by an abnormal immune response that targets the body's own tissues and organs. With over 80 identified types, autoimmune diseases affect various systems in the body, ranging from the joints and skin to internal organs such as the thyroid and gastrointestinal tract. While the exact causes often involve a combination of genetic, environmental, and immunological factors, their impact can be profound and systemic

REFERENCES

- [1]. Ilchmann-Diounou, Hanna, and Sandrine Menard. "Psychological stress, intestinal barrier dysfunctions, and autoimmune disorders: an overview." *Frontiers in immunology* 11 (2020): 1823.
- [2]. Miller, Frederick W. "The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention." *Current opinion in immunology* 80 (2023): 102266.
- [3]. Angum, Fariha, et al. "The prevalence of autoimmune disorders in women: a narrative review." *Cureus* 12.5 (2020).
- [4]. Nigrovic, Peter A., Pui Y. Lee, and Hal M. Hoffman. "Monogenic autoinflammatory disorders: conceptual overview, phenotype, and clinical approach." *Journal of Allergy and Clinical Immunology* 146.5 (2020): 925-937
- [5]. Mohd Zaid, Nurul Amirah, et al. "Promising natural products in new drug design, development, and therapy for skin disorders: An overview of scientific evidence and understanding their mechanism of action." *Drug design, development and therapy* (2023): 23-66.
- [6]. Matson, Daniel R., and David T. Yang. "Autoimmune lymphoproliferative syndrome: an overview." *Archives of pathology & laboratory medicine* 144.2 (2020): 245-251.
- [7]. Alexander, Tobias, and Raffaella Greco. "Hematopoietic stem cell transplantation and cellular therapies for autoimmune diseases: overview and future considerations from the Autoimmune Diseases Working Party (ADWP) of the European Society for Blood and Marrow Transplantation (EBMT)." *Bone marrow transplantation* 57.7 (2022): 1055-1062.
- [8]. Kadasah, Sultan F., and Mohamed O. Radwan. "Overview of ursolic acid potential for the treatment of metabolic disorders, autoimmune diseases, and cancers via nuclear receptor pathways." *Biomedicine* 11.10 (2023): 2845.

- [9]. Cuthrell, Kimberly Morton, Nikolaos Tzenios, and Javeria Umber. "Burden of Autoimmune Disorders; a review." *Asian Journal of Immunology* 6.3 (2022): 1-3.
- [10]. Achuthan, Adrian A., Kevin MC Lee, and John A. Hamilton. "Targeting GM-CSF in inflammatory and autoimmune disorders." *Seminars in immunology*. Vol. 54. Academic Press, 2021.
- [11]. Nettis, Maria Antonietta. "Minocycline in major depressive disorder: and overview with considerations on treatment-resistance and comparisons with other psychiatric disorders." *Brain, behavior, & immunity-health* 17 (2021): 100335.
- [12]. Cuthrell, Kimberly Morton, Nikolaos Tzenios, and Javeria Umber. "Burden of Autoimmune Disorders; a review." *Asian Journal of Immunology* 6.3 (2022): 1-3.
- [13]. Achuthan, Adrian A., Kevin MC Lee, and John A. Hamilton. "Targeting GM-CSF in inflammatory and autoimmune disorders." *Seminars in immunology*. Vol. 54. Academic Press, 2021.
- [14]. Koźmiński, Przemysław, et al. "Overview of dual-acting drug methotrexate in different neurological diseases, autoimmune pathologies and cancers." *International journal of molecular sciences* 21.10 (2020): 3483
- [15]. Bhagavati, Satyakam. "Autoimmune disorders of the nervous system: pathophysiology, clinical features, and therapy." *Frontiers in neurology* 12 (2021): 664664.
- [16]. Shuid, Ahmad Naqib, et al. "Association between viral infections and risk of autistic disorder: an overview." *International journal of environmental research and public health* 18.6 (2021): 2817
- [17]. Banday, Mujeeb Z., Aga S. Sameer, and Saniya Nissar. "Pathophysiology of diabetes: An overview." *Avicenna journal of medicine* 10.04 (2020): 174-188.
- [18]. Betterle, Corrado, et al. "Autoimmune polyendocrine syndromes (APS) or multiple autoimmune syndromes (MAS) an overview." *Polyendocrine disorders and endocrine neoplastic syndromes* (2021): 3-50.
- [19]. Brummer, Tobias, et al. "Treatment approaches to patients with multiple sclerosis and coexisting autoimmune disorders." *Therapeutic advances in neurological disorders* 14 (2021): 17562864211035542.
- [20]. Lu, Mengrou, et al. "The role of extracellular vesicles in the pathogenesis and treatment of autoimmune disorders." *Frontiers in Immunology* 12 (2021): 5662