Researchers Guide to IMMUNOLOGY

From the Real World to the Lab

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Contents

Section 1:

Understanding Autoimmune Disorders

What is the immune system?

The immune system acts as the body's defense against foreign invaders such as viruses and bacteria. Humans have a sophisticated two-fold immune response that includes the innate and adaptive immune systems. The innate response is a fast acting, generic reaction that utilizes white blood cells to attack invaders in a non-specific manner. The more advanced adaptive response is specific to the type of invading pathogen. Although slower to initiate, the adaptive response offers long-lasting immunity from specific pathogens.

What is an autoimmune disorder?

Healthy immune systems are able to detect pathogens and neutralize them before they cause extensive damage to the body. In some instances, however, the immune system is hyperactive and fails to differentiate the body's own tissues from invaders. As a result, the adaptive immune system attacks healthy host tissue as it would a foreign pathogen. This leads to a broad spectrum of diseases classified as autoimmune disorders where the body attacks its own tissues. Over 80 different types of autoimmune diseases are currently recognized.

What are the general symptoms of an autoimmune disorder?

Symptoms for autoimmune diseases vary greatly according to the types of tissues involved. In general, initial symptoms include fatigue, muscle ache, a low grade fever, and general ill-feeling (malaise). A hallmark indication of an autoimmune disease is inflammation, which causes redness, heat, pain, and swelling.

Do patients always experience symptoms of their autoimmune disease?

Most autoimmune diseases cause symptoms during "flare-ups" or active periods of the disease which can last anywhere from a few hours to several years. At other times, the disease remains in a period of quiescence, or an asymptomatic state. During this time, patients still receive treatment to control potential flare-ups. Autoimmune diseases are chronic and therefore, necessitate ongoing observation and treatment.

What is the difference between systemic and localized infections?
Autoimmune diseases are characterized as either systemic or localized. Systemic diseases affect multiple organs, often targeting connective tissues (skin, muscles, and joints), endocrine glands (thyroid, pancreas, and adrenal glands), and components of the blood (red blood cells). Examples of systemic autoimmune diseases include systemic lupus erythematosus (SLE), which can harm the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system, and rheumatoid arthritis (RA), which primarily affects joints but can also affect the eyes, mouth, and lungs.

Localized autoimmune diseases are limited to one specific organ. Examples include Crohn's disease and ulcerative colitis both of which target the gastrointestinal tract and Graves' disease which is caused by an overactive thyroid.

Who is affected by autoimmune disorders?
Autoimmune diseases affect men and women of all socioeconomic, racial, and ethnic backgrounds. However, most autoimmune diseases disproportionately affect women, particularly those of African, Hispanic, or Native American descent. For example, SLE is 9 times more prevalent in women than men and 2-3 times more prevalent in African American, Hispanic, Asian, and Native American populations than in Caucasians.

Evidence also suggests that individuals with a family history of some types of autoimmune diseases are genetically predisposed to develop the disease. Research indicates that approximately one-third of the risk for developing an autoimmune disease can be attributed to genetic factors.

Although all ages can be diagnosed with an autoimmune disease, onset generally occurs in childhood to late adulthood, depending on the specific autoimmune disease.

Examples of Autoimmune Disorders

Autoimmune Disease	Symptoms
Systemic Lupus Erythematosus (SLE) SLE is the most severe form of lupus because affects multiple organ systems. As a result, diagnosing and treating this disease is especially challenging. Tests used to diagnose SLE include antibody tests (including tests for antinuclear antibodies or ANA), complete blood counts (CBC), chest X-rays, kidney biopsies, and urinalyses. Research indicates that a combination of genetic, hormonal, environmental, and immune system factors contribute to the cause of SLE. Women between the ages of 15 and 45 of African, Asian, and Native American descent are most susceptible.	Primary • Fatigue • Fever • Arthritic pain • Malar (“butterfly” shaped) facial rash, flaky spots on upper body, sores/bumps on face and chest • Swollen glands • Light sensitivity • Hair loss • Swelling of the extremities • Headaches • Sudden chest pain Secondary • Weight loss • Memory loss • Bloody urine • Numbness • Anxiety/depression • Anemia • Complications of any organ
Rheumatoid Arthritis (RA) RA affects about 1% of the U.S. population. It is caused by inflammatory substances produced by immune cells in joint tissues resulting in irritation and eventual wearing down of cartilage. Over time, cartilage loss allows bones to rub against each other causing extensive pain and bone damage. X-rays and blood tests are used in diagnosis. Women between the ages of 40 and 60 with a family history of the disease are most susceptible.	• Fatigue • Appetite loss • Fever • Muscle and joint aches • Rheumatoid nodules • Symmetric arthritis • Morning stiffness • Red/swollen joint • Bone deformity • Hoarse voice

Autoimmune Disease	Symptoms	
Sarcoidosis Sarcoidosis primarily affects the lungs and lymph glands. It causes the formation of granulomas–abnormal masses or nodules consisting of inflamed tissues–that can alter the normal structure and function of the affected organ. Chest X-rays, CT scans, pulmonary function tests, and bronchoscopies are utilized in diagnosis. Sarcoidosis is more prevalent in women and typically occurs between the ages of 20 and 40. African Americans are 10-17 times more susceptible than Caucasians.	• Small lumps on the interior and/or exterior of the body • Chest pain • Dry cough • Shortness of breath • Fatigue • Fever • Joint pain • Weight loss • Hair loss • Red skin sore • Rash • Random scarring • Lesions	• Anemia • Hyperkalemia • Headache • Seizures • Dry, itchy, burning eyes • Vision loss • Dry mouth • Nosebleed • Upper abdominal swelling • Streaking rashes • Swollen lymph nodes • Meningitis
Scleroderma Scleroderma causes the skin to thicken and harden, losing its ability to stretch. This can cause swelling and pain in muscles and joints. Diagnosis includes a physical exam, lab tests, and a skin biopsy. More women than men are affected by scleroderma. It generally affects people between the ages of 30 and 50.	• Swelling of hands/feet • Red spots on skin • Calcium deposits in skin • Joint contractures • Tight facial skin • Fingertip ulcerations • Joint pain/stiffness • Persistent cough • Shortness of breath • Heartburn • Difficulty swallowing • GI problems • Anemia • Fatigue • Hair loss • Constipation	

Autoimmune Disease	Symptoms
Sjogren's Syndrome Sjogren's Syndrome results from an immune system attack on the glands that make tears and saliva. Diagnosis includes blood tests, X-rays, and tests that measure eye and saliva production. Women over the age of 40 have the greatest risk of developing Sjogren's Syndrome, particularly if they have another rheumatic disease such as lupus.	• Dry eyes • Dry mouth • Joint pain, swelling, and stiffness • Swollen salivary glands • Skin rashes or dry skin • Vaginal dryness • Persistent dry cough • Prolonged fatigue
Psoriasis Psoriasis is a skin condition that causes skin cells to grow too quickly, resulting in thick patches of skin on the knees, elbows, scalp, hands, feet, and lower back. Psoriasis flare-ups typically last anywhere from a few weeks to several months and are separated by periods of remission. Psoriasis is diagnosed following a physical exam, medical history evaluation, and skin biopsy. Risk factors include a family history of the disease, certain viral and bacterial infections, high stress levels, obesity, and smoking.	• Red patches of skin covered with silvery scales • Small scaling spots • Dry, cracked skin that may bleed • Itching, burning, or soreness • Thickened, pitted, or ridged nails • Swollen and stiff joints

Autoimmune Disease	Symptoms
Ankylosing Spondylitis Ankylosing spondylitis causes inflammation in the spine that leads to vertebrae fusion. X-rays, computerized tomography (CT), and magnetic resonance imaging (MRI) are utilized in diagnosis. Unlike the majority of autoimmune diseases, men are more susceptible than women. Symptoms typically appear between the ages of 15 and 35.	• Pain and stiffness in the lower back, buttocks, ribs, shoulder blades, hips, thighs, and heels. • Mild fever • Loss of appetite • Loss of spinal mobility • Acute iritis–inflammation of the colored area of the eye
Ulcerative Colitis Ulcerative colitis is an inflammatory bowel disease that affects only the innermost lining of the large intestine (colon) and rectum. Tests used in diagnosis include blood tests, stool tests, colonoscopies or sigmoidoscopies, and other imaging tests. Symptoms typically present before the age of 30 and in patients with a family history of the disease.	• Anemia • Severe tiredness • Weight loss • Loss of appetite • Bleeding from the rectum • Sores on the skin • Joint pain • Growth failure in children
Crohn's Disease Crohn's disease is an inflammatory bowel disease that can affect the deep layers of the intestines. Diagnosis utilizes blood tests, fecal occult blood tests, colonoscopies, endoscopies, CT scans, and MRIs. Crohn's disease usually presents between the ages of 15 and 35 but can occur at any age. It is most prevalent in industrialized nations, northern climates, and in people of Jewish descent.	• Diarrhea • Abdominal pain and cramping • Blood in the stool • Ulcers • Reduced appetite and weight loss • Fever • Fatigue • Arthritis • Eye inflammation • Mouth sores • Skin disorders • Inflammation of the liver or bile ducts • Delayed growth or sexual development in children

Autoimmune Disease	Symptoms
Multiple Sclerosis (MS) Multiple sclerosis damages the myelin sheath that surrounds and protects nerve cells, delaying or preventing the relay of messages between the body and the brain. Women are twice as likely as men to develop MS. A family history of the disease, certain viral infections, and an ethnicity with roots in northern Europe also increase the likelihood of occurrence.	• Blurred or double vision • Thinking problems • Clumsiness or a lack of coordination • Loss of balance • Numbness • Tingling sensations • Weakness in an arm or leg

Interesting Autoimmune Statistics

- The American Autoimmune Related Diseases Association estimates that about 50 million Americans currently suffer from at least one of the over 80 autoimmune diseases currently recognized.
- Autoimmune disease is one of the top 10 leading causes of death in female children and women in all age groups up to 64 years of age.[1]
- NIH estimates annual direct health care costs for autoimmune diseases to be around $100 billion. For comparison, cancer costs are approximately $57 billion and heart and stroke costs approach $200 billion.[2]
- NIH funding for autoimmune disease research in 2013 was $871 million.[3]

[1]http://www.aarda.org/autoimmune-information/autoimmune-statistics/
[2]source: NIH presentation by Dr. Fauci, NIAID on AARDA website
[3]http://report.nih.gov/categorical_spending.aspx

Rheumatoid Arthritis (RA)

Arthritis Foundation

- Affects over 1 million Americans.
- Is 2.5 times more likely to occur in women than in men.
- Accounts for 22% of all deaths from arthritis and other rheumatic conditions.
- Along with other forms of arthritis, costs the U.S. economy nearly $128 billion per year. in medical care and indirect expenses such as lost wages and productivity.
- People with RA are 2x more likely to die than persons of the same age without RA in the general population.
- Was responsible for 2.9 million ambulatory care visits in the U.S. in 2007.
- Compared with people without arthritis, people with RA are more likely to change occupation (3.3% vs 0%), reduce work hours (12.2% vs 1.7%), lose their job (3.3% vs 0%), retire early (26.3% vs 5.2%), and be unable to find a job (15.3% vs 5.2%).[4]

Systemic Lupus Erythematosus (SLE)

CDC

- The FDA approval of belimumab in 2011 was the first new treatment for lupus in over 50 years.
- Lupus was listed for 1,032,000 ambulatory care visits annually from 2001-2005.[5]

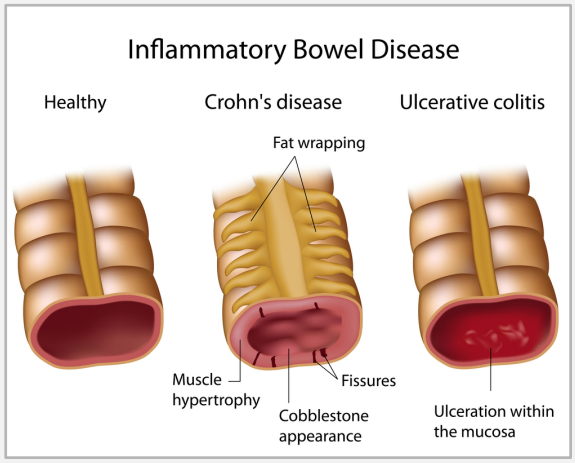
SLE Lupus Foundation

- Approximately 1.5 million Americans have lupus.
- 9 in 10 people with lupus are female
- Lupus is more prevalent in women who are African American, Hispanic/Latino, Asian, or Native American.
- Lupus is one of the leading causes of kidney disease, stroke, and heart disease in women of childbearing age.[6]

Crohn's Disease

CDC

- IBD is one of the five most prevalent gastrointestinal disease burdens in the United States, with an overall healthcare cost of more than $1.7 billion annually.
- Each year in the United States, IBD accounts for more than 700,000 physician visits, 100,000 hospitalizations, and disability in 119,000 patients.
- Over the long term, up to 75% of patients with Crohn's disease and 25% of those with ulcerative colitis will require surgery.[7]



[4]http://www.arthritis.org/files/images/AF_Connect/Departments/Public_Relations/Rheumatoid-Arthritis-Final-3-7-12.pdf
[5]http://www.cdc.gov/arthritis/basics/lupus.htm
[6]http://www.lupusny.org/sites/default/files/Lupus_WYSK.pdf
[7]http://www.cdc.gov/ibd/#impactIBD

Section 2:

From the Real World to the Lab

The Process of Diagnosing Autoimmune Disorders

Diagnosing autoimmune disorders is generally very difficult. Each autoimmune disease presents with common, generic symptoms in addition to subtle underlying differentiators that must be identified for proper diagnosis and treatment. Further complicating diagnosis is the common presence of multiple autoimmune disorders in a single patient.

Tests used to diagnose an autoimmune disorder commonly include:

- **Antinuclear antibody tests (ANA)** - A type of autoantibody test that recognizes antinuclear antibodies, which attack the cell nucleus
- **Autoantibody tests** - Specialized tests that identify specific antibodies from the body's own tissues
- **Complete blood count (CBC)** - Measures the numbers of red and white blood cells in the blood. Both counts will be abnormal when the immune system is actively fighting an infection or attacking healthy tissue
- **C-reactive protein (CRP)** - Elevated CRP indicates inflammation throughout the body
- **Erythrocyte sedimentation rate (ESR)** - Indirectly measures the degree of inflammation in the body

How Patients are Treated and Where to Find Them

Treatment for autoimmune disease seeks to accomplish three goals:
1. Reduce symptom prevalence
2. Control the autoimmune process
3. Maintain the body's ability to fight against disease

The broad spectrum of autoimmune disorders necessitates specialized treatment for each individual based on his or her diagnosis, symptoms, and level of severity. Some patients require vitamin and hormone supplements to compensate for their body's shortage. Those with diseases affecting the blood may require transfusions. Physical therapy may be used in conjunction with medication to improve movement and mobility in patients with diseases, such as RA and scleroderma that aggravate joints, muscles, and/or bones.

Physicians Involved in Diagnosis and Treatment

Patients with autoimmune diseases are treated by physicians who specialize in the organ system immediately affected. Patients are generally referred to a specialist following a visit with their primary care physician. Additionally, many patients suffer from multiple concurrent autoimmune diseases, and therefore may have several physicians involved in their treatment.

List of Specialists Involved in Autoimmune Disease Treatment

- **Nephrologist** - A doctor who treats kidney problems, such as inflamed kidneys caused by lupus.
- **Rheumatologist** - A doctor who treats arthritis and other rheumatic diseases, such as scleroderma and lupus.
- **Endocrinologist** - A doctor who treats gland and hormone problems, such as diabetes and thyroid disease.
- **Neurologist** - A doctor who treats nerve problems, such as multiple sclerosis and myasthenia gravis.
- **Hematologist** - A doctor who treats diseases that affect blood, such as some forms of anemia.
- **Gastroenterologist** - A doctor who treats problems with the digestive system, such as Crohn's disease and ulcerative colitis.
- **Dermatologist** - A doctor who treats diseases that affect the skin, hair, and nails, such as psoriasis and lupus.[8]

[8]http://www.womenshealth.gov/publications/our-publications/fact-sheet/autoimmune-diseases.cfm#f

Treatment and Side Effects

The degree of specialization required to treat autoimmune diseases presents a challenge in assimilating histories and treatment options for these patients. Because many underlying issues are common to several autoimmune disorders, novel treatments originating in one specialty could prove successful in another. However, due to the limited collective approach currently employed in treating and studying autoimmune diseases, innovative solutions for autoimmune diseases have been limited.

Most medications prescribed to autoimmune patients are immunosuppressive and are intended to control or reduce the immune system's response to limit damage to healthy tissues. These medications include corticosteroids (such as prednisone), and nonsteroid drugs such as azathioprine, cyclophosphamide, mycophenolate, sirolimus, or tacrolimus.

The most common side effect of immunosuppressant drugs is immunodeficiency, which leaves patients vulnerable to an increased risk of infection. As a result, patients must be especially careful around individuals with communicable diseases such as colds or stomach viruses. Frequent hand washing and limited contact with sick individuals is suggested.

Other side effects of immunosuppressant drugs include:

- **Hypertension** - high blood pressure
- **Dyslipidemia** - abnormal amount of lipids in the blood
- **Hyperglycemia** - high glucose levels
- **Peptic ulcers** - ulcer in the gastrointestinal tract
- **Lipodystrophy** - degeneration of the body's adipose tissue
- **Moon face** - caused by a buildup of fat on the sides of the face due to high cortisol levels
- **Liver and kidney injury**

Drugs that treat autoimmune disorders can affect the metabolism and action of other medications. Consequently, prescription contraindications and dosage must be carefully monitored.

Section 3:

Research Challenges

Understanding the clinical experiences of autoimmune patients is a key element in effectively researching these diseases. Complicating this endeavor, however, is the divide between the research environment and the clinical setting. While doctors focus primarily on healing patients, researchers focus more on understanding the nuances of diseases in order to develop potential treatment options. Bridging this gap can help scientists understand the possibilities and limitations of specimen procurement, so they can more efficiently and effectively design their research projects.

Rheumatoid Arthritis (RA)

The activity level of rheumatoid arthritis is defined in one of three ways. However, there is no clear consensus on the issue.

1. **Mild RA** - A person with mild RA has some of these symptoms: joint pain, inflammation of 3+ joints with no inflammation in other tissues, negative rheumatoid factor (RF) test, elevated ESR or CRP levels, no bone and/or cartilage damage.

2. **Moderate RA** - A person with moderate RA has a combination of these symptoms: 6-20 inflamed joints with no inflammation in other tissues, elevated ESR or CRP levels, positive RF test or positive anti-cyclic citrullinated peptide (anti-CCP) test, no bone and/or damage.

3. **Severe RA** - A person with severe RA has one or more of these symptoms: 20+ persistently inflamed joints with inflammation in other tissues, rapid loss of functional ability, elevated ESR or CRP levels, anemia related to chronic illness, low blood albumin level, positive RF test, bone and/or cartilage damage.

It is not possible to target patients with above-baseline RA symptoms, but it is possible to target patients who have active RA. Because defining the level of activity is subjective, targeting by activity stage is difficult but not impossible.

Most suspected RA patients are immediately placed on some type of NSAID. As the disease progresses towards joint damage, more potent RA drugs, such as the biologics and anti-TNFs, are prescribed. Examples of Anti-TNFs include: etanercept/Enbrel, infliximab/Remicade, adalimumab/Humira, golimumab/Simponi, abatacept/Orencia, certolizumab pergol/Cimzia, tocilizumab/Actemra. There is a brief time to catch patients pre-treatment, but it is extremely difficult to locate these patients.

Targeting a patient based on their CRP score or ESR is possible; however, patients would be targeted based on their prior scores. Their current scores will be known only after collection and analysis when the tests are performed.

A high disease activity (DAS28) score generally indicates a high CRP score. However, a high DAS28 score does not always guarantee a patient will have a high CRP score. Targeting patients with a high DAS28 score is one of the best ways to target a patient that will likely have a high CRP score, but the method is not fail proof.

Systemic Lupus Erythematosus (SLE)

The activity level of SLE is determined in much the same way as RA. There are three levels:

1. **Mild SLE** - Symptoms are easily recognized and treated. i.e. – skin rash, headaches, fatigue, and mild pain.

2. **Moderate SLE** - Abnormal blood counts – white or red blood cells. Typically this classification is blended with the severe category since blood involvement almost always indicates future organ system involvement.

3. **Severe SLE** - Disease is affecting major organs/ organ systems.

Over 90% of patients treated for lupus-related systems are currently treated regardless of how active or inactive the disease is at the moment. The traditional concept of “lines of treatment” does not directly apply to SLE due to the incredibly unpredictable and variable nature of the disease. However, anti-inflammatory drugs are the first and most often prescribed courses of treatment by rheumatologists.

Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), is a scale designed to assess and categorize the level of disease activity in SLE. It is often used by researchers in clinical trials, but rarely, if ever, by the physicians treating lupus patients. It includes clinical tests (rashes, hair loss, etc.) and laboratory tests (blood tests, urinalysis, etc.) in the scoring index. Scores range from 0 to 105; a score greater than 20 is rare.

SLEDAI SCALE
A score of 6 or more corresponds to active disease, though this is not what a physician will use to define active disease. Physicians define active as “symptomatic:” is the patient experiencing symptoms of their lupus or not?
mild/moderate flare is defined as a change >3 points from patients previous score
severe flare is a change >12

This test can be performed and provided with additional data, but it is not something that can be targeted. Tissue removal is not a part of treatment for patients with SLE, so tissue is not something that can be targeted from consented patients.

Ulcerative Colitis (UC) and Crohn's Disease

Patients suffering from UC or Crohn's are encouraged to change their diet and generally put on medications specifically designed to reduce inflammation and immune response. The last line of treatment is surgery. Therefore, tissue specimens are often more difficult to acquire than blood samples. Tissue samples may take longer to accrue, but the request for tissue samples is not impossible to fulfill.

During a surgery for UC, surgeons usually remove the entire colon and rectum. Surgery is only likely for patients with higher Mayo scores (10-12); these are the most severe cases, and it is only these cases which require surgery. The Mayo Scoring System (sometimes referred to as Disease Activity Index) for ulcerative colitis has 4 categories with 4 options per category with a maximum score of 12. The categories are: stool frequency, rectal bleeding, endoscopic findings and physician's global assessment. The four categories are averaged to get the final score.

Remission	Mild	Moderate	Severe
0 - 2	3 - 5	6 - 10	11 - 12

Surgery for patients with Crohn's will involve the patient having sections of unhealthy intestines removed and then having the healthy sections reattached. They may also have a procedure known as strictureplasty performed which widens a segment or segments of the intestines which have become too narrow. Additionally, surgeons may perform surgeries to drain abscesses and close fistulas. A patient will often have to have surgery multiple times.

Multiple Sclerosis (MS)

It is more difficult to identify some courses of MS for sample collection. Eighty-five percent of patients are diagnosed with relapsing-remitting MS, so this is the course that is the easiest to target. The different MS courses are explained below.

1

Relapsing-Remitting MS - *Approximately 85% of people are initially diagnosed with relapsing-remitting MS.*

People with this type of MS experience clearly defined attacks of worsening neurologic function. These attacks—which are called relapses, flare-ups, or exacerbations—are followed by partial or complete recovery periods (remissions), during which no disease progression occurs.

2

Secondary-Progressive MS - *Approximately 50% of people with relapsing-remitting MS develope this form of the disease within 10 years.*

People are usually not initially diagnosed with Secondary-Progressive MS; they develop Secondary MS from Relapsing-Remitting MS. Following an initial period of relapsing-remitting MS, many people develop a secondary-progressive disease course in which the disease worsens more steadily, with or without occasional flare-ups, minor recoveries (remissions), or plateaus.

3

Primary-Progressive MS - *Approximately 10% of people are initially diagnosed with primary-progressive MS.*

This disease course is characterized by slowly worsening neurologic function from the beginning, with no distinct relapses or remissions. The rate of progression may vary over time, with occasional plateaus and temporary minor improvements.

4

Progressive-Relapsing MS - *Approximately 5% of people are diagnosed with this form of the disease. This is a rare course of MS.*

In this course of the disease, people experience steadily worsening disease symptoms from the beginning, but with clear attacks of worsening neurologic function along the way. They may or may not experience some recovery following these relapses, but the disease continues to progress without remissions.

At this time, the most useful test to confirm the diagnosis of MS is an MRI. Generally this is paired with a review of a patient's medical history, cerebrospinal fluid (CSF) testing, visual evoked potential testing, and McDonald criteria evaluation. CSF can be difficult to target and does not guarantee a definitive diagnosis of MS. A patient could have a negative result in CSF analysis and still have a MS diagnosis. Therefore, an MRI is still the most common test used to confirm diagnosis of MS, not CSF

Tissue is not resected in the course of treatment for a patient with MS, and bone marrow procedures are not used to diagnose the presence of MS.

Patients who are experiencing an attack, relapse, or exacerbation can be targeted because these are identifiable states. An exacerbation of MS (also known as a relapse, attack) causes new symptoms or the worsening of old symptoms. It can be very mild or severe enough to interfere with a person's ability to function at home and at work. No two exacerbations are alike, and symptoms vary from person to person and from one exacerbation to another. For example, the exacerbation might be an episode of optic neuritis (caused by inflammation of the optic nerve that impairs vision) or problems with balance or severe fatigue. Some relapses produce only one symptom (related to inflammation in a single area of the central nervous system) while other relapses cause two or more symptoms at the same time (related to inflammation in more than one area of the central nervous system).

To be a true exacerbation, the attack must last at least 24 hours and be separated from the previous attack by at least 30 days. Most exacerbations last from a few days to several weeks or even months.

For severe exacerbations (involving loss of vision, severe weakness or poor balance, etc.), which interfere with a person's mobility, safety, or overall ability to function, most neurologists recommend a short course of high-dose steroids to reduce the inflammation and bring the relapse to an end more quickly.

Section 4:

How We Can Help

At Conversant Bio, we offer a wide variety of samples from patients with autoimmune diseases. Some of the most popular autoimmune disease products include whole blood, peripheral blood mononuclear cells (PBMCs), plasma, and serum. Don't hesitate to contact us with your specific requests.

Peripheral Blood Mononuclear Cells (PBMC)

Mononuclear cells, mainly consisting of monocytes and lymphocytes, are obtained by gradient centrifugation using Ficoll. These cells are aliquotted and cryopreserved at -150°C in a manner that maintains post-thaw cellular viability.

Key Applications
• drug testing and drug target discovery • assessing immune responses • toxicology studies • genetic studies

Peripheral Blood Plasma

Plasma is the liquid, non-cellular portion of blood. It contains a variety of proteins, nutrients, ions, hormones, and clotting factors.

Key Applications

- biomarker identification/ validation
- genetic studies

Peripheral Blood Serum

Serum is the liquid, non-cellular portion of blood lacking clotting factors. It contains a variety of proteins, nutrients, ions, and hormones.

Key Applications

- biomarker identification/ validation
- genetic studies

Section 5:

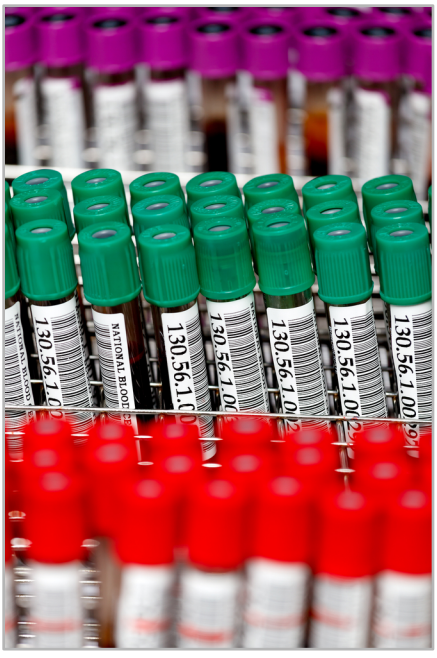
Case Studies

Case 1 - Data, Data, Data

Conversant Bio provided approximately 90 unique samples from rheumatoid arthritis patients for a pharmaceutical company. The inclusion/exclusion criteria involved current treatment, treatment history, and comorbidities. Conversant Bio's access to patient records allowed the targeting of patients meeting these specific criteria. All previous and current clinical lab data (e.g. ESR, CRP, Anti-CCP, RF, CBC, etc.) found was provided to the researcher.

Case 2 - Large Patient Numbers Across Multiple Autoimmune Indications

Conversant Bio's extensive site network allowed for the collection of patients from a variety of autoimmune disorders including: Lupus, Psoriasis, Rheumatoid Arthritis, Crohn's Disease, Sarcoidosis, Scleroderma, Ulcerative Colitis, as well as normal controls. There were approximately 700 total unique patients and donors enrolled for this study. Conversant Bio's lab processed the samples to PBMCs, plasma, or serum.



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