The Flame Within Autoimmune disorders, Prevention, Risk Factors, Diagnosis & Treatments.

Preface to the second edition:

The autoimmune disorders have become the biggest threat to humans larger than AIDS, SARS and Polio combined. In the second edition I have published treatment for Asthma, anxiety, depression, attention deficit disorder (ADD), eclampsia, chronic fatigue, schizophrenia, obsessive compulsive disorder, Vitiligo, Parkinsons and many others. In this edition I have mentioned uses of electro medicine and alternative treatments for autoimmune disorders. Evidence suggests that the leading cause of death in the world is due to infections, the common antibiotics can control these infections.

This book is dedicated to my parents Salahuddin Khan & Nasreen Khanum. It was due to the dedication of my parents that a child with attention deficit disorder and learning disorder would grow to become a source of help for ailing humanity. Another motivation to write this book on autoimmune disorders was the fact that soon after my marriage, my wife developed ankle arthritis. Then following her first pregnancy, she had difficulty walking and developed severe stiffness. In retrospect, it took her several years and multiple visits to many doctors before a diagnosis of Takayasu diseases was finally reached, by an internist. The next hurdle was to start a treatment and the only option was steroids. At the time of diagnosis she had no pulses in the wrists. I was determined to find a cure for this disease. It took twenty years and since then I have treated young girls with Takayasu who have fully recovered within two weeks with doxycycline. That's what you find in this book, treatments that reverse the disease process!

Medical Science is complicated and each patient is unique and different. Even if the diagnosis is MS or Alzheimer's, the treatment is not the same, in each patient the cause of the disease may be different in each patient. The response of medication is different due to the strength of the immune system. I accept no liability of any professional harm from recommendations in this book, as the treatment of the disease should be done by a professional doctor after careful evaluation of the patient. Majority of the information in this book comes from the National Library of Medicine U.S.A.

Thanks and please watch for the **coming book, natural treatment of all cancers**.

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Glossary

AIDS: Acquired Immune Deficiency Syndrome. HIV virus invades the T4 lymphocytes and multiplies, causing a breakdown in the body's immune system, leading to infection, cancer, autoimmune diseases.

A.I.D.P. Acute (sudden onset) Inflammatory Demyelinating Polyradiculoneuropathy

A.I.O.N. Anterior Ischemic Optic Neuropathy, loss of vision due to inflammation in posterior ciliary artery circulation in the optic nerve head.

Anaerobic: Of, relating to, or being activity in which the body incurs an oxygen debt (for example weight training or resistive exercises) and does not immediately burn off a lot of calories and fat.

Anti-inflammatory: Reducing inflammation by acting on body mechanisms, without directly acting on the cause of inflammation, e.g., glucocorticoids, aspirin. Fish Oil

Autoantibodies: Autoantibodies are Y shaped proteins that attack specific proteins or other substances found in specific tissues or organs of the body. They are created by the immune system when it fails to distinguish between "self" and "non-self." (They can be called the bad antibodies, e.g. "antinuclear antibody",).

Autoimmune Disease: One of a large group of diseases in which the immune system turns against the body's own cells, tissues and organs, leading to chronic inflammation and often serious conditions.

Autonomic failure or dysautonomia develops when the small nerves controlling heart rate, blood pressure, bowel movements, and skin color and hair integrity get involved with disease. Patients either have low blood pressure or high blood pressure, heart rate slow or fast. Caused by autoimmune disease.

Axonal *degeneration,* called the "dying-back" phenomenon, results in axonal degeneration at the most far end of the axon. Axonal degenerative polyneuropathies are usually symmetric, and as the disorder progresses, the axons typically degenerate from toes toward hands. Axonal degeneration is often attributed to a "metabolic" etiology.

Carotenoids: Carotenoids are a group of more than 700 compounds that produce the red, yellow, and orange colors found in many fruits and vegetables. Beta carotene (also called provitamin A) is the most widely studied carotenoid, but others are proving to be of great interest. Carotenoids are proving to be vital for health.

C.D.C. Center of Disease Control in the U.S.A. which issues disease alerts.

Cynocobalamine Vitamin B12 an essential vitamin not made by our body

Bacteria: Microscopic germs. Some bacteria are "harmful" and can cause disease, while other "friendly" bacteria protect the body from harmful invading organisms.

Borrelia burgdorferi a Spirochete which causes Lymes Disease has World Wide distribution. Symptoms of Lyme disease vary, and do not appear until 6–8 weeks after the tick bite, the infection is difficult to diagnose.

Bronchitis: Inflammation of the mucous membrane of the bronchial tubes, frequently accompanied by cough, hypersecretion of mucus, and expectoration of sputum. Acute bronchitis is usually caused by an infectious agent. Chronic bronchitis the result of smoking,is **Chronic Obstructive Pulmonary Disease** (COPD) or **Emphysema**.

Cancer: Refers to the various types of malignant neoplasms that contain cells growing out of control and invading adjacent tissues, which may metastasize to distant tissues.

Candidiasis: Infection of the skin with any species of candida, usually *Candida albicans*. The infection is usually localized to the skin, nails, mouth, vagina, bronchi, or lungs, but may invade the bloodstream. It is a common inhabitant of the GI tract. Growth is encouraged by a weakened immune system, or with the prolonged use of antibiotics. Vaginal **symptoms** include itching, pain when urinating, and vaginal discharge.

Clarithromycin or Biaxin is an antibiotic used to treat certain infections caused by bacteria, such as pneumonia; bronchitis; and ear, lung, sinus, stomach, skin, and throat infections. It also is used to prevent disseminated Mycobacterium avium complex (MAC) infection and reverse SLE.

C.N.S: Central Nervous System (Brain and spinal cord).

Chronic: Usually Chronic illness: Illness extending over a long period of time.

Ciliary: Often Ciliary activity: Activity of the eyelashes or any hairlike processes (cilia).

Cold agglutinins: are abnormal proteins in the blood. They act as antibodies, causing red blood cells to clump together and die prematurely — especially at temperatures colder than normal body temperature

CRP: C-REACTIVE PROTEIN a test that measures autoimmune disease activity (0 is normal)

C.T. scan; Computed tomography scan makes pictures of the body by using x-rays and a computer.

Cytokines: Are chemical messengers that control immune responses. Secreted by white blood cells, T cells, and epithelial cells. There are at least 17 different kinds of interleuken and 3 classes of interferon called alpha, beta and gamma and various subsets. Interleukens and interferons are called “cytokines”

Demyelination refers to focal loss of the **myelin** (outer nerve sheath) sheath with sparing of the axon (central fibers in the nerve). This reaction can be seen in focal mononeuropathies (single nerve injury) or generalized sensorimotor or predominantly motor neuropathies. Demyelination in the brain and spinal cord causes Multiple Sclerosis and in the peripheral nerves it causes (CIDP). Also called white matter disease.

D.H.E.A. A precursor hormone of testosterone. Used in the treatment of Chronic Fatigue & anti-ageing.

D.I : Diabetes Insipidus. Some people with D.I have kidneys that don't concentrate urine very well (meaning their urine is more diluted). They have to urinate very often. People with D.I are thirsty all the time

Diabetes Mellitus: A disease with increased blood glucose levels due to lack or ineffectiveness of insulin.

E.A.U.: experimental autoimmune uveitis (inflammation of the eye)

E.C.G.: electro**c**ardio**g**raph an electrical recording of heart waves.

E.E.G. Electro **E**ncephalo**g**raphic Recording is a test to record electrical brain waves to help diagnose Epilepsy, sleep disorders and brain death.

E.S.R. test used to measure inflammation, infection (10 – 15 mm is normal) also called **Sed rate**

Fibromyalgia: (FMS): A disease affecting the fascia and causing pain and stiffness.

F.D.A: Food and Drug Administration (agency monitoring safety of new drugs through drug trials) The treatment guidelines of FDA are followed by physicians, governments all over the World.

F-wave is a variable response and is obtained infrequently after nerve stimulation. Commonly, several supramaximal stimuli are needed before an F-response is seen since only few stimuli reach the anterior horn cell at the appropriate time to stimulate it.

G.B.S. Guillain-Barre Syndrome, sudden or slow onset of weakness after flu due to autoimmune disease.

Gingivitis: Inflammation of the fibrous tissues that surround the teeth. (Main cause of heart disease)

Glucose: A sugar that is the simplest form of carbohydrate, serves as the primary fuel for the muscles and the brain.

HAART: A multi drug therapy for treatment of AIDS.

HIV: Human immunodeficiency virus, a man made virus which causes AIDS.

Hormones: Chemical secreted by body organs are carried by the bloodstream and influence cells some distance from the source of production. Examples adrenal hormones such as corticosteroids and aldosterone; glucagon, growth hormone, insulin, testosterone, estrogens, progesterone, DHEA, melatonin, and thyroid hormones.

Horners: Horner syndrome is a small pupil (miosis), droopy eyelid (ptosis), and shrunken eyeball (enophthalmos) and reduction of sweating on the ipsilateral side of the face and neck,; occasionally the development of cataracts; same side loss of sweating (hemifacial anhidrosis) .

H.S.P. Heat shock proteins, or *stress proteins*, are a group of proteins that are present in all cells in all life forms. They are induced when a cell undergoes environmental stresses like heat, cold and oxygen deprivation.

Hyperkeplexia: Startle disease (hyperekplexia) is a rare non-epileptic disorder characterized by hypertonia, generalized stiffness and brief muscle jerks in response to unexpected auditory, sensory and visual stimuli.

I.C. Interstitial cystitis a bladder infection induced autoimmune disorder

Immune System: A complex that protects the body from disease organisms and other foreign bodies.
I.O.I. Intraocular inflammation of the eye

Irritable Bowel Syndrome: (IBS) is inflammation of intestines with pain in the lower abdomen; bloating, alternating diarrhea and constipation; mucous in stools; indigestion; constant tiredness; low back pain; painful intercourse in women.

I.V.I.G. Intra Venous Immune Globulin a solution containing IgG antibodies from Humans.

Leukemia: Cancer of the lymph glands and bone marrow resulting in overproduction of white blood cells (related to Hodgkin's disease).

Leukocyte: A white blood cell which appears 5,000 to 10,000 times in each cubic millimeter of normal human blood. Among the functions are destroying bacteria, fungi and viruses and rendering harmless poisonous substances.

Lyme disease caused by a spirochete called **Borrelia burgdorferi.** First recognized in the United States, following a mysterious outbreak of juvenile rheumatoid arthritis near the community of Lyme, Connecticut.

Metabolism: The chemical processes of living cells in which energy is produced Responsible for the production of energy, biosynthesis of important substances, and degradation of various compounds.

Mold: Molds are Fungi which produce allergens (substances that can cause allergic reactions), irritants, and in some cases, potentially toxic substances (mycotoxins). Inhaling or touching mold or mold spores may cause allergic reactions in sensitive patients. Allergic responses include sneezing, runny nose, red eyes, and skin rash.

Myelin: Wrapping around the nerve fibers, Myelin conduct electrical impulses faster. (loss of myelin causes cidp)

M.R.I. Magnetic resonance imaging scan used to make pictures of the body by using magnets with a computer.

MTHFR stands for **M**ethylene-**T**etra-**H**ydro-**F**olate-**R**eductase. MTHFR is an enzyme it is needed to metabolize and get rid of homocysteine. High homocysteine levels are a risk factor for blood clots in the veins or arteries. Levels of homocysteine can be lowered by taking a multiple vitamin with a high content of folic acid (400 mcg = 0.4 mg), vitamin B6 (pyridoxine; 25 mg) and B12 (cobalamin; 1 mg).

N.I.H. National Institutes of Health (Medical Research Agency in USA)

O.C.D. Obsessive-compulsive disorder an autoimmune psychiatric disorder

Parasite: An organism living in or on another organism.
PFOA stands for Perfluorooctanoic Acid, a man-made chemical. PFOA (sometimes also called "C8") is used by companies, such as DuPont (Teflon, Stainmaster, Scotchguard), to make fluoro-polymers for use in non-stick cookware and all-weather clothing. PFOA have been commonly found in humans across the globe

PLEDS: Periodic lateralized epileptiform discharges (PLEDs) are seen, as a rule, following acute brain damage. (These are large EEG waves present over one are of the brain

Pyelonephritis: Inflammation of the renal pelvis.

Raynaud's syndrome is a disorder of blood circulation in the fingers. Exposure to cold reduces blood circulation causing the fingers to become pale, white or purple. Raynaud's most commonly associated with hand-arm vibration

Rickettsia: Bacteria, are carried by many ticks, fleas, and lice, and cause diseases such as typhus, rickettsialpox, Rocky Mountain spotted fever, Like viruses, they grow only in living cells.

Rituximab: The first monoclonal antibody therapy approved in the United States for the treatment of relapsed or refractory non-Hodgkin's lymphoma (NHL).

E.S.R. Erythrocyte Sedimentation Rate is used to measure inflammation, infection (10 – 15 mm is normal)

Syndrome number of symptoms described together, Example; dry eyes and dry mouth is Sjogrens syndrome.

Tilt Test: People with syncope are placed on a Tilt table and their blood pressure and pulse is monitored. If the person gets symptoms or the blood pressure falls after standing up then the test is considered positive.

TMJ: Tempero-mandibular joint - hinge of the. This gets tight jaw usually due to muscle pain

Urea breath test Is a procedure for diagnosing the presence of a bacterium, Helicobacter pylori (H. pylori) that causes inflammation, ulcers, and atrophy of the stomach.

Virus: A small bug with a DNA and/or RNA that reproduces in the cells of the infected host.

White Blood Cell: (WBC): A blood cell also called as leukocyte that does not contain hemoglobin and is responsible for maintaining the body's immune surveillance system against invasion by foreign media.

White Matter Disease: caused by destruction of Myelin in the Brain, in Multiple Sclerosis or outside the brain in CIDP (loss of myelin in nerves). Please also see under demyelination.

- Chapter 1 Introduction to Inflammation (the flame within)

Autoimmune diseases (AD) reign as the number one disease process on planet Earth. These autoimmune diseases are the cause of heart disease, alzheimers, arthritis, diabetes, autism, Fibromyalgia and multiple sclerosis. In the past heart disease and diabetes were the leading causes of disease. If the autoimmune process is diagnosed early, then people can heal faster and expect to live longer and healthier life. Why wait for the autoimmune disease to get you, when you can learn to avoid and treat these diseases. **This book gives you the knowledge to change your lifestyle and follow a diet to prevent AD**. In many diseases a protocol for cure of the disease is provided. A quick way to avoid diseases to eliminate toxins (chemicals), from your food and environment, eat a raw diet full of vitamins, minerals and detoxify with fasting.

Autoimmune diseases affect women three times more commonly then men. Women have a robust immune system as compared to men; and it acts as a double edged sword, protecting them from diseases and attacking them to cause diseases. Females get more urinary tract infections, menstrual periods, **pregnancy and suffer from stress,** which all trigger autoimmune diseases. Men, around the age of forty, start to get autoimmune diseases, due to declining **testosterone** levels. Some common symptoms the men experience are pains and numbness in the feet due to autoimmune neuropathy (C.I.D.P). This numbness usually gets misdiagnosed as a diabetic polyneuropathy, in a few years this untreated inflammation can take the life of this misdiagnosed patient as it will cause cardiac conduction defects and cardiac arrest. Other factors responsible for men to fall prey to autoimmune diseases, are exposures to chemicals, pestacides, germs, alcohol and a poor diet mainly of grains and meat.
Autoimmune skin lesions in women get misdiagnosed as herpes and patients are commonly placed on acyclovir without any help. The most common symptom of autoimmune disease is fatigue. Women with fatigue never get an evaluation for autoimmune disease and suffer unnecessarily. Women get dark circles under their eyes after pregnancy due to a condition called meleasma / cholasma, both are easily preventable and treatable. Chronic inflammation, spurred by the immune system, plays a crucial role in most medical diseases (evils) including arthritis, Alzheimer's, multiple sclerosis, diabetes, cancer and heart disease.
Microorganisms like Chlamydia pneumonia, Mycoplasma (smallest living organism), Helicobacter-pylori (ulcer bug), Borrelia Burgdorferi (Lymes bug), and mold (Fungus) are important triggering events for autoimmune disease (AD). The AD can also be triggered by

chronic stress, excessive physical activity, surgery, food, vaccination and trauma (accidents). These events are usually triggered in genetically predisposed patients, who have a tendency to develop autoantibodies (antibodies that attack self proteins). Helicobacter pylori (H-pylori) is a bacteria which has developed with the humans since Adams arrival, it is present in the stomach linings of humans worldwide, known for causing stomach ulcers, skin diseases and stomach cancers. Daily use of green tea, milk and yogurt has been found to inhibit H-pylori growth.

The flame within is turned on by a rogue protein that is inhaled, by infection, by exposure to chemicals, by contimanted food, other factors like chronic stress, excessive physical activity, medication, vaccination, accidents and surgery play a role in activating autoimmune diseases. Some diseases get turned on in specific decades of life. Kawasaki and childhood epilepsies get turned on, in the first decade of life; others like multiple sclerosis and S.L.E. are activated in the second decade, while Alzheimers and Temporal arteritis are turned on in the last decades of life. There is an association of Kawasaki disease (causes cardiac inflammation in infants) to carpet shampoo exposure, even a spot cleaner no matter what brand will trigger off this deadly disease in infants. Kawasaki is also triggered by the placement of a humidifier in the infant's room. I recommend cleaning the carpets with hot water, especially when an infant is in the house.

Prevention is the key to avoid A.D; simply by consuming an anti-inflammatory diet, enjoying mild physical activity and by losing the fat, which pumps chemicals which drives inflammation. Stay away from chemicals in your toothpaste, chemicals in soda drinks and chemicals in diet. Early onset alopecia, arthritis and CNS vasculitis are seen more commonly in repeated consanguineous marriage (**cousin marriage**). There are usually multiple factors involved in falling prey to autoimmune diseases. A product of multiple cousin marriage, then gets a trivial head injury, which is enough to fire off the weakened immune system. A single cousin marriage has no effect on autoimmune diseases, repeated marriage may affect some families but not others. Since the creation of Adam, we are all cousins.

A very common cause of autoimmune diseases is gingivitis, so dental hygiene is very important to prevent heart diseases, arthritis, strokes and cancer. I have provided instructions on Oil pulling in the last chapter, which will get rid of gingivitis, make your teeth sparkling white and make you healthy.

Inflammation is not always considered harmful. Inflammation is part of the typical immune response which is essential for battling germs and healing wounds. The familiar redness, heat, swelling and pain from, any injury or a splinter are signs of inflammation helping protect us. Problem starts, when the inflammatory process fails to shut off, after an infection or injury is over. Persistent, low level inflammation paves the way, for the chronic autoimmune diseases in later life. Persistent inflammation is probably, the reason why men and women around age of forty start experiencing autoimmune diseases. To prevent low level inflammation, a daily 32 mg aspirin (crush a 320 mg aspirin into ten parts), or use **omega-3 oil 3000mg** daily and a balanced diet is recommended (described in the diet chapter).

Chronic inflammation is similar in all AD such as, cardiac, kidneys, arthritis, lungs (asthma) or brain (epilepsy, alzheimers). They are all caused by an antibody mediated diseases process, "inflammatory" and the treatment is similar for all these diseases, "anti-inflammatory" or

immune modulation. Modulation here means to modify the immune system by medication supplements or lifestyle change. Treatment of al AD is generally based upon the same principals.

Heart attacks historically have been related to be caused by cholesterol. Blood vessels became clogged with atherosclerotic plaque called "bad" (LDL) cholesterol, which was deposited on vessel walls. Current thinking has changed, scientist have discovered, the misguided immune system targets a blood vessel, resulting in inflammation within arteries, where cholesterol then gets deposited, narrowing the vessel. The site of inflammation, in a blood vessel, is the place where cholesterol gets deposited and eventually blocks it. Center of Disease Control reports, “Mycoplasma pneumoniae (MP) and Chlamydia pneumoniae (CP) within the blood vessels of the heart, results in inflammation and blockage.” Inflammation is now seen as the cause of heart disease. To test the level of inflammation within the body a test called **CRP** (C-reactive protein) is done. American Heart Association has raised awareness that bacteria like **Chlamydia pneumonia, Helicobacter pylori** are the cause of inflammation in heart disease. Complete discussion on how to get rid of disease causing bacteria in heart disease is provided in the cardiac chapter. Diabetes is linked to inflammation; the immune system attacks the pancreatic islet cells which produce insulin resulting in reduced production of insulin. Other factors that can cause inflammation are, low vitamin levels of Folate, Vitamin –D, Vitamin -C, & low hormonal levels like testosterone will also trigger inflammation.

Two studies which show that sewer rats have better immune systems than rats living in clean antiseptic labs, the lesson for humans are that clean living may make us all sick. These studies gives weight to a 17-year-old theory that the sanitized Western world may be partly to blame for soaring rates of human allergy, asthma cases and autoimmune diseases, such as Type I diabetes and rheumatoid arthritis. The **Hygiene Hypothesis**," is that children who are around numerous other children or animals early in life are exposed to more microbes, and their immune systems develop more tolerance for the irritants that cause asthma. Those who do not get these exposures in childhood start to react abnormally to irritants in later life. Children who get an H-pylori infection early in life are protected from acquiring asthma later in life.

Diet is an important factor in reducing inflammation, as processed foods and trans-fats increases inflammation. A diet rich in coloured fruits and vegetables helps in reducing the inflammation. Normal intake of fiber increase intestinal motility reduces inflammation, as toxins like H-pylori are moved forward within intestines and less of them get absorbed into the body. A low fat diet combined by heavy exercise is detrimental for the immune system. Dietary fats are not the cause of disease, but inflammation triggered due to essential fat deficiency will cause disease. Essential fatty acids available in fish oil, butter oil, virgin olive oil, flax seed oil, and castor oil, walnuts, almonds, peanuts & coconut should be part of our regular diet.

It is recommended that people over thirty take a baby aspirin daily (to suppress the smoldering inflammation, avoid aspirin if you have a bleeding disorder or gastric ulcers. **Omega-3 taken on a daily basis in your diet will suppress inflammation**. People taking these supplements show lower values on the CRP test. I believe that essential fatty acids is combined with the recommended diet, this combination will prevents inflammatory diseases later in life. To obtain Omega-3 children and adults should first use Cod Liver Oil during winters, in summers **Flax seed oil**, **Fish oil**, **Olive oil**, coconut oil can be consumed.

The size of the patients belly is an important risk factor for disease, a man having a belly over 40 inches is unhealthy, and this weight will trigger an inflammatory reaction. Excess weight causes hypertension, and insulin resistance resulting in a higher cholesterol levels. By lowering weight one can lower the risk of heart disease as hypertension, cholesterol and insulin resistance.

The Attack on Self Tissues: Immune cells are the protective forces maintained in our body. The weakened immune system in predisposed individuals gets tricked into attacking self tissues, this phenomena is triggered by bacteria, pesticides or other toxins which cause an autoimmune disease. Every cell in the body has a specific protein tag (antigen); bacteria entering our body carry antigens similar to cells in the human body. Our immune system in trying to defend itself develops specific antibodies to target these bacteria, the antibodies attach to the bacteria and eliminate them. However, some antibodies also attach to body cells that carry similar antigens as of the bacteria. The cells where an antibody has attached are destroyed by the immune system. In early stages of the disease the body tries to repair the damaged tissue. If the repair is effective, the person feels better, which is called a remission. If the body is exposed to the bacteria again, then a second attack takes place and the person feels weak again, this worsening is called a relapse. Frequent remissions and relapses will weaken the affected human.

Autoimmune diseases can affect any organ in the body. For instance, an autoimmune attack directed against the brain results in multiple sclerosis. An attack against the intestines results in crohn's disease. In other diseases, like systemic lupus erythematosus (SLE), any part of the body can be attacked. (Heart, lung, kidney, brain, intestines, skin, muscles). Some of the autoimmune diseases are considered rare; however as a group these diseases afflict millions of people and animals and are the commonest cause of disease on Planet Earth and the Universe.

Stages of autoimmune disease: (Khans inflammatory staging)

Inflammatory stage: The autoimmune diseases can attack the human body usually in three stages, the first stage happens when the attack is just starting and the disease has **flare-ups**. This is described as remitting-**relapsing type disease**. The person has good and bad days. I have termed this the **inflammatory stage** of an autoimmune disease. In this phase the body cells are under an inflammatory attack. Biopsy of tissue obtained in early stages will show some inflammation, some repair (fibrosis) and some atrophy. **A combination of atrophy, repair and inflammation seen in a histology slide is the hallmark of all autoimmune diseases**. Similar tissue reactions are observed in polymyositis, atrophic gastritis, and inflammation of the ovary (oophoritis). Usually this stage lasts up to the first 15 months following the first symptoms. If the person is fully functional with an active autoimmune disease, then they are in the inflammatory stage of disease. In the inflammatory stage proper treatment can reverse and cure the disease.

Remission stage: In this phase an autoimmune disease is inactive, no new attacks are taking place. Disease activity measured by the CRP or ESR will show low values. In the remission stage the person needs to be continued on treatment only if the CRP or erythrocyte sedimentation (ESR) rate is abnormal. However anti-inflammatory diet should be continued.

Progressive Stage: After being in the inflammatory stage without treatment, the autoimmune diseases can enter a progressive stage. This will not be seen in all the patients. Spontaneous

improvement is termed **disease burnout**, some how the immune attack stops in many patients. In progressive stage, remissions and relapses are not seen, but there is just a progressive down hill course. Some diseases like Multiple Sclerosis take a few years to enter this phase others like Giant cell Myocarditis enter this phase within a few weeks of onset. In the progressive stage of disease, the treatment should be high dose and aggressive. Some patients have been saved with aggressive treatments even in the progressive stage.

-Chapter 2: Causative factors in autoimmune disease:

1ncidence of autoimmune diseases are higher in the underdeveloped countries where pollution and chemical contimanation combined by diets (high in processed foods and calories) fuel the inflammatory process. Excessive exposure to 60 Hertz electrical fields, microwaves, cell phone towers, chemicals and Pork in the diet is harmful. Children who did not get colostrum (premilk produced after pregnancy), are at risk of getting more infections and higher risk of autoimmune diseases. Children who spent their third semester in uterus during the winters while their mothers were exposed to infections also show a slightly higher rate of autoimmune disease. Children should get mothers milk for at least two years. Colostrum has strong anti-inflammatory properties and is produced from the mammary glands after the termination of pregnancy. Fresh colostrum is packed with antibodies, growth factors, and nutrients. In pregnancy the mother is passing a lot of her antibodies to the baby. There is a natural vaccination against some diseases in colostrum. The natural vaccination by nature is without any side effects.

The autoimmune diseases are often chronic, requiring lifelong care and monitoring. Currently many autoimmune diseases can be **cured** or made to "**disappea**r" with **early treatment**. Myasthenia Gravis can be cured in most patients with the removal of Thymus Gland in the neck. Kawasaki disease in children can be cured if IVIg, steroids or aspirin are provided soon after the diagnosis. Celiac diseases can be cured by removing Gluten from the diet. Antibiotics will reverse arthritis, Alzheimer's, skin diseases, asthma, vasculitis, SLE, Takayasu, Fibromyalgia, CIDP and multiple sclerosis. Early treatment in autoimmune diseases has resulted in long term remissions. Majority of patients with autoimmune diseases live normal lives, provided the disease is anticipated early and treated promptly.

Genetic Factors: The genes we inherit do not contribute to the susceptibility for developing an autoimmune disease. Family members with autoimmune diseases may inherit and share a set of abnormal genes, although they may develop different autoimmune diseases. Mother may have diabetes, the daughter gets vasculitis and granddaughter may have asthma. Then do we really have genes to get all those diseases or **we are getting chemical and bacterial exposures**.
In the group of children with asthmatic mothers, **those exposed to a cat were significantly more likely to wheeze as compared to those with no cat exposure**. In fact, the risk of wheezing increased in each of the five years of the child's life. By the third year, the risk of wheezing doubled, and by the fifth year it more than tripled. **Toxins are the real** cause that makes our **genes ineffective**. Its **not really the genetics** that **we are being made to believe** but **the chemicals, bacteria and toxins** that alter the expression of our genes.

Diet: Inflammation can be triggerd by an inadequate diet, which is deficient in nutrients but exceeds in **toxins**. In many conditions like Alzheimer's, Epilepsy, Migraine, Fibromyalgia, ALS

and chronic fatigue there is a magnesium deficiency seen in patients. Deficiency of magnesium is associated with a higher CRP level, which if left untreated will trigger autoimmune diseases. Magnesium supplements are used to stop epilepsy attacks. Magnesium is deficient in patients who eat white flour, only 16% of magnesium is left in white flour when compared to whole wheat. Patients suffering from clinical depression were given magnesium supplements and showed a sudden reversal of symptoms.

Aluminum and **Fluoride** exposure results in osteoporosis due to magnesium and calcium deficiency. Buffered aspirin contains aluminum, antacids, antiperspirants, diapers and famous anti diarrhea products contain aluminum. People with chronic renal failure treated with aluminum-containing medications and pre-term infants fed on aluminum containing formula are at high risk of aluminum toxicity. The healthy human body can defend itself adequately from aluminum's toxic effects, but long term aluminum exposure has to be avoided
Vitamin deficiency like, Cynocobalamin (B12), Folic acid, Pyridoxine (B6), Thiamine (B1) and Vitamin-D have all been associated with inflammation. In the entire western world there is a higher incidence of Multiple Sclerosis. **The countries with a highest incidence of MS have the lowest amount of sunlight year round. Reduced sunlight in turn causes vitamin-D deficiency; supplements of vitamin-D independently improve symptoms of MS. I would recommend Cod Liver Oil 1000mg supplements for children and adults during winters** to prevent all autoimmune diseases specially multiple sclerosis. If too much cod liver oil is consumed it will cause skin spots on the face that is time to reduce the dose. Those people who are deficient in vitamins can take supplements but the best way to replace vitamins is through a proper diet high in nutrients. A few people will need supplements; among them are those who have had H.pylori infections resulting in stomach ulceration.

Homocysteine is an intermediate compound formed during metabolism of methionine (an amino acid). Elevated serum homocysteine levels are a known risk factor for heart disease, stroke and autoimmune disorders. The plasma levels of homocysteine are dependent on the intake of folic acid, vitamin B6 (pyridoxine), and vitamin B12 (cobalamine). We have no accurate laboratory test to measure minimum levels of B12 deficiency. Even if a lab tests shows a normal rage of B12 and normal serum folate levels, the body may actually be deficient in B-12. A more sensitive indicator of B-12 deficiency is **homocysteine.** If homocysteine levels are high which means higher inflammation then sub-lingual supplements of vitamin B12, B-6 and folic acid help reduce serums homocysteine levels, this vitamin replacement will also reducing the risk of myocardial infarction and stroke. Homocysteine is an important marker and a risk factor for autoimmune diseases. Instead of testing homocysteine levels in every patient **I recommend a diet rich in the vegetables and fruits.** In those patients who are clinically anemic I recommend supplements of these vitamins to <u>be given by sublingual route.</u> The sublingual combination of folic acid, pyridoxine and Cynocobalamin is available in health food stores.

Sunshine & Environment: Many of the autoimmune disorders are triggered by excessive cold, protective clothing is required in cold weather. A nerve disorder like facial paralysis is triggered by cold exposure. Summer heat and the hot afternoon Sun will trigger skin disorders and sun stroke; proper protection from the hot afternoon sun is a requirement. When the skin turns red on exposure to the sun, this redness is a sign of inflammation which should be avoided by using proper clot. Multiple sclerosis and neuropathy are aggravated by heat exposure. Extremes of

temperatures will produce *stress proteins* which causes inflammation in the body. To read more about stress proteins please see the immunology chapter.

Sunlight stimulates the pineal gland in the brain; pineal produces certain chemicals called 'tryptamines'. The human body requires a prolonged exposure to the sun to produce vitamin-D and keep our mood happy with the tryptamines. **Avoid routine use of sunglasses, especially on cloudy days, allowing the sunshine to light up the Pineal gland for increased production of tryptamines.**

Vaccination: The association of vaccination and resulting autoimmune disease is well known. The Centers of Disease Control (C.D.C.) reported an association between flu vaccine and Guillian Barre Syndrome (GBS). The affected person in whom the disease is triggered by a vaccine should get immediate high dose steroids or IVIg, the whole vaccine triggered disease process should resolve. **Physicians need to be aware that potential treatment exists, that is by using steroids or IVIg soon after the reaction**. The incidence of GBS after flu vaccine is usually seen within the first 6 weeks. Fortunately incidence is low at 9 cases of GBS per million vaccines given. Post vaccination GBS is also reported with tetanus toxoid and tetanus-diphtheria toxoid. The reaction happens most likely due to antibodies present in the vaccine triggering an autoimmune response against self. If someone develops a reaction don't wait ask for IVIg or 100-mg of prednisone. I have seen patients who developed chronic fatigue and CIDP following vaccination. Thimerosal is a mercury-containing preservative which was linked to autism. Today, with the exception of some Influenza (flu) vaccines, none of the vaccines used in the U.S. to protect preschool children against 12 infectious diseases contain thimerosal as a preservative. Is your country providing Thimerosal free vaccine? **I would not strand in line to receive a flu vaccine**. In many cases vaccinations with tetanus and flu shots have triggered an autoimmune disease; in retrospect the patients who suffered from such reactions had undiagnosed **immune deficiency**. After the 9-11 incidents, USA congress passed the **Patriot act**, in which was piggybacked a bill that made the vaccine companies immune to any lawsuits. There are some benefits of flu shot vaccine; among them is improvement in those people who have frequent runny noses or allergies with just one shot. Avoid flu shots if you have autoimmune disorders. In USA the government offers financial package to the parents of any baby whose death is caused by vaccination.

Injury: Injury has been studied for many years as a cause of autoimmune disease. Railway spine was a term used in early 1900 for chronic pains seen in people following a railway accident that was later termed the railway brain as a way for people seeking compensation. The railway spine condition was discredited. However the modern malady of Fibromyalgia is similar to the railroad spine and is triggered by an injury and considered a valid entity.
For over a century, patients and physicians have dealt with the phenomena that trauma may precede the onset of multiple sclerosis but multiple studies have failed to show such a relationship. The literature does show Pemphigus, Fibromyalgia, eye injury (sympathetic ophthalmia), renal failure (glomerulonephritis) and long term neuropathies are triggerd by trauma. Multiple studies from earthquake injured personnel show long term sensory motor neuropathies caused by trauma. Scientists think swelling in the anterior and posterior compartments in the leg, due to injury causes the neuropathies (nerve injury). These observations are helpful for future prevention of autoimmune disease, by administering a dose of prednisone

at the time of injury the person can avoid swelling in the tissue and prevent these nerve injuries. Activation of stress proteins at the time of injury can cause inflammation and swelling. **You can suppress the stress proteins after an injury by consuming Omega-3 Oil 1000 mg for children and 3000mg for adults.** (**Flaxseed oil, Fish oil, Olive oil**). Need to take omega-3 after any surgery, injury or child birth for a month to prevent autoimmune disease.

Injury can triggers an immune reaction, just look at the swollen feet of an injured athlete. No bones are broken, the muscles are intact but the swelling is an immune reaction. In any injury the naturally protected proteins in the body get exposed to the immune system. Following the exposure, the immune system mounts an attack against them. After a head injury inflammation develops in the brain, this is triggered by *stress proteins.* **The head injury may not be seen on a MRI scan but the rise in inflammation can be measured by the C-reactive protein test.** Steroid or Omega-3 treatment following an injury prevents *stress proteins* from activating. Steroids or Omega-3 use at the time of injury results in a lower incidence of autoimmune disease later in life. **I recommend that omega-3 oils to be used to suppress inflammation.**

Stress: Stress can trigger autoimmune diseases; *stress proteins* are produced by the cells, which trigger inflammation within the body. Stress related neuropsychiatric disorders like P.T.S.D. (post traumatic stress syndrome) are associated with immune system activation, resulting in inflammation. Healthy people living in conditions of chronic stress frequently show lower urinary and plasma cortisol, which will allow more inflammation. PTSD can happen following a sexual assault, car accident, chronic job stress (soldier, policeman, and fireman) or being in a natural disaster. Once the cortisol levels are depressed, inflammatory markers like CRP start rising up. In a study done on women in Israel, who were exposed to stress, their CRP levels were found to be elevated. Those suffering from chronic fatigue syndrome and Fibromyalgia have lower levels of cortisol (hormone). In untreated PTSD patients cortisol levels are lower and inflammatory levels are high, both factors pave the way for autoimmune diseases. Stress leads to early symptoms of stiffness, neck pain and difficulty sleeping. Early intervention by restoring the normal levels of cortisol can stop the stress process. The correct medicine to stop stress in PTSD will be omega-3 or DHEA (De**h**ydro**e**pi**a**ndrosterone). DHEA is an over the counter hormone precursor which will help reduce inflammation. The routine psychiatric medications like serotonin reuptake inhibitors will not relive the inflammation associated with PTSD, resulting in the high mortality as a result of suicide, often seen in servicemen returning from war duty. **Aspirin, prednisone and omega-3 oils will prevent inflammation in PTSD.** To control stress see the lifestyle and diet chapter.

Excessive Exercise and Low fat a bad combination: Excessive exercise has resulted in athletes to develop autoimmune diseases. Exercise should be done with rest periods. In older patients excessive exercise causes heart failure. Chronic fatigue, CIDP, ALS are among the diseases which can develop after excessive exercise or activity. Moderate exercise enhances the immune status, but when athletes exercise to the maximum, it stresses the immune system, especially when they are training heavily and don't get enough rest, this leaves them susceptible to neuro-muscular diseases. Switching from a low to moderate fat diet dramatically increased the number of natural killer cells, according to a research study. The study shows, "**a low-fat diet,** adhered to by competitive athletes, may not be best for the immune system, by increasing dietary fat to moderate levels improves the immune functions. Lowering fat in the diet triggers higher

cholesterol levels which results in more inflammation. **To lower body cholesterol we need to increase good dietary fat, there is an inverse relationship between essential fatty acids and cholesterol, poorly understood by physicians and the lay people alike.**

Commonly seen autoimmune disease in athletes is cardiomyopathy (CM) which initially present with the athlete having symptoms of dizziness. CM is a dangerous condition which requires immediate rest for 2-3 months duration. Inflammation in CM is triggered by a low-fat diet and over exercise. For the management of athlete-myocarditis please read the cardiac section. Before any exercise the body needs to be well hydrated, for the intense metabolism the body needs normal **fat**, protein and carbohydrates. Majority of the athletes who start an exercise plan, combined with a low fat, low carbohydrate diet will lead to the release of excessive *stress proteins*, resulting in more stiffness and weakness of the muscles. Our bodies require more omega-3 type fats and less omega-6. The correct proportion was placed by nature in whole wheat and whole brown rice, flax seed, coconut, walnut, almonds and peanuts.

Chemical & air inhalation Exposure: Single or repeated chemical or contaminated inhalation exposure can result in autoimmune diseases. Exposure to fumes, toxins, pesticides and contaminated air has triggered diseases. In infants **even a single exposure to carpet shampoo will trigger Kawasaki disease in infants**. **Fluoridated water or chlorine can cause Myasthenia Gravis**. **Pesticides have been linked to cause Parkinsonism**. Recent Pork plant workers exposed to **inhalation** of pork brains resulted in many developing CIDP, in USA. Inhaling cocaine and other drugs may also trigger autoimmune reactions. Chemicals are everywhere and also contained in drugs. In a recent study, done on people who had been exposed to amphetamines (drugs used for sleep disorders and attention disorders) a relationship between the amphetamine and development of Parkinsons was discovered. Tobacco smoke contains a mixture of over 4700 chemical components many of which are toxic and have been implicated in the etiology of chronic obstructive pulmonary disease (COPD), asthma, cancer and cardiovascular disease. Some chemicals like Agent Orange not only give rise to autoimmune diseases, but parent's exposure to Agent Orange appears to be associated with an increased risk of birth defects in their children. A drug called MPTP caused Parkinson in M.J. Fox and many young people, which is an autoimmune triggered reaction of the drug to the substantia-niagra (dopamine producing region in the brain) which can improve with immunomodulation. A higher incidence of Parkinsons is seen in gardeners and farmers directly linked to pesticides. Chemicals activate *stress proteins* which results in inflammatory diseases. Single or multiple exposures to chemicals can cause an autoimmune reaction to be trigged in genetically predisposed patients. Pesticides induced problem can be avoided by using gloves, masks and taking a shower soon after work. **Do not walk your kids in the Garden section of superstores filled with the smell of pesticides**. If you are living in a city where smoke and exhaust fumes are present then triggering of autoimmune disease due to these toxins will be seen. The air in the house needs to be clean and without any smell of mold. Try to ventilate your homes so there is no smells of new carpets, new paint as the particles in these are toxic for your health. Don't let children stand around when the deck or furniture is being varnished. As a child I saw my father growing silk worms, one day they were placed in a room from where a pesticide bag had been removed, the smell present in the room resulted in the death of all the silk worms overnight.

Multiple sclerosis (MS) has a higher incidence in patients with dental amalgam which contains **mercury** and sliver fillings. Significant deposits of **mercury**, previously non-existent, have been found in the lungs, kidneys, endocrine organs, liver, and heart of patients with amalgam. Amalgam has not only been associated with heart disease but also M.S. and cancer. **Mercury and silver absorbed from the amalgam can easily be removed by taking cilantro.**

Chemical analysis of the umbilical cord blood, done in infants showed 270 different chemicals in an average baby's blood. These chemicals can harm the development of the brain and nervous system, cause skin rash, allergies, cancer, birth defects, liver and kidney damage. (These toxins include mercury, flame retardants and pesticides). In an average home, we see carpet cleaners, window cleaners, and grill cleaners these are all toxic. **If you can smell the chemicals you are inhaling them**. Infants are particularly vulnerable as their immune system is developing and these chemicals can cause immune dysfunction. PFQA a chemical in Teflon finds its way to the baby in the uterus. PFQA takes years to leave the body and can be found in the environment and animals as far away from sources as polar bears in the Artic and dolphins in the Mediterranean. Traces of PFQA have been found in patients all over the world. EPA began its investigation into PFQA, they found it is very persistent in the environment; PFQA was present at low levels both in the environment and in the blood of the general US population. Though only trace amounts of PFQA exist in Teflon products when they hit the market, some scientists believe the chemical may be released as Teflon ages. Other scientists have suggested that PFQA, which is also used in stain and grease-resistant carpets, clothing and fast-food packaging, may be released into water supplies when carpets or clothing are washed. Children can crawl and lick the carpets. PFQA is found in french-fry boxes, microwave popcorn bags, and hamburger wraps. Bisphenol is used in polycarbonate plastic baby bottles and in resins that line food cans, it have been found to alter brain structure, neurochemistry, behavior, reproduction and immune response in animals. **You can replace all your chemical cleaners and toothpaste by using Baking Soda as a universal cleaner. Ask for paper containers when you purchase food, or carry your own cotton bag. Do not purchase Teflon coated products, neither will you cook in non stick pots and pans.** Avoid feeding your babies in plastic bottles, avoid drinks in plastic containers. Avoid refrigerated drinks in aluminum containers. Ask for glass bottles, silver or earthen containers will be best.

Poisoning: The most common cause of poisoning in the US is exposure to carbon monoxide. Carbon monoxide exposure not only results in a reduction in Oxygen saturation but it also triggers an inflammatory response. The inflammatory response is seen from after any chemical exposure including diesel and kerosene fumes. Food poisoning may also trigger autoimmune diseases. After an exposure to any poisoning if the symptoms in the affected person do not improve not improve with treatment, then a CRP test should be done to look for inflammation, if CRP is elevated then the inflammation should be treated with either aspirin, steroids, **omega-3** or IVIg. Heavy metal intoxication with gold, mercury, and manganese, are known stimulants of the immune system and has been implicated as causes of autoimmune diseases. After an exposure to any poison use a mud bath by covering your face arms and legs with clay, then wash your skin with water, avoid soaps. You can consume some clay and it will clean your bowels.

Biggest Cause of autoimmune diseases is infections: There are lots of bacteria and viruses around us that will trigger autoimmune diseases **(Helicobacter pylori, Chlamydia pneumonia,**

Mycoplasma). We do not have to worry about getting them you already have them in your body. People who put metallic objects in their mouths have higher counts of these organisms. Once an organism enters our body, the immune system recognizes the biological identification markers on this invader. Then the immune system mounts an attack on the organism, but in people with weak immune systems this attack also damages their own body. We are all carriers of Mycoplasma which may have spread from various bugs including mosquitoes.

Molecular mimicry is one mechanism by which infectious agents can trigger an immune response against self. According to this hypothesis a host acquires an infection with an agent that has antigens that are similar to the host antigens but differ sufficiently to induce an immune response. The resulting immune response will attack the infecting organism and also damage specific host cells that resemble the antigen. A scientist found that an infection with a rotavirus, a type of gastro-enteritis which infects almost all young children, triggers type-1 (childhood) diabetes in susceptible patients. It was noticed that some parts of the virus proteins are very similar to proteins on the surface of pancreatic cells. Because of this similarity, the body's immune system attacks both the invading virus, and the body's own pancreatic tissues. Diabetes develops, when the immune system attacks pancreatic cells, reducing the production of insulin. It was found that the children who went on to develop diabetes experienced a big jump in anti-pancreatic antibodies every time they became infected with Rotavirus. Molecular mimicry of the pancreatic proteins by the Rotavirus may cause the immune system to attack the pancreatic cells.

Idiopathic thrombocytopenic purpura (ITP) a blood disorder that causes destruction of the small sticky platelets, is caused by autoantibodies sticking to platelets which leads to destruction of platelets, ITP has been associated with Helicobacter pylori infection. Myocarditis (heart enlargement) is triggerd off by Coxsackie-virus, Cytomegalovirus-virus and streptococcus infections. Ankylosing spondylitis (arthritis) is triggered by Yersinia or Salmonella. Multiple Sclerosis can be triggered by Epstein-Barr-Virus, Coronavirus, Acinetobacter and Pseudomonas aeruginosa. Early infection should be promptly treated and a full course of the antibiotic should be taken, to effectively eradicate even a low grade infection. **Specific antibiotic treatment helps prevent the triggering of autoimmune disease**.

In a large study a group of American dental patients, were studied by measuring their CRP. The CRP which measures inflammation was elevated in those patients with **extensive periodontal disease**. Regular cleaning of the teeth and gums helps us stay healthy and keep the inflammatory levels low. Dental disease is associated with higher risk of heart disease, stroke and infections. Use baking or herbal toothpaste to clean your teeth. Avoid the toothpaste that is full of **fluoride** especially in children. Please read about **oil pulling** in the last chapter, which is a technique to revive unhealthy gums and it also cleans and whitens the teeth naturally.

The best prevention for diseases is to wash your hands with water only, before you eat or touch food. Kissing can easily spread thousands of bugs, present in the mouth if the affected person has periodontal disease. (Intimate kissing with multiple partners) has caused many serious infections like meningococcal disease. Infectious mononucleosis (mono) or glandular fever is often called the **kissing disease**, but more commonly coughing, sneezing, or sharing a glass or cup transmits mononucleosis. Similarly, infections have originated after the people have kissed their pets. Pets should not be allowed near new born who have a weak immune system. Sex with multiple

unprotected partners should be avoided. Multiple partners expose you to multiple types of the organisms, especially those who have metallic objects in their genitals are full of germs.

Pharmaceutical triggers: Some of the medications like minocin, IVIg, anti-cholesterol medications, monoclonal antibodies, Botox, statins, antibiotics can induce inflammatory diseases which are usually reversible after discontinuation of the drug. If a drug induces an autoimmune disease then to reduce inflammation with omega-3 oils, Turmeric, Curcumin or steroids.

Immune reconstitution inflammatory syndrome (IRIS): This is a condition seen in some cases of AIDS or immunosuppression, in which the immune system during recovery from the infection, responds to a previously acquired infection with an overwhelming inflammatory response that paradoxically makes the symptoms of infection worse.
A sudden increase in the inflammatory response produces nonspecific symptoms such as fever, and in some cases a worsening of damage to the infected tissue.
Though these symptoms can be dangerous, they also indicate that the body may now have a better chance to defeat the infection. The most common treatment is to administer antibiotics or antiviral drugs against the infectious organism, and in some cases corticosteroids to suppress inflammation until the infection has been eliminated.

Infections most commonly associated with IRIS include cytomegalovirus, herpes-zoster, Mycobacterium avium complex (MAC), Pneumocystis-pneumonia, and tuberculosis. AIDS patients are more at risk for IRIS when they are starting HAART for the first time, or if they have recently been treated for an opportunistic infection.

Aids spread was rapid in India, however the same Aids Virus did not spread in neighbouring neighoubring Pakistan the cause of not spreading was simple. The males in Pakistan are circumscribed at birth which inhabits the genital transmission of Aids. Not a single case of SARS in Muslim countries as they do not eat Pork. Hepatitis is rampant in all the third world and Muslim countries due to poor personal hygiene and poor sanitary conditions in restaurants. People have died after consuming meals in Hepatitis Virus laden restaurants. Those people who have used an **electronic pulsar** do not get this illness.

- Chapter 3 Diagnosis of Autoimmune Disease

Autoimmune diseases are simply to diagnose based upon the **disease cycle**. The **weakness, fatigue, pain or fever comes on** and then in a few hours or in a few days it is gone. The cycle of a disease getting better and then worse only happens in autoimmune diseases. This up and down cycle is a important clue. Once you have the clue from the history then just a specific examination of the particular person will clinch the diagnosis. I have described the specific examination findings under each disease. **Rarely** some special lab tests are required which are described under each disease.

Diagnostic clues seen in autoimmune disease are symptoms which, "**remit and relapse** "or "**wax & wane**". The patient may have weakness, fatigue for a month, or days and then they feel better. **Relapsing** (starting) or **Remitting** (ending) disease is commonly seen in Multiple

Sclerosis, Fibromyalgia, Chronic Fatigue and Myasthenia. Any treatment given at the start of a remission may seem to help, one has to observe the treatment for a year or more to see if the disease **relapses** (comes back). Thus symptoms which get better and worst are autoimmune.

Some early symptoms of autoimmune disease: The symptoms start with complaints of **fatigue** and tiredness, followed by feeling of pain numbness and weakness. Patients have difficulty in concentration. Visit to the doctor's office will result in **normal** evaluations. Generally the doctor will refer the patient to a **psychiatrist** or start antidepressants. In the short run any prescription or placebo may seem to help. The autoimmune diseases are **remitting and relapsing** so no matter what drug is used the patient may enter a "remission phase", refers to the situation where the disease disappears completely. Remission can happen even without treatments.

Autoimmune diseases behave like the stock market; some symptoms become worse on some days while other ones improve. The up and down cycles in a disease process should alert the physician of an underlying autoimmune disease process. **These cycles are a diagnostic marker for autoimmune disorders.** There are days similar to a stock market collapse when all the symptoms are worse which are associated with a low atmospheric pressure.

When a person has multiple complaints consisting of fatigue, tiredness, reduced energy, pain and stiffness then a diagnosis of autoimmune diseases in general, and Fibromyalgia, Chronic Fatigue and S.L.E in particular should be considered.

Common autoimmune symptoms, with possible causes and strategies to avoid them:

Fatigue, Insomnia & memory problems: The person **feels tired all the time** and does not sleep well. Their reserve of energy depletes quickly with activity. In the morning it feels like a truck ran over their body, this exhausted feeling with memory loss due to poor sleep. People with Fibromyalgia and arthritis have poor sleep in stages 2 & 3 of sleep cycle. Supplements of magnesium, Fish / Flaxseed oil, DHEA and **sublingual vitamin B-12** help improve these sleep symptoms. For details please read the **fibromyalgia** and Chronic Fatigue section.

Depression: Depressed patients feel a difficulty in doing their daily tasks. During the day they appear overwhelmed and demonstrate **stress** which turns into depression. Depression is caused by inflammation and low serotonin levels in the brain. Tryptophans in milk are activated by warming the milk, the Tryptophan in warm milk once inside the body is converted to serotonin. Consumption of **warm milk** helps overcome the symptoms of depression. Tryptophans are also present in brown rice, yogurt, cheese, meat, peanut and sesame seeds or tryptophan supplement. To reduce inflammation seen in depression, take supplements of fish and flaxseed oil and aspirin may help. Read the chapter on PTSD & depression for more help.

Gastrointestinal Problems: Some people will have symptoms of gas, bloating, cramps, diarrhea, constipation and irritable bowel syndrome following a meal. This is because their stomach cannot tolerate digesting a large meal or they are allergic to the food. The meals stay longer in their stomach, causing fermentation and gas buildup. These patients may need to eat small snacks in place of large meals and avoid any allergens to eliminate their symptoms.

Remember to eat proteins and carbohydrates at different times, taken together they will cause fermentation and gas in some patients. If this does not help then try eating a diet of fruits, vegetables, milk products, chicken, beef and fish for four months. (No gluten, no wheat, rye, barley, millet or oat. (No beer).Use honey in the morning and **yogurt** three times a day to help with gastric motility problems. Read the diet section and celiac disease for more help.

Chemical Sensitivity & Allergies: A dysfunctional immune system starts to react abnormally to various chemical toxins. Chemical exposure to new carpet smell will cause headaches and fatigue, tiredness and pain. To reduce chemical sensitivities, use cilantro to eliminate toxins, Omega-3 to reduce the inflammatory response and check the diet page which guides you to avoid toxins and eat the proper whole foods.

Pain: The most common cause of pain in the whole world is myofacial pain disorder. In myofacial pain parts of the muscle fibers form knots called trigger points which result in pain. These trigger points are seen with every autoimmune disorder, common in MS, Parkinsons and arthritis. Try to stretch your joints first thing in the morning and every three hours during the day. Massage painful areas with olive oil. Magnesium supplement may help reduce stiffness and please read the diet section and muscle stiffness section for detailed help.

Dry Eyes: Some autoimmune disorders because reduced tear production, dry vagina, and eyes get dry and become light sensitive. Keeping the eyes moist and using sunglasses during the day with consumption of sublingual **vitamin B-12** to help reduce inflammation and dryness. Place a drop of Honey in red dry eyes, it will cause burning, tearing for a few minutes, then will ease chronic symptoms. Please read the Sjogrens chapter for more information.

Loud Sounds: cause a startle. Ears become hypersensitive and they can not pay attention to one speaker in a crowd. This is due to the Stapedius muscle going into a spasm. Frequently seen in Stiff person syndrome, Fibromyalgia, post concussion and myofacial pain disorder involving the neck, usually the excessive startle will responds to vitamin B-12 and magnesium supplements, stretching neck muscles and plugging the ears with cotton wool or swimmers plugs helps.

Candida or Yeast infections: Tongue may have white or dark coating. Women may get vaginal yeast infections caused by candida overgrowth usually seen in Southern US due to high humidity. Any infection can cause a number of autoimmune type symptoms**. Apple Cider Vinegar** helps to get rid of fungal infections if taken one teaspoon twice a day. Reduction in the use of antibiotics and supplementing with yogurt helps reduce yeast growth.

Cold feet, Cold hands: Some people have cold proteins called, cold agglutinin or Raynaud's disease which will result in feeling of pain on exposure to cold. Use warm gloves along with a course of **Doxycycline.** Keep yourself warm and hydrated, please read the Cryoglobulin and Takayasu disease chapter for more details.

Simple Blood tests to check inflammation: We recommend that the (C reactive protein) **C.R.P**. and **Erythrocyte Sedimentation rate** (ESR) should be done in every patient. Simple blood test like the ESR is elevated in inflammatory disease. The C.R.P. is also elevated in autoimmune diseases; normally the C-reactive protein should be zero. C.R.P is a more specific measure of

inflammation and should be done in suspected patients to see if inflammation is causing the disease. To access disease activity on a monthly basis only an E.S.R. needs to be repeated as the cost to perform the test is cheaper. Many cases will present with a normal ESR, even when the ESR is normal one should look at the history and clinical findings to properly diagnose the disease and the underlying autoimmune disease process.

Inflammation is also triggered by reduced vitamin levels. The normal lab test to check vitamins in the blood is inaccurate as the normal values have been set **too low**. So another way to check them is by measuring the **homocysteine level**. If the level of homocysteine is high this means more inflammation is present due to vitamin deficiency. To lower the homocysteine level use Cynocobalamin, pyridoxine and folic acid sublingual supplements.

Simple Tests for immune deficiency: Some people who develop autoimmune diseases may have underlying immune deficiency. Diagnosis of immune deficiency is important because these patients can easily be treated. These immune deficient patients present with symptoms of fatigue or with frequent viral or bacterial infections like sinusitis, bronchitis and with frequent episodes of allergies. IgG or immunoglobulin-G is the most common antibody that helps us fight germs. Testing our **IgG levels**, **IgG Subclass levels** and **IgA level** is important test to clinch the diagnosis of immune deficiency. Usually the IgG subclass-2 or the IgG subclass-3 will be deficient in these people. The people with low IgG levels respond well to small doses of IVIg (intravenous immune globulin) at 400mg/kg per month. In Celiac disease the IgG subclass 4 is usually elevated. The IgA levels are only elevated in Hench Scholein purpura.

Screening Antibody tests for autoimmune disease: Not all the physicians agree on doing these antibody tests. **The argument given is if you suspect an autoimmune disease then treat it with a test dose of steroids or I.V.I.G and if the patient responds you have a working diagnosis**. Insurance requirements in USA require some tests results before they authorize expensive treatment like IVIg. For preliminary testing of autoimmune diseases the initial tests are **Rheumatoid factor**, **antinuclear antibody (A.N.A**), **anti-Thyroid Antibodies** and **Anticardiolipin Antibodies** (aCL antibody). If an antibody test is slightly positive it should be considered diagnostic for autoimmune diseases.

There are a lot of specific tests for autoimmune diseases. Like Infertility is associated with **Anticardiolipin Antibodies** (aCL antibody) in women and **antisperm antibodies** in men, Myasthenia is associated with **Acetylcholine receptor antibody** and in Multiple Sclerosis (M.S.) there is no associated antibody but is diagnosed by a Magnetic Resonance Imaging scan (M.R.I). The absence of antibody does not rule out the disease. A person can have Myasthenia and serum tests may still show that the Acetylcholine receptor antibody is negative. In thirty percent of the patients with the disease there will be no antibody on their tests. This is called sero-negative disease. Coming back to M.S. even if the M.R.I. scan shows multiple white spots,

other diseases like Celiac disease need to be considered. Celiac disease is associated with **antgliadin antibody**, this can easily be tested to secure a diagnosis. It is important to consider Celiac, as simple dietary restriction can help the person. **Specific antibody tests** are presented in disease sections**. <u>These antibody tests are expensive, unreliable and usually not recommended.</u>** I do not order antibody tests, as I diagnose the disease based upon history.

Most of the autoimmune diseases are diagnosed by history alone. The diagnosis is confirmed by elevated CRP or sedimentation rate. Some rare diseases may need specific test like a MRI for Moyamoya (a disease causing inflammation of blood vessels in the brain).

Therapeutic trial for a Diagnosis: If any patient has symptoms of fatigue, tiredness, weakness, then it is best to obtain the diagnosis by a **therapeutic trial** of treatment. Try giving the affected person **Doxycycline**, vitamins, honey, and change the diet (celiac diet) and look for a change. Improvement suggests an autoimmune disease process. On the contrary if the person gets palpitations or weakness after taking the Doxycycline that is an indication of severe disease. This reaction can be called a **herxheimers** reaction, (a reaction seen after an antibiotic is given, which results from host cells reacting to the death of dying organism). When I see a herx reaction in a patient I will continue the antibiotic on alternate days for a long term until all the symptoms are resolved. To reduce a herx reaction omega-3 oils or curcumin, turmeric is used.

Chapter 4- Diet and Lifestyle changes for prevention of autoimmune disease:

This anti-inflammatory diet should be consumed to avoid inflammation. This anti-inflammatory diet will help prevent all the disease mentioned in this book and is recommended for all humans.

Inflammation is triggered by many causes; by decreasing inflammation through diet one reduces the rate of disease and ageing, as inflammation is fueling stress, cancer, ageing, and allergies.

Fats are good for brain functions and nerves, fats are needed for digestion and help is storage and distribution of vitamins. Reducing **the essential fats** in the diet **harms the body** and even causes pre-mature heart attacks, with reduction in the circulating hormone levels. Excessive intake of vitamins B-6 causes permanent neurological damage. Even moderate alcohol intake causes neuronal damage. Thus we need to adopt a balanced diet which contains a combination of carbohydrates, fats, proteins and nutrients. Increased protein intake triggers attacks of gout and porphyria, too many carbohydrates can predispose to insulin resistance thus we need a balanced diet. The correct balance is provided to us by nature, in whole wheat, whole brown rice, nuts, fruits and vegetables. We need to avoid the processed foods like white sugar, white flour and processed oils.

Magnesium is an important mineral for our bones, nerves and blood vessels. Found in green leafy vegetable salads, sesame seeds, pumpkin seeds, peanuts, halibut and black beans. Magnesium (Mg) deficiency is seen in many conditions. The conditions aggravated by Mg

deficiency include migraine, multiple sclerosis, glaucoma, osteoporosis, Alzheimer's disease, muscle stiffness, pain, asthma, and fatigue. I recommend that everyone should take magnesium rich foods. If a medical problem occurs only at night, or in certain periods of the year like winter and autumn (minimum sunshine) then supplemental magnesium will help the patient. Epilepsy or migraines which happen at night are relived by magnesium supplements at 400 mg taken two or three times a day.

Zinc deficiency is a frequent human dietary problem in the United States and is associated with diseases like alcoholism, renal disorders, hair loss, skin lesions, gastrointestinal tract disorders, memory problems and asthma. Modest deficits in zinc cause reduced immune capacity and lower white cell counts. A suboptimal intake of zinc causes marked atrophy of the thymus, a reduction in leukocytes (white blood cells), and a reduction in immune functions. Zinc is needed for lymphocyte development and antibody production, particularly immunoglobulin-G. Zinc is contained in beef, yogurt, liver, whole wheat, sesame and pumpkin seeds. To maintain **proper immune functions our body needs Zinc**. High zinc intake may cause seizures.

Silver throughout history has been used as an antibacterial compound. The royalty in Europe used to eat from silver spoons and drink in silver cups due to which their skin color looked bluish (referred to as blue blooded). The blue discoloration seen in the skin is due to excessive intake of silver a harmless condition called **Agyria**. The Food and Drug Administration today classifies **colloidal silver** as a pre-1938 drug. Robert O. Becker, M.D., author of *The Body Electric*, discovered that silver ions **promote bone growth, improve immune function and kill surrounding bacteria**. I recommend drinking out of silver cups and using a silver spoon to eat, wear silver bracelets or you can get supplemental silver.

Aluminum is toxic for humans; it has been associated with dementia. It is present in intravenous feedings called (TPN) and can cause seizures in infants. Avoid aluminum in buffered asprin, anti-diarrhea products, cream filled cookies, powder and roll-on-deodorants and Mylanta.

Copper deficiency, will cause progressive symptoms, of weakness, fatigue, tiredness, **alopecia**, **white hair growth**, anemia, infections, constipation, **neuropathy** and difficulty walking. Serum levels of copper are elevated up to threefold above normal with **inflammations** and with many chronic and infectious diseases, apparently because the body mobilizes all tissue stores of copper to fight the condition. During remissions the copper levels return back to normal. Taking high dose of zinc creates a relative copper deficiency and helps to prevent formation of new blood vessels. Copper is available in a wide variety of foods, including fruits, nuts, legumes, avocadoes, and shellfish, but deficiencies may occur in adults who have **celiac disease** or are on very restrictive diets. Wearing a copper bracelet has helped many golfers improve their game. Consider using **copper bracelets** on your wrist to reduce joint pain.

Fluoride is toxic for all life forms a high dose will cause death in infants. Milder doses in restaurants and schools have resulted in abdominal pains. Chronic low doses will stunt growth and have resulted in hypothyroidism. It’s recommended that you drink the non fluoride water. Finland, Sweden and Holland have cut tooth decay rates by 90%, 80% and 70% respectively over the past 20 years, without using Fluoride in their water supply. A scientific study showed people taking Fluoride in the water had lower amount of infection fighting cells. Trees do not

grow well with Fluoride in the water and to compensate trees will produce more magnesium to trap the fluoride. **Toothpaste**, pesticides, automotive wheel cleaners all can contain fluoride. Ingestion may cause low calcium in the blood, epilepsy, irregular heart beats, and coma. In hospitals calcium chloride and magnesium salts are given to reverse fluoride intoxication. Do not leave fluoride products within the reach of children. (Read the labels on these products). The best teeth and gums that I have seen are of people who use Muswak on their teeth. Muswak is the skin peeled of trees, then people use this as a brush on their gums and teeth.

Avoid **Dental amalgam** (an alloy made of silver, copper, tin and zinc, bound by elemental **mercury**). If you cannot get an amalgam free cavity filling can say goodbye to the tooth. Some of the dental amalgams contained mercury. The use of mercury in amalgam has been related to development of Multiple Sclerosis. To remove excess mercury, from the body **Cilantro can be used,** cilantro chelates mercury out of your body within a week if used twice daily.

Some of the treatments to avoid are **Ayurvedic medications** which contain herbs, minerals, metals, or animal products and are made in standardized and nonstandardized formulations. During 2000-2003, a total of 12 cases of lead poisoning among adults in five states were associated with ayurvedic medications or remedies as reported by CDC.

Hydrogen peroxide bought from heath food stores in the US and ingested in concentrated form has resulted in instant strokes, facial burns and skin burns. Hydrogen peroxide should not be ingested **in high concentration**. The patients who died after the ingestion of hydrogen peroxide were trying to use the supplement to improve their oxygen levels. The proper way to consume Hydrogen peroxide will be to dilute it according to instructions written on the package.

Omega-3 Fats & Oil: Fats and oils are important for the body especially for the brain and nerves. Myelin is made from lipids, enzymes and body functions are related to amount of lipids in the body. Higher intake of oils containing omega-3 will lower cholesterol. I have seen many young doctors who died from fatal arrhythmias caused by low fat diet and heavy exercise. Low fat diet causes athletes to develop cardiac arrhythmias. The processed and refined oils on store shelves are useless and are low in **essential fatty acids** (E.F.A). **Natural butter**, **olive oil**, **flaxseed oil, fish oil** and walnut oil are good sources of E.F.A and **omega-3**. I recommend taking two tea spoons of EFA daily. **Coconut oil** has medium chain fatty acids which are similar to mother's milk called Lauric acid. Consumption of **coconut** will increase your dietary fiber, **improve immune** functions and help get rid of viruses and bacteria. This oil will not elevate your triglyceride levels or cholesterol. Coconut is an anti-ageing food.

Alpha-linolenic acid (ALA) is one of the two essential fatty acids in humans. ALA is important in important in the prevention coronary heart disease. Like other fatty acids from marine origin, it prevents cardiac arrhythmias and sudden cardiac death. The optimal dietary intake of alpha-linolenic acid is 2 g per day. The main sources of alpha-linolenic acid are **flaxseed oil (linseed-oil),** nuts (walnut), ground linseeds and green leafy vegetables such as purslane.

Flax seed oil is a wonder oil to protect us from many autoimmune ailments and cancer, the recommended way to consume Flax seed oil is by mixing it with cottage cheese and consuming it in the morning fresh. Highest content of Omega -3 is in Flax Seed Oil.

People frequently ask me about good cooking oils? We need to understand how the cooking oils are manufactured; the manufacturer is concerned about the long shelf life of their oil. So they will process oils extensively and most will lose their nutritional value. To increase the production manufactured oils are produced by chemical extraction. These chemicals further destroy the nutritional value of cooking oils. Processed oil is odorless and looks all clear, while **pure olive oil** will have **a cloudy precipitate** at the bottom of the container which disappears upon shaking. For **light cooking** one should use, water mixed with **Butter oil**, Mustard oil, Palm oil. The Canola oil is made from rapeseed, heavy pesticides have been used in the cultivation of rapeseed and may still remain in the oil. Some authors reported that long term users of Canola may develop vitamin-E deficiency. Canola oil is not recommended. **Coconut oil** can be used; it has a good taste and is the main ingredient in chocolates. For frying foods one needs to use a Hydrogenated oil or Ghee as they will withstand higher temperature of cooking as compared to oils. It is best to avoid cooking and eat raw foods and vegetables and fruits. Cook lightly, well done foods are useless. Stay healthy and try to eat a raw diet, without cooking.

If you have Celiac or Autoimmune diseases try a Gluten free diet, this diet should be tried by those who have weight gain, early ageing, temper problems or autoimmune diseases. The diet is simple; Use only milk, rice, vegetables, corn, fruits, meats, fish, chicken, honey, juices and water. See how you feel? No pasta, no beer, no alcohol, no bread, cakes or cookies. The cornbread, corn flour is perfectly ok to eat with a gluten free diet. The grains not allowed are wheat, rye, millet, barley, and oats. At least for three months the above diet should be tried to see if it helps you. Some people do well on a lactovegetarian diet (a diet of milk, vegetables and fruits). White bread is often tolerated well by celiac disease patients.

Children and adults who snack frequently on high carbohydrate foods may develop, "**auto-brewery syndrome**". These patients may have short intestines to begin with; they show features of alcohol intoxication because of abnormal yeast proliferation after ingesting carbohydrate-rich meals. Blood test on a person who had no external alcohol, showed an ethanol concentration of 15-mmol. These people have a tendency to fall asleep after a heavy meal, due to the production of large amount of alcohol from the fermentation in the autogenous brewery. Treatment is simple start fasting and take low carbohydrate foods.

Organic Foods: One should eat whole foods and avoid processed foods. Naturally grown food will not contain the **poisonous pesticides** present in non organically grown foods.

The recommended breakfast should consist of oatmeal with whole milk along with teaspoon of organic honey and a tea spoon of olive oil. Alternate with a whole boiled egg, the main nutrients in the egg are found in the yellow portion which helps reduce heart disease, the white portion is full of protein called albumin. Take some blue berries, walnuts and almonds. A slice of toast made from muti-grain bread. (**Avoid white bread**). Avoid **white sugar and candy**. Brown sugar is much better then white sugar. Tea has antioxidants and taken three times a day is very beneficial for health. Coffee causes too much stimulation and some people may see symptoms of fatigue after drinking coffee. Green tea is more healthy and taken four times a day will keep you healthy and reduce inflammation. Many studies have shown that green tea drinkers have a lower incidence of stomach cancer because it gets rid of *h pylori* from the stomach. Yogurt or milk

taken three times a day regularly will aid in reducing *h pylori*. Breakfast is the most important meal of the day so please eat this meal.

Snacks between meals should consist of fruits and **nuts**, **fruits** and water. Those of you who are going to do extreme exercise they need to take a high load of **carbohydrates** before the activity. Athletes should take a normal amount of **fat** as a low fat diet predisposes them to immune dysfunction. More fat in the diet helps the body in providing readily available energy. Otherwise the body has to turn into anaerobic mode does not sound good. Lunch should consist of high vegetables & some protein (peas, chicken, Fish, and well cooked beef). Eat plenty of fruits, carbohydrates and replenish your fluids by drinking water. The best lunch will be green salad mixed with fruits and nuts with a dressing of **vinegar** and olive oil. Men need to avoid **Tofu** (tends to increase feminine hormones). Regular use of at least **two tea spoons of apple cider vinegar** will clear all fungal infections in the body. The nail and skin fungus will come back within one week of stopping vinegar. Sweets after lunch are good for the brain.

For dinner eat a high vegetables & protein diet (peas, lentils, Chicken, fish, Beef) with vegetables, fruit and water. Remember to use only whole multi grain bread. The best dinner will be green salad mixed with fruits and nuts with a dressing of vinegar and olive oil.

AVOID PORK! (All **the countries that got SARS were those who consumed Pork, countries where Pork was not eaten did not get SARS**). Please visit the farms in North Carolina to see how dirty the filthy the farms are where the pigs are raised!

Chew your food well, chewing food in the mouth will allow more absorption of vitamins from the sublingual area. **Eat slowly** and chew food to small particles before **swallowing.** This helps avoid choking. **Don't drink and breathe at the same time**. This will put enough fluid in the wrong pipe to give you a scare and tears. Eat slowly and chew the food so you get the most nutritional value out of your food.

I recommend eating unpolished brown rice. The polished white rice has the bran coating removed and has lost most of its nutrients (thiamine). Basmati rice has low carbohydrate value and is recommended. Whole wheat bread has omega -3 oils in the husk. People who eat white bread develop magnesium deficiency which leads to obesity and inflammation. Whole brown rice lowers cholesterol.

Avoid sweeteners: (Sweeteners like aspartame which can cause seizures, fatigue and headaches). In sensitive people seizures have been caused by a sweetener. To get rid of ants sprinkle a packet of Splenda in your house. Splenda can kill ants.Sativa is safe.

All the vitamins and supplements are found in food. Thus I recommend that you get your vitamins from fruits, milk, honey, lentils, grains and vegetables. The most common vitamin deficiency seen in clinical practice is **B12**. If you have tingling numbness or weakness, dry mouth your doctor may check the B12 level in you. If the level is low they will prescribe you a B12 injection. The alternative is sublingual B12. **Most patients with B12 deficiency on testing show a normal B12 level**. There are some people who need vitamin supplements, especially those who have damaged stomach lining and cannot absorb nutrients. There is increased risk of

stroke, heart attack, epilepsy, headaches if homocysteine levels are elevated. Treatment with several B group vitamins (**B12-B6 -Folic acid**) has been shown to reduce the level of homocysteine in the blood; even in persons whose serum levels of these vitamins is in the range currently considered normal. For better absorption a sublingual form of the vitamins is recommended. In place of multivitamins we recommend a teaspoon full of honey (organic), regular milk, fruits and vegetables.

A good multivitamin supplement with zinc is needed for those who have a poor diet. Some people self prescribe sublingual B6 for their neuropathy. This may lead to excessive high levels of B6 in your body and result in a permanent neuropathy.

Avoid processed meats like, (hotdog, sausage, salami or pastrami). Processed meats increase the incidence of cancer. Nature created foods with a proper balance of minerals, fats, proteins, carbohydrates and vitamins. Processing of food disturbs the natural balance within meals. Processing leads to poor absorption of minerals and nutrients resulting in inflammation. Protein intake is essential for the human body, proteins should be present in every meal, and proteins can be taken in the form of nuts, beans, lentils or meat. People with **gout** should avoid high protein intake and alcohol in their diet. **Remember the Brain and nerves can only consume carbohydrates for fuel,** so pure protein diets may drop some IQ points and causes Gout. Uric acid can be lowered by excessive water intake without medications.

Carbohydrates are a very important food source of readily available energy. Every cell in the body is dependent on carbohydrates as energy sources specially the brain cells. We need to avoid the processed carbohydrates which make the collagen under the skin weaker and cause wrinkles. People with **porphyria** usually have darker urine if left in sunlight. These people should only use a **high carbohydrate** diets and avoid alcohol and high proteins. Children using carbohydrates before an examination perform better in their tests. Carbohydrates increase exercise tolerance and performance. I recommend that carbohydrates be consumed in the form of dried fruits, fruits and fresh fruit juices. **Sativa** is a plant in South America which is used to make a low calorie natural sugar. I would recommend the intake of **Sativa**.

Fluids: Start your day in the morning with a glass of water. Life on Earth will not be possible without water. Drinks a total of 8 glasses of water a day, (Iced tea, water, lemonade, tea, milk). Regular fluid intake increases the motility of the stomach and intestines, washing the bacteria away. This results in getting rid of constipation, hemorrhoids, dizziness and weakness. Taking care of fluids will avoid kidney stones, keep your teeth clean, avoid fatigue, improve memory, reduce cholesterol and reduce blood clots. Proper fluid intake will help you lose weight as you will not feel hungry. Some constipated people have held 40lbs of fecal material in their guts, increasing fluids will get rid of constipation. Milk is a very important fluid. Daily intake of milk or yogurt has been associated with low incidence of *H. pylori* a bug that induces many of the autoimmune diseases. Milk should be consumed as a whole product no one should be using low fat milk. Green tea also inhibits *H. pylori* in the stomach.

Soda consists of acid which increase the risk of tooth decay and Osteoporosis. The sugar and acid will damage the enamel especially in children. Organic milk is the best drink as it does not have growth hormone and pesticides. Soda intake will also increase acidity and contribute to

cancer. The only good time to take a soda drink is after a heavy protein intake, thus it will help improve digestion.

Beer has been shown to be toxic to the brain, nerves and muscles. Vinegar provides all the benefits of improving blood flow similar to alcohol but without the hangover. Alcohol causes nerve damage (neuropathy), muscle damage (myopathy) and liver toxicity. Scientists have reported that a single glass of beer is able to destroy millions of neurons. Those patients who are suffering form mold related issues need to pay attention to the fact that darker the beer means higher the mold content.

Breathing & Atmosphere: The best drug on Earth is **Oxygen**. It is considered a drug in the US and thus requires a doctor's prescription to be dispensed. **We cannot survive a millisecond without oxygen**. So breathe deeply specially in the morning, deep breathing every morning will help the immune system eliminate toxic bugs. Try to live close to **sea level** as the atmospheric pressure is higher. (No prescription no pharmacy involved). If you live at sea level and decide to visit the mountains **do not go** hiking on the first day. It takes time for your body to produce more red cells and adjust to the lower atmospheric pressure. If you have cardiac or autoimmune-disease then avoid **high altitude.**

We breathe **20, 000 Liters** a day. Every filter need to be cleaned. For a huge body we carry a small filter in the nose, we need to clean this at least once a day. More **oxygen** kills *Borrelia* the cause of Lymes disease. Remember to take deep breaths, this helps burn calories. Studies show that oxygen concentration has decreased on planet Earth. Some of the planets mass extinctions of dinosaurs occurred during or after geologically sudden drops in atmospheric oxygen**.** The atmospheric concentration of oxygen then probably was about 35 percent; the current oxygen concentration is 21 percent.

Half of the world's **oxygen** is produced via phytoplankton photosynthesis. The other half is produced via photosynthesis on land by trees, shrubs, and grasses. The concentration of oxygen in the air is the same at all altitudes, but atmospheric pressure which determines how much air enters the lungs with each breath does decrease with altitude. As less air enters the lungs, the body tries to compensate by breathing faster and deeper. This begins a chain of reactions that can result in altitude sickness. Simple way to recover from this is to breathe faster at high altitudes.

When a storm is approaching and the Barometer falls, that affects the amount of oxygen entering our lungs. Slightly less oxygen combined with increased swelling in the body, produced by the falling barometer results in a feeling of stiffness and pain, felt by people with autoimmune muscle and nerve problems. Lower atmospheric pressure makes our body swell up, causes an uncomfortable feeling to patients with Fibromyalgia and migraine.

Carbon dioxide levels are now 35 percent higher than at any point in the last 650,000 years. There is a higher concentration of Carbon Dioxide (CO_2) under a tree at night. (A location to avoid at night and do not sleep there). The rising levels of CO_2 have led to a near doubling of dissolved organic carbon, (DOC), in rivers over the past 15 years. When DOC reacts with the chlorine, used to disinfect water supplies, it forms, chemicals, such as trihalomethane and

haloacetic acids, that have been linked to bladder cancer, stillbirths and birth defects. You need to avoid these chemical in your water supply. Water Filters are a necessity.

Approximately, 14 million U.S. adults and 9 million children have asthma, according to 2001 CDC figures. Childhood asthma rates have more than doubled in the U.S.A., since 1984 in a trend that has largely baffled scientists. Atmospheric CO2 may be the main culprit. Recent studies identified CO2 levels in large U.S, which are at times up to 60% higher than in rural areas. A recent study suggested that ragweed, is responding to the higher CO2 levels in the atmosphere by producing more pollen. Need to avoid, congested poorly ventilated buildings where CO2 levels are even higher. Rural locations have better air than urban. Children who are exposed to other children in a child care center or those who grow up in farms have a lower incidence of asthma. Children who are exposed to a **cat** at the young age have a higher incidence of asthma in later life.

Avoid pollution and dirty air; avoid the fumes of motor vehicles and machinery, which are toxic for your health. Fumes of stored chemicals, paints, new carpets are detrimental for health.

Exercise: The best exercise is to stretch all your joints and walk. For someone who has Polyneuropathy (numb feet) they should use a stationary Bike or simply the exercise pedals which you can place next to your favorite couch. Use them for 10 minutes at a time four times a day. This will reduce pain, and improve strength by improving the blood circulation. Best of all it can be done in the security of your environment. The next best thing is walking and if extremes of temperature bother you use the local mall. At least 30-40 minutes a day should be devoted to exercise.

Stretch: Before you get out of bed, stretch like a cat or a baby. This will lessen the stiffness in the joints when you start walking early in the morning. People who stop stretching tend to develop osteoporosis. Remember to change your position and stretch regularly. Stretching exercises are recommended about five times a day. Turn your neck from side to side, Bend down on the hips and touch your hands to the floor do this about 20 times. Sit down on a chair and stand up for 20 times. If you can manage, then perform twenty push ups daily. Remember to stretch, five times a day. For back pain lay down on your stomach and then try to raise your chest up by pushing against the floor with your hands, repeat this about 20 times a day, until the pain is gone.

Avoid sitting in front of a cold draft. Cool air makes you stiff. New Born babies will cry if they are not wrapped due to a feeling of coldness. Thiamine deficiency predisposes people to develop stiffness after exposure to a cold draft.

Smoking: Chronic heavy smoking reduces blood flow to your vital organs, (Brain). **The Surgeon General has shown that smoking causes lung cancer.** Smokers have lower incidence of some autoimmune diseases including Alzheimer and Parkinson. This is thought to be due to Nicotine, and the same benefit is seen in tea and coffee drinkers. Get the beneficial effects by tea and coffee. **4000 Americans die, per year, of lung cancer and 37,000 due to heart disease, caused by other people's passive smoke.** Smoking from a water pipe carries the same risk as from other sources. Smoking reduces the incidence of Parkinsonism.

While driving in heavy traffic try recirculation the air in the cabin, which helps to avoid inhaling the fumes of other vehicles. **The best air in New York is on the day the buses go on strike**. Higher, indoor air pollution happens in homes with coal burning and open fireplace. Homes with central heating have less indoor pollution. Do not place humidifiers in an infant's room; they have been associated with induction of (Kawasaki's disease). Do not use chemicals to clean the carpets, use hot water instead. Even a small spray of carpet cleaner has caused (Kawasaki disease) in infants. Water is a universal cleaner just boil it to clean any carpet stain.

Clothing: Do not wear synthetic clothing, cotton keeps you feeling healthy. (Silk underwear's can cause fungal infections). Sleeping on silk sheets is very cumbersome as they slip off at night. Having sex in silk clothing has been promoted by the Mogul Emperors in India. Wear light color clothing in the summer as light colors reflect heat, dark colors should be used in the winters as they trap heat. Cover your face, arms legs in intense sunshine.

Sunlight: Do not use sun glasses early in the morning. Sunglasses reduce your melatonin and Thymosin production. This may end up causing you to be fatigued later in the day. If your eyes twitch, blink and hurt then expose them to regular sunlight early morning and evening without glasses and the symptoms will improve. Melatonin is a very important chemical and acts as an anti oxidant and free radical scavenger and deficiency is linked to aging. Curiously St. Johns wort is used for depression that is a melatonin stimulator. Tests on florescent lighting in a school in Florida, showed evidence for increased Hyperactivity, Irritability, Depression and Fatigue among exposed children. A two hour exposure daily to Sunlight cuts down on depression, hyperactivity and fatigue. Infants should only be exposed to the early morning Sun.

Personnel hygiene: Do not forget personnel hygiene. Take a bath everyday with water to wash off the bacteria. Brush your teeth twice a day minimum, use dental floss or Colostrum to clean plaque, and wash your mouth five times a day with water to get rid of bacteria. The biggest cause of Heart disease is the bacteria which enter from your mouth directly in your blood stream. Honey prevents gingivitis and periodontal disease, if applied to gums three times a day after meals. Wash your hands before every meal. No bad odors should come from you, your clothes or your home. Bad odors suggest mold, bacteria or toxins. Good smells improve health (aromatherapy) works so use natural perfumes around the house. Make sure you wash your hands all the time you cannot afford another infection. Use coconut oil or mustard oil on your hair at night. Use virgin olive oil and honey mix on your face at night to reduce redness and dark spots. Use tea tree oil, flax seed oil on your nails to get rid of fungus.

Clay is a natural source of nutrients; we need to use the clay coming out of mines as it is safe. The clay exposed to the open atmosphere has been polluted. **Bentonite** is a special form of clay found to have medicinal value. Use this clay in place of soap, to rub your face and body, then take a cold shower. A cold bath is considered by some to help lose weight. The clay if left on the hair will hold the hair in place and leave its yellow stain for a day or two until it dries and falls.

Spirituality & soul: Spirituality is a measure of the strength of our sprite inside the body. To achieving inner peace, reduce stress start by taking care of your soul. When we load software on a computer suddenly it comes alive. Without software a computer has no soul its dead. Our soul can communicate with the sprite of dead people during sleep; we see episodes in dreams which

have specific meanings or warnings, when you have such a dream then discuss these with other people to find a solution. When you see dead parents in your dream, then they are actually visiting you that night. Warnings are sent to you in dreams. A constant sensation of fear is caused by other people planning against you (time to start praying). A sensation of fear which comes up on entering a particular place and goes away on leaving that room is caused by "Evil Jinn or demon" in the room leave some written prayers and these feelings will vanish.

Help your soul get stronger by **meditating, praying** and focus on telling yourself that you are improving daily. If you think positively, keep a smile on your face and walk with energy. **Remember to thank God** on a daily basis. Remember to be honest, to help people. Then things around you will change. If there is too much stress at work then start talking to others so you do not have to pay to the psychiatrist. Exercise which involves stretching will help in overcoming stress. Think positively and only of good things, stop all negative thoughts. Do not worry about things, worry will not solve any problems, worry increases stress. While you pray your soul relaxes. When a problem arises, think and seek help from others (teamwork). Soul needs a reason to live on that is **love**. (Love someone, something and see what it will do to you). You need to have a **purpose**, a **project** need to involve yourself in something. Try to help other people and then you receive an automatic reward which makes you feel good and relaxed. Do **not lose your temper** or raise your voice, stay cool and smile often. If someone dislikes you and you want them attracted towards you, then while you are resting with your eyes closed, think and see the image of the person who is acting negatively towards you, if you practice this for a week you will see the feelings of the other person change positively towards you.

Finally we are but a projection of our conscious. Some can control the environment around us. Some can look in the future. There is a lot more to learn about **ESP** or the sixth sense, **the best person is instinctive, if your inner voice tells you that something is wrong then pays attention to the inner voice and change course**. (This is a form of ESP message and not a seizure). Remember not to get upset from the news. Do not let adversity bother you, learn to forgive, forget and relax. Stay calm ignore others attitudes. One needs to learn to accept fault no matter how minor. When any one offers criticism take it positively. Learn, Improve and Excel. (Perseverance command success).

Doing negative things, (Hate, Rage, reduces tolerance), depresses the immune functions, raises inflammation. Helping other people, staying happy automatically gives you satisfaction, helps boost your immune function, and reduces stress. When you talk negatively about others or do negative criticism your body may suffer more inflammation as it makes you angry. **So tolerate, forgive and love this attitude will let you live longer and healthier**. All the worldly goods are left back even the body stays in the grave. Your soul will be with you forever. (**All the hidden treasures of the Pharos were stolen by 1000BC**.) Always think of positive things, do not let negative thoughts in your head. Think of success, learn to forgive your mistakes, (error is human). Even if you work hard you may not always see success, but you should not give up. You cannot make all the people happy, so concentrate on doing things that make you happy.

Medical research has shown that **prayer** and **mediation** makes beneficial changes in the body. Enjoy your partner; bring the positive out of them. Enjoy your work, focus on the positive and suppress the negative. You should be the last person to consider surgical treatment of any organ

for pain relief. Most of the autoimmune diseases can be taken care of without surgery, (herniated discs in the back and neck, aneurysms, prostate problems, chronic pelvic pain and pancreatitis). Avoid unnecessary surgery.

Fasting: Benjamin Franklin - "The best of all medicines are rest and fasting"

Fasting is the world's most ancient and natural healing mechanism. Fasting triggers a truly wondrous cleansing process that reaches right down to each and every cell and tissue in the body. The entire alimentary canal is swept clean. By rebuilding immunity, health is naturally restored and disease disappears. Fasting promotes cleansing and healing; helps normalize weight, blood pressure, cholesterol; rebuilds the immune system; and **helps reverse the aging** process. To get rid of accumulated poisons out of our bodies we must fast. By fasting we give our bodies a physiological rest.

Fasting is abstinence from all food and drink for a limited period of time to maintain or improve health, or treat a specific illness. Most of the research into the therapeutic value of fasting has explored the water only method, during which drink water but abstaining from all food. A short fast, lasting from one day can generally be tolerated by most people. An extended fast up to three days is not recommended. Fasting has been known since ancient times. (References in the Bible, Koran, Torah, ancient Chinese and Greek medical texts).

“For to fast is to do well to yourselves - if you but knew it.” “He from among you who is ill or suffers from an ailment of the head shall redeem himself by fasting”. Koran

People of all religions have fasted as part of religious rituals well known is the Muslims Ramadan. Fasting to benefit health is an old practice and is generally practiced today only in prosperous Western societies. The **Natural Hygiene system** practice was started by Isaac Jennings, M.D. a Yale graduate who rejected the therapeutic use of drugs to treat specific ailments and instead developed a treatment program that included periodic fasting, a vegetarian diet, pure water, sunshine, clean air, exercise, and rest.

“**Instead of using medicine rather fast a day**.” Avicenna, the great Iranian physician often prescribed fasting for three weeks or more. It is claimed that, as a result of fasting, people often recover from arthritis, asthma, digestive problems, high blood pressure, heart problems, and many other diseases. Fasting means eating nothing, drinking only water and getting lots of rest during the day, eat a small meal at night and early morning. Autolysis or self-digestion is a state the body enters about the fourth day of a fast; according to Dr Herbert Shelton, in this state the body can break down even cancerous tissues.

Recent research shows **skipping meals** may be good for you. Researchers from the National Institute on Aging found that mice that fasted every other day, and then were allowed to eat what they wanted on the intervening days, seemed more resistant to diabetes than did control mice or animals on calorie-restricted diets. They were also resistant to Alzheimer's disease. In addition, the intermittently fasting mice produce more of a chemical called brain-derived neurotrophic factor (BDNF), which promotes learning, memory and the growth and survival of nerve cells. This BDNF appears to make the animals more resistant to a neurotoxin that produces brain

damage similar to Alzheimer's disease. The intermittently fasting animal cells also become more adept at scavenging glucose from blood; this **is an anti-diabetic effect**, detectable on glucose tolerance tests. In a trial of 16 patients, with classical rheumatoid arthritis (RA) who underwent fasting for ten days, followed by a nine week period on a lacto vegetarian (milk, vegetarian diet). After fasting, 5 of 15 patients showed objective signs of improvement**. The fasting patients showed reduction in all of the following, pain, stiffness, consumption of analgesics, and serum concentration of orosomucoid** (a protein found in blood plasma, an indicator of inflammation). **Study concluded that fasting may produce subjective and objective improvements in RA.**

Studies have shown fasting reduces inflammation in rheumatoid arthritis and helps patients with Fibromyalgia. The simple fasting can be done by not eating anything from morning to evening; you can have water within that period. Doctors have known that **fasting can cause attacks of acute intermittent porphyria**, and that a high-carbohydrate diet can help relieve these attacks.

Spices: Things like ginger, garlic, turmeric, cloves, black seed, cilantro, saffron, and cinnamon, are all neuron protective and they demonstrate anticancer activity and get rid of over a hundred infections. Spices should be included in every diet. UCLA's Alzheimer's disease Research Center found that **(turmeric)** has one additional property not shared by most spices. It directly inhibits the production of amyloid plaques, the sticky substances that directly causes Alzheimer's disease. Turmeric, in fact, seems to cut the number of amyloid plaques in half. I prescribe a tea spoon of turmeric to be consumed twice a day by all my patients. They will usually mix it in some warm water or milk and consume it daily. The consumption of turmeric is associated with reduced arthritis, cholesterol and improved memory. Sixty percent of the nutritional value of turmeric is destroyed by cooking. Embracing a cuisine rich in spices, as well as in fruits and vegetables, may further enhance the chemopreventive capacity of one's diet. Spice up your life, with extra spices in your food. All the spices have been show to reduce inflammation and enhance the immune system.

From 1991 -1993 an epidemic of optic and peripheral neuropathy affected more than 50,000 people in Cuba. With loss of vision, diminished color vision, optic-nerve pallor, and decreased sensitivity to vibration and temperature in the legs of affected people, was seen. Tobacco use, particularly cigar smoking and poor nutrition was associated with an increased risk of optic neuropathy (nerve blindness). The number of new cases decreased after the initiation of vitamin supplementation in the population. The risk was reduced among subjects with higher dietary intakes of methionine, vitamin B_{12}, riboflavin, and niacin and higher serum concentrations of antioxidant carotenoids.

Except for the USA bitter almonds are sold all over the world. California's trees are of the sweet-almond variety. Sale of bitter almonds is illegal in the USA. Bitter almonds contain a small quantity of a substance that, in the presence of water, forms deadly prussic acid. This substance is also present in the kernels of prunes, peaches and apricots and other fruit trees that, like the almond, belong to the rose family. Heat destroys the poison, so cooking renders it harmless. Childen are at high risk of death after eating 7-8 bitter almonds. There are some **benefits** in consuming these bitter kernels as they provide an **anti cancer** protection.

Fennels are tiny tasty seeds consumed after food in Indian and Pakistan to aid in digestion and helps reduce gas production in the stomach. Fennel & Liquorice are beneficial for women.

Liquorice (Mulethi) is a Remedy which offers vital protection against Heart Disease, Stroke and Ulcerative Colitis. Hordeum leaf extract reduces the amount of LDL (Low Density Lipoprotein) cholesterol. Hordeum (barley grass) helps reverse this by stimulating the growth of friendly bacteria, which in turn helps reduce inflammation and improves symptoms.

Cats Claw is an herb grown in South America which is considered to have antibiotic properties. It has been used in infections like Borrelia or Lymes disease. MRSA is a super bug which has no treatment, yet has been successfully treated with another natural antibiotic Honey.

Echinacea (eucalyptus globulus): has long been used as an antiviral remedy for colds and flu. It appears to work by boosting production of interferon, the bodies own antiviral fighter, as well as, stimulating infection-fighting white blood cells.

Garlic (allium sativum): Compounds that are rich in sulfur content are found in abundance in garlic and are active against the virus responsible for flu. Reduce cholesterol.

Ginger (zingiber officinale): A phenolic compound in ginger is responsible for relaxing the muscles of the stomach, and explains ginger's effect in easing **motion sickness**. Fresh or dried root has been shown to minimize vomiting, protect the liver, help sore throat and reduce gastric pain. Ginger tea can be used to treat sore throat, cough and Flu as it has anti viral properties, you can also chew upon the ginger to obtain help in sore throat

Goldenseal (hydrastis canadensis): Berberine increases blood flow to the spleen and stimulate the activity of macrophages, blood cells that are an important part of the immune system.

Eucalyptus (eucalyptus globulus): Eucalyptus oil helps eliminate viruses.

Juniper (juniperus): Inhibits herpes, flu and many other types of viruses.

The **Silky hair of corn** is wrapped around the kernel, can be removed and placed in a liter of water which is then boiled for 15 minutes. After cooling this warm water can be consumed throughout the day and will clean out the kidney, it will also remove any stones in the kidney. Regular consumption will lower cholesterol.

Milk thistle is an herb used extensively to treat Hepatitis.

Cassava is the third-most important food source in tropical countries, but it has one major problem: The roots and leaves of poorly processed cassava plants contain a substance that, when eaten, can trigger the production of cyanide. Cassava has caused spastic paralysis and optic atrophy in Nigeria.

Eat a balanced diet, rotating different foods which include, vegetables and fruits should be consumed according to the seasonal fresh growth of these items.

Chapter 5- Immune System

The immune system is our private army and police which act as a double edged sword; it defends against microorganisms and toxins and rarely this army (immune system) mistakenly will attacks the persons own body (**Friendly Fire**). At the heart of the immune response is the ability to distinguish between self and non-self. Every cell carries a distinctive molecules that distinguishes it as "self." Normally the body's defenses cannot attack tissues that carry a self marker.

The organs of the immune system, are positioned throughout the body, are called lymphoid organs. The word "lymph" in Greek means a pure, clear stream. Lymph nodes are small, bean-shaped structures that are laced throughout the body along the lymphatic routes. Lymph nodes contain specialized compartments where immune cells congregate, and where they can encounter antigens. **T**hymus the master immune gland located in the chest makes **T**-cells; they are released in the bloodstream after being tested in the thymus that they will not attack their own body cells. In autoimmune diseases the thymus allows T-cells to attack the body. Removing part of the abnormal thymus helps cure some autoimmune diseases. Spleen is a large organ which helps get rid of cells tagged by antibodies. Tonsils are one of the primary sites of the immune system which encounters bacteria and triggers an immune response. All of the immune cells originate from the **stem cell** in the bone marrow. In autoimmune and immune deficiency diseases replacing the stem cell provides a new immune system. The attacking cells in our immune system are of two following subtypes of cells called leukocytes:

- The **phagocytes** cells are like scavengers that engulf and destroy the germs.
- The **lymphocytes** cells are the learning cells which remember the germs.

The most common phagocyte is the Neutrophils which fights bacteria. In a bacterial infection, the number of neutrophils increases.

Two types of Lymphocytes are part of the immune system, **B-lymphocytes** and **T lymphocytes**. B-Lymphocytes come from bone marrow, T-cells develop in the **t**hymus gland. **B**-lymphocytes are the **B**odyguards, which look for invaders and make specific antibodies against them. **T**-cells act like **T**anks, who destroy the invaders identified by the B cell.

A foreign substance invading the body has many antigens example (body parts of H-pylori or Mycoplasma). On detection of an antigen, immune cells activate the B-lymphocytes to produce specific antibodies. Antibodies are specialized Y shaped proteins that attach onto specific antigens. Antibodies and antigens lock together, like a key into a lock. In a disease, the T-

lymphocyte is responsible for not attacking the body. In autoimmune disease the T-cell is deceived into attacking the body by a process called molecular mimicry.

Once the B-lymphocytes have produced antibodies, these antibodies then continue to exist in a person's body for a lifetime. If the same antigen is presented again, the antibodies already present do their job of attaching to the antigen and these antigen antibody complexes are then destroyed by the phagocyte. If we get **measles** once, then we do not get measles again, as antibodies against measles are present. Immunization is used to prevent diseases by injecting an **attenuated antigen** which produces antibodies for protection, thus an attack by the real germ should have no effect, as antibodies are already present. B-cells make the following types of antibodies, (**IgA, IgG, IgM, IgE, and IgD**). IgG is the most important antibody and helps us fight infections; IgG has four sub types called (IgG subclass-1, IgG subclass-2, IgG subclass-3, and IgG subclass-4.). Those people who are immune deficient will either have IgG deficiency or IgG subclass deficiency.

Antibodies will find an antigen and attach to it, to destroy antigens tagged by antibodies is the job of the T-cell. In an infection an antibody will attach to the bacteria and then comes the phagocyte to eat them up. A sub type of the T-cell is called Natural-Killer T-cells (NKT), they are the immune systems emergency response team to find and destroy bacteria and cancer cells. There are other types of T-cells, named helper, suppressor and cytotoxic. Cytokines are chemical messengers which are the chief tool of T-cells. Lymphocytes, including both T-cells and B-cells, secrete lymphokines, while monocytes and macrophages secrete monokines. Cytokines recruit many other cells and substances to the field of action. Cytokines encourage cell growth, promote cell activation, direct inflammatory traffic, and destroy target cells including cancer. Antibodies produced by B-cells can neutralize toxins (poisonous or damaging substances) produced by different organisms.

Antibodies can activate a group of proteins called **complement** that are also part of the immune system. Complement assists in killing bacteria, viruses, or infected cells by destroying the cell walls. N-meningitides infections, SLE, glomerulonephritis, arthralgia, and uveitis occur commonly in complement deficiency. Complement is activated and increases in heart attack patients after **streptokinase** is given, but can be lowered by a high dose of magnesium sulphate.

The immune system protects the body against cancer and disease. This protection is called immunity. Humans have three types of immunity called innate, adaptive, and passive.

Innate Immunity: Innate immunity provides a swift response against infectious agents prior to the initiation of adaptive immune responses. Cells involved in innate immune responses include macrophages, neutrophils, eosinophils, and natural killer T (NKT) cells.

Adaptive Immunity: A slower response by lymphocytes, developed by repeated exposure to infections and vaccination. The lymphocytes are learning cells, they remember the attacking organism and send out T-cells, to hunt the attacking cells.

Passive Immunity: This is a temporary immunity provided to the body, which is removed in a month. Antibodies in a mother's milk (colostrum) provide an infant with temporary immunity to diseases, that the mother has been exposed to. This can help protect the infant against infection during the early months of childhood. IVIg usually offers protection for 4 weeks

As a person gets older, they usually become immune against many germs; this is due to repeated exposures to these germs due to which their immune system develops many antibodies. Adults get fewer infections as compared to children, adult immune system learns to recognize and immediately attack many of the viruses that cause colds and flu.

Heat shock proteins (**HSP**), also named ***stress proteins***, these proteins are present in all cells of all life forms. They are activated when a cell is exposed to environmental stresses like heat, cold and oxygen deprivation. *HSP* are present in cells under normal conditions. Abnormal peptides are formed inside sick cells which need to be transported to outside the cell's surface. Inside the cell, heat shock proteins take these peptides (antigens) and hand them over to other molecules. The immune system sees these peptides as red flags, which triggers an immune response. These abnormal peptides are **antigens,** a term that describes any substance capable of triggering an immune response. If a normal cell dies then no *HSP* are produced and no inflammation results. The normal death of cells does not trigger inflammation. Cells under stress will start producing *stress proteins*, which start getting the immune systems attention and will results in inflammation. **Apoptosis** or programmed cell death is also called cellular suicide. For no reason at all the cells can undergo apoptosis and die, which can cause failure of an organ and also be the cause of human death. In cancer patients aptosis is not seen. Those dyeing due to swelling of organs are undergoing a programmed death or apoptosis without any external cause.

The Immune System Disorders:

- Immunodeficiency disorders: Due to reduced immunoglobulin's or antibodies.
- Autoimmune disorders: In which the body's immune system attacks its own tissue.
- Allergic disorders: An immediate reaction which can cause death in response to an antigen. Epinephrine or electrical stimulation is used to turn it off.

Our body has Y shaped antibodies they are of four types IgG, IgA, IgM and IgE. The IgG antibodies are further subdivided into four sub-classes called IgG-subclass-1, subclass-2, subclass-3 and subclass-4. If the IgG levels are normal and the patient still has symptoms of immune deficiency then their subclasses need to be checked. The IgG antibodies have a subtype called the **antiidotype** antibody, these antiidotype can attach to many different types of antigens and inactivate them, these antiidotype antibodies are useful in many autoimmune disease. People who get autoimmune diseases have less antiidotype antibodies. Other antibodies are called the **autoantibodies** which tend to attack our own body cells. In autoimmune diseases autoantibodies are increased, removing them with plasmapheresis or stopping their production by IVIg, steroids, omega-3 will result in improving the autoimmune disease.

To keep our immune system healthy we need to keep our body clean. Wash the hands and mouth five to six times a day. Learn to meditate, stop worrying and nutrients. Learn to drink more water and eat mainly vegetables and fruits, this will help keep the inflammation at low levels. Stay clear of chemicals and detoxify. To remove toxins, mud baths, leafy vegetable consumption is recommended. Try to eat a raw diet, eat the grain kernels when they are about to sprout as they will then provide more nutrition. Eat the fruits which come in the season, avoid refrigerated foods and water. Water should be stored in glass or earthen containers.

-Chapter 6 Neurological Autoimmune Disorders & Their treatment

Acute Disseminated Encephalomyelitis (ADEM)

Acute disseminated encephalomyelitis (ADEM) is an autoimmune disorder characterized by inflammation of the brain and spinal cord caused by damage to the myelin sheath. The myelin sheath is the fatty covering, which acts as an insulator, on nerve fibers in the brain. ADEM may occur in association with a viral or bacterial infection, as a complication of vaccination, or without a preceding cause. **The numbers of children developing this condition are increasing 0.4/100,000/year**; the incidence quadrupled during 1998-2000.

Symptoms: Onset of the disorder is sudden in a child following flu like illness or vaccination. The person starts to develop headaches, aches and pains, followed by confusion and may become comatose. Symptoms vary among patients, headache, vomiting, tiredness, confusion, fever, difficulty walking, **stiff neck**, vision loss, weakness in the legs, coma, and seizures may be seen. The disorder occurs in children more often than in adults. Some may mistakenly call this Multiple Sclerosis however Multiple Sclerosis does not present with fever. Some patients present with weakness on side of the body they usually have a Mycoplasma infection. Jerking of arms due to Myoclonic seizures can be seen. Rarely children may become confused and be misdiagnosed as **psychosis**. Some children may develop double vision due to brainstem involvement and this may be the first symptom of A.D.E.M.

Tests: Anti-Streptolysin-O titer (ASO) is obtained which is usually elevated and throat cultures for streptococcal infection and Chlamydia are obtained. Magnetic resonance imaging (MRI) scan of the brain usually shows multiple white spots, rarely some bleeding is seen in the brain and tumor like lesions may also be seen. Spinal tap is done to look for raised levels of inflammatory cells, and to look for an inflammatory marker called oligoclonal bands which are absent in ADEM, oligoclonal band are associated with Multiple Sclerosis. The spinal fluid proteins are usually elevated. **Herpes encephalitis** needs to be ruled out, in Herpes the CSF chemistry is as follows, cell count is usually 100 WBC with a **few hundred red cells**, glucose is normal with MRI showing bilateral or unilateral temporal lobe lesions. Vitamin levels for B-6 (pyridoxine), B-12 (Cynocobalamin), and Thiamine need to be checked with serum homocysteine levels.

Treatment of ADEM:

- Group beta hemolytic **streptococcal** bacteria are usually the cause, confirmed by elevated **ASO titers**, these streptococcal bacteria are treated with **penicillin**. ADEM is also caused by Chlamydia pneumoniae infection. The diagnosis is established by a

checking a tracheal swab for increasing titres of Chlamydia-IgM antibody. The patient can then be treated with **doxycycline 100mg twice a day** and **prednisone** resulting in complete recovery. Other antibiotics like, **ciprofloxacin**, chloramphenicol or **azithromycin** are appropriate under most circumstances.

- Following vaccination A.D.E.M. can be treated with steroids or **IVIg** plus **doxycycline**. To control inflammation prednisone works 90% of the time and in resistant 10% cases IVIg is used at a dose of 500mg/kg/day for 4 days. Rarely plasmapheresis or cytotoxic drugs are used.
- Treatment of herpes encephalitis is **Acyclovir (30mg/kg/day), infuse in three divided doses daily, each dose infused over 1 hour, and treat for 10-14 days.**
- Check homocysteine, if elevated give vitamin B12, folic acid, B6 and B1 are given.

In some cases complete resolution is noted within a few days, while others may take a few weeks or months. About 5-10% of the cases may go on to develop M.S, so I recommend a good diet with omega-3 to reduce future inflammation. During the winter months give cod–liver oil as it contains vitamin-D to all patients who have suffered from MS or ADEM.

Autoimmune Epilepsy: Epilepsy is among the commonest symptom and diseases, in the past an etiological explanation could not be identified. Evidence shows that autoimmune mechanisms play a role in causing epilepsy. Autoimmune epilepsy is commonly associated with Myoclonic (sudden muscular jerk) or photosensitive epilepsy (epilepsy triggered by light), temporal lobe and all childhood epilepsies. Just like any autoimmune disorder the symptoms of epilepsy are remitting and relapsing. Epilepsy is associated with injury, surgery, vaccination, infection and often seen in patients suffering from other autoimmune disorders. Numerous publications have shown an association of serum auto-antibodies in patients with epilepsy syndromes, which responded to immunomodulation treatment. Following a generalized seizure increased inflammatory markers like white cells, elevated proteins, elevated CRP and increased levels of interleukin-6 (IL-6) are seen in patients with recent tonic-clonic seizure. The involvement of inflammation with epilepsy is common.

In my experience I see a close association of autoimmune phenomena in epilepsy. Many of the patients, who had been labeled as intractable epilepsy for years, are simply controlled by drug manipulation (reduction in dose) and introduction of an anti-inflammatory diet. Autoimmune epilepsy is seen frequently with thyroid disorders, SLE (Lupus), Sjogrens (dry mouth) or arthritis and antiphospholipid antibody disorder, if these patients get a seizure it is likely related to a autoimmune process. The autoimmune epilepsy starts suddenly and appears unresponsive to medical treatment (refractory). Later a pattern of remission and relapses is seen. Light sensitive patients, with light induced seizures, and those who have seizures at night are more likely to have autoimmune epilepsy.

In women and young men new onset of autoimmune epilepsy can be confirmed by checking for, antiphospholipid antibodies, antinuclear factor, and glutamic acid decarboxylase (GAD). The GAD antibodies are higher in diabetics with associated epilepsy. Thyroid antibodies and thyroid functions need to be checked in all patients. If a patient suffering from Lupus gets epilepsy then common sense is used to think about an autoimmune cause. If a patient is not responding to epilepsy medication it is worthwhile to start them on omega-3 fatty acids, steroid and **Vibramycine** and see if the seizures respond and the brain lesions disappear on MRI. Micro-electronic device can also be used to control epilepsy described later.

One to five percent of the epilepsy patients have **Celiac disease**, these patients do not respond to epilepsy medications and **they have unexplained weight loss**. Anti Gliadin antibody can be positive in Celiac disease. Every patient with epilepsy needs to try the fruit vegetable, protein, rice and milk diet which is free of wheat, rye, barley, millets and oats **for four months**. No beer or alcoholic dinks allowed. **Within that period if a benefit** is seen then the diet should be continued. Some patients may show dramatic **calcifications** (white lesions) in the occipital regions of the brain, which clears off with magnetic stimulation. I do not recommend mass screening for Celiac Disease instead, increased alertness should be observed in patients who have **epilepsy and weight loss**. Celiac disease patients have abnormal thyroid function tests, may have diabetes along with serum **Carnitine deficiency** (an amino acid in proteins)

Landau-Kleffner syndrome (LKS), known as acquired epileptiform aphasia (aphasia means difficulty in speech communication). LKS is an autoimmune childhood disorder characterized by deterioration in language skills in association with seizures or seizure activity (spike wave) on the E.E.G. LKS affects children, between the ages of 3 and 8 years.
Symptoms: The children usually experience an abrupt loss of language and comprehension and a reduction in their ability to express themselves. New onset of **stuttering** can be due to LKS. Approximately 70-80% of children with LKS have seizures; however, the presence of seizures is not a requirement for a diagnosis. Usually an improvement is seen between attacks of LKS, just like any autoimmune disease.
Tests: With PET scanning the area affected in the brain is in the left temporal Lobe, a region next to the left ear. This area in the brain is responsible for human speech and hearing sounds. The **EEG** recorded during sleep is diagnostic and shows spike wave discharges predominantly in the **temporal** (in front of ears) and **parietal** regions (area in the center of the head). Onset of seizures can be related to previous infections. Autoantibodies directed against brain cells have been identified in LKS.
Diagnostic criteria:

- Abnormal EEG with epileptiform (spike & wave) activity.
- Aphasia (language & communication disorder); children are unable to respond to their name and have difficulty understanding environmental sounds, such as a door bell, telephone ring.

- Autistic behaviors (avoidance of human contact, extreme pickiness over food, sleep disturbances, pain insensitivity, inappropriate bizarre repetitive play)
- Behavioral problems (hyperactivity, aggressiveness, decreased attention, easily distracted, temper tantrums, and social withdrawal)
- Expressive language difficulties (the ability to speak is often seriously affected; some children lose their speech completely)
- Loss of bladder and bowel control
- Seizures (generalized or complex partial seizures in sleep)
- Visual problem (difficulty recognizing family and friends or common objects)
- Positive antibodies (IgG anti-brain autoantibodies) 45-50% patients.

(**Treatment of LKS is explained later with all epilepsy syndromes**)

Lennox-Gastaut syndrome: LGS is autoimmune epilepsy which is seen during 2 to 8 years of age. LGS is one of the most severe forms of epilepsy. It accounts for up to 10 percent of all cases of childhood epilepsy, with slightly more males than females are affected. It usually develops in children at an average age of 3 years.

Types of seizures seen in LGS

- **Tonic**: These attacks consist of stiffening of the body, with the eyes rolling upwards, dilation of the pupils and shallow, irregular breathing.
- **Atonic** or drop attacks: brief loss of muscle tone and consciousness, causing abrupt falls.
- **Myoclonic**: consist of sudden arm or leg movement.
- **Atypical absence**: staring spells with some jerking and eye movements.

(**Treatment of LGS is explained later with all epilepsy syndromes**)

West Syndrome (WS): West Syndrome starts in the first year of life. The seizure of WS is a sudden bending forward and stiffening of the body, arms, and legs. Spasms tend to begin soon after arousal from sleep. Sometimes only the head and eyes are involved. The spasms typically last for 1 to 5 seconds and occur in clusters, ranging from 2 to 50 spasms at a time. Infants may have many clusters and several spasms per day. After five years of age these spasms are often replaced by other seizure types.

West Syndrome is characterized by:

- **Infantile spasms**, (**Salam attacks**, it's as if the baby is bowing down for a greeting)
- Brief head drop
- **Hypsarrhythmia** (disorganized, chaotic brain wave patterns, seen in EEG),
- Mental retardation.

(**Treatment of epilepsy is explained later with all epilepsy syndromes**)

Absence Epilepsy: Usually seen in children this condition starts with **episodes of stareing** which can last upto twenty seconds or more. There is associated **blinking** and the child does not **respond** during the attack to other people. Absence epilepsy has been seen in autoimmune diseases and in some cases only responds to treatment with **steroids**. It can be associated with Vasculitis such as Moyamoya disease. Absence Syndrome is characterized by 3-per second spike and wave attacks seen on EEG.

Epilepsia Partialis Continua (EPC): This can be seen in a variety of conditions including infections (herpes) or strokes. EPC can present like a finger jerking, to hand and arm movements spreading to the whole body. The seizures can last a long time up to days. They are associated with GAD antibodies and respond to steroids, Omega-3, IVIG & plasmapheresis.

Rasmussen's Encephalitis (RE) & Parry-Romberg syndrome (PRS):

Rasmussen's syndrome is a chronic inflammation of the brain with recurrent seizures; it is a rare neurological autoimmune disorder, in which inflammation can spread to the whole affected side of the brain. There can be some atrophy of brain and extremities PRS presents with unilateral facial atrophy, seizures and sometimes vasculitis causing aneurysms.

Symptoms of RE: The disease starts slowly with weakness of the arm or leg giving the appearance of a stroke. The weakness will get worse with time and at the same time seizures start. These children may develop difficulty with talking. Usually it appears they have a stroke, as the baby stops using one hand, older children can have memory problems. Atrophy of the face is common in PRS (Parry-Romberg syndrome).

Diagnosis of RE: Magnetic resonance imaging (MRI) shows unilateral cerebral atrophy (shrinkage of brain) and areas of white dots (increased signal intensity in grey and white matter of the brain. Multiple **white matter** lesions are seen on the MRI scan which can disappear with treatment. EEG will show seizure activity and slowing of EEG activity on the affected side. Antibodies against glutamate receptor are seen in Rasmussen disease. Patients with PRS may have **calcifications** in the brain which disappear with magnetic stimulation.

Treatment of RE: Recently it has been shown that if IVIg is given early, it stops the progression of the disease, seizures are controlled, and a complete reversal of the disease process is seen. It takes a month to see a complete improvement. Other therapies have included antiepileptics, **steroids**, antiviral agents, alpha-interferon, and immunoglobulin. In the past surgical removal of the involved brain was the only long-term treatment.

Juvenile Myoclonic Epilepsy: This is common epilepsy usually seen in teenagers and young adults. I have seen prominent neurologist diagnose this as tics. A common presentation is movements at shoulder muscles and sudden jerks of shoulder muscles, other patients may start a seizure with odd loud sounds. Activity makes these seizures worse. Life long treatment is recommended and the condition runs in the families. These seizures respond very well to a

nanostimulator which I have developed without medication and they also respond to Valporate. ASO titers are often elevated in these patients.

Causes of autoimmune epilepsy: The causes of autoimmune epilepsy are injury, post-vaccination, infections (Lymes, Mycoplasma, enteroviral meningoencephalitis, Toxoplasma gondii, Herpes encephalitis, AIDS-toxoplasmosis, streptococci) and many autoimmune diseases like SLE. Autoimmune epilepsy is also seen in paraneoplastic disorders with anti-Hu antibodies. Patients may have anti-GAD antibodies in blood and spinal fluid.
The commonest causes of epilepsy syndromes in infants are infection due to cytomegalovirus and toxoplasmosis during the prenatal stage and the purulent meningitis, tuberculous meningitis and herpetic encephalitis during the neonatal and postnatal periods. The evidence of epilepsies in meningo-encephalitis varies according to the organism.
All patients with LKS, WS, and LGS need to be tested for IgG antibodies against Toxoplasma gondii. Cats can be the source of infection in the kids. Infants who have been exposed to cats are likely to have toxoplasmosis. Valporic acid has an affect against Toxoplasma and is an antiepilepsy drug of choice for such cases. Presence of IgG antibodies against Toxoplasma gondii infection should be taken into account as a possible cause of Landau-Kleffner syndrome. In immunocompetent hosts **pyrimethamine** plus **sulfadiazine** are used for treating Toxoplasma infections.

Tests for autoimmune epilepsy: (I consider **all epilepsy** syndromes as **autoimmune**)

- Glutamic acid decarboxylase antibodies (GAD), Antiphospholipid antibodies and Antinuclear antibody positivity and anti-GluR3 (anti Glutamate) antibodies.
- The spinal fluid IgG level, protein level and cell count need to be checked along with GAD antibodies. Elevated spinal fluid protein and elevated cell count are an indication of autoimmune disease. The spinal fluid glucose remains normal.
- Serum IgG level, IgG-subclass levels and IgA levels need to be measured. If the **IgA** level is **low** it indicates **celiac disease**, a **high IgA** level will suggest **Henoch-Scholein** purpura. Low IgG and low IgG-subclasses will be due to immune deficiency, Dilantin can cause low IgG-subclass levels. Higher IgG-subclass levels are seen in response to an infection. Check magnesium and calcium levels as reduced levels can trigger epilepsy.
- M.R.I. scan or C.T. scan is done to look for damage. The EEG can show seizure activity and is especially effective if T1 and T2 electrodes are used in front of the ears. This helps record deep brain waves not usually seen by surface electrodes.
- Urinary porphyrin levels are checked to evaluate for Porphyria.

Treatment for all autoimmune Epilepsy syndromes: The treatment for autoimmune epilepsy is multi pronged. First fix any vitamin deficiency, fix mineral and fluid deficiency, use the correct drug, use the least amount of drug and use anti-inflammatory medication. If the

seizures frequency increases in a patient then respond by increasing steroids rather then anti epilepsy medication. In porphyria patients the only epileptic drug that can be used is gabapentin. The following three steps are only for infants. I use magnetic stimulation in patients who have increased seizures to reduce their frequency. Nanopulser have been used to stop epilepsy.

- **Diagnostic EEG** is done, to determine whether patient's seizures; and EEG abnormalities, are related to pyridoxine deficiency. In this approach, administer **pyridoxal phosphate** (vitamin **B-6**), 50-100 mg IV during diagnostic EEG; if dramatic improvement is noted in EEG, then the patient is having pyridoxine-dependent seizures.
- **Pyridoxal phosphate** dose for all epilepsy patients is 10 mg/kg intravenous, then 10 mg/kg/day in four divided doses. (repeated if the seizures do not stop)
- In patients responding to above treatment, start a combination therapy consisting of high-dose **pyridoxal phosphate** (40-50 mg/kg/day) and low-dose synthetic **ACTH** (0.01 mg/kg/day). Monotherapy with pyridoxal phosphate provided excellent seizure control. Measure weekly B-6 levels to adjust dose.
- **Diet:** Use a gluten free diet with (chicken, fish, beef, rice, vegetables, fruits, milk products, sugar, jams and fruit juices). Things to strictly avoid are Gluten containing foods like Wheat, Rye, Barley, Millets and Oats. **No beer** or alcoholic products should be allowed. Above diet should be tried for three months if there is a benefit it should be continued and the person is evaluated for Celiac disease. (See the gastrointestinal section). Magnesium supplements are very effective in controlling seizures (**Magnesium** and **calcium** levels should be checked in epilepsy. Magnesium supplements have an anti-inflammatory effect. Magnesium is also used in pregnancy induced epilepsy).
- **Fluids:** Maintain good hydration with frequent intake of water.
- **Steroids:** Solumedrol, one gram can be infused over one hour. Then oral prednisone or ACTH can be used. After the prednisone is given a decline in clinical seizures and reduction in anti-GAD antibodies can be seen. Patients with Myoclonic epilepsy respond even faster to steroids. Higher doses of steroids can aggravate seizures.
- **Oral corticosteroids** are used more often and usually need to be maintained for a long period of time to prevent relapses. The recommended dose of Prednisone is 1mg/kg/day for 12 weeks (for 6 weeks daily steroids are given and from 7 to 12 weeks prednisone is tapered.). Treatment is long term, in long term immunosuppression look at the list of all the drugs used in the CIDP section.
- **Antiepileptic drugs:** For initial therapy, **Lamictal**, **topiramate (TOP), Valporate** is often chosen as it has anti inflammatory properties. TOP should start at the same time as steroids, at a dose of 1 mg/kg/day this dose can be adjusted with increase of 0.5mg/kg/day. Fifty percent of the patients are controlled by **TOP** alone, in the rest a combination of TOP and lamotrigine can be used. In some cases that have absence epilepsy, ethosuximide can be used. Other available drugs can be used are, Valporate and Felbatol. **If clinical seizures increase try reducing the medications**, most seizures stop

after reduction of the epilepsy drugs. This reduction in dose is accompanied by reduced clinical seizures, this phenomena is commonly seen when multiple drugs are being used. Inflammation and irritation of the brain is triggered by higher antiepilepsy drug levels. If the EEG shows epilepsy activity, do not increase the dose of anti epilepsy drug. Increased activity may be due to inflammation, for which you need steroids, melatonin or pyridoxal. **Valproate reduces L-Carnitine levels,** thus Carnitine supplements should be used with valporate.

- **Benzodiazepines:** In West syndrome and LGS, Clonazepam is used to prevent the Myoclonic jerks. **Clonazepam** is a long acting drug replace it with **Lorezepam** which has less side effects and a shorter half life. Lorezepam can also be used as a sub lingual tablet to help stop the progression of a seizure, it will stop seizures within minutes..
- **Supplement** 3mg of **Melatonin** for uncontrolled seizures occurring at night, provides improvement in control of nocturnal epilepsy. It takes a month to see all the benefits. Melatonin dose can be increased to 6 mg. Melatonin also improves the sleep cycle. Once, Melatonin it is withdrawn seizures will return. Melatonin helps the Myoclonic epilepsy the best, and makes a good combination with Toprimate.
- **Immunotherapy for epilepsy: IVIg** or **steroids** should be the first line treatment in all these syndromes described above. IVIg can be started at a dose of, 0.5 g/kg body weight per day for 4 consecutive days. Then 500mg/kg can be given every 2 weeks to 4 weeks, for 5-6 months. During that period low dose of steroid can be used. The use of IVIG has been associated with an initial dramatic response in some patients. Some patients had an immediate response to IVIG initially and relapsed before eventually achieving a long-term sustained remission. To avoid relapses steroids should be given with IVIg and maintained based upon clinical reponce for three to six months.
- **Cyclophosphamide** can also be used to control seizures. In a case report, of a 2-year-old girl, who developed sudden onset of right hemiplegia, followed by generalized seizures, chorea-type movements, and severe weakness. Intravenous cyclophosphamide pulse therapy resulted in a complete improvement of her clinical symptoms. At age of six, she had recovered from epilepsy. Autoimmune mechanisms involving the antiphospholipid syndrome were considered to be the pathogenesis of this case."
- An **electronic external stimulator** is a **simple cheap electronic stimulator** developed by **Nanotech Lahore** which if used daily **controls all seizure types**. Patients have been taken off medications after using this stimulator. The treatment is reserved for patients who have not responded to multiple medical therapies, has been followed in selected cases by a marked improvement in language skills and behavior.
- Cod Liver oil and Omega-3 oil supplements act like anti-inflammatory medication and are useful for controlling epilepsy, green colored. The oil treatment has evolved into a lipid diet found very useful in many children. In this diet low carbohydrates are used along with an excess of lipids to help control seizures.

Alzheimer's: Alzheimer's disease (AD) is an age-related autoimmune disorder that presents with a **progressive loss in recent memory** and **deterioration of brain functions**. The brain of a patient with AD has deposits called **senile plaques** of **amyloid-beta-peptide**, **intracellular neurofibrillary tangles** that consist of tau protein and a loss of neurons that innervate the **hippocampus.** In Alzheimer's disease (AD) there is evidence that **neurotoxicity is caused by CNS inflammatory processes**. Central nervous system (CNS) inflammation may predate the development of senile plaques and neurofibrillary tangles in AD and may prove to be a more sensitive marker of prodromal AD. Epidemiological studies suggest a **protective effect of NSAIDs** against development of AD. Patients with Alzheimer's have **lower levels of anti-beta-amyloid antibodies**.
In a study, Yale university investigators treated eight patients with IVIg. Of the eight treated patients, seven had completed six months of treatment. All **the patients treated with IVIg improved and the disease showed a reversal in them**, similar results were reported in a second study with IVIg in Alzheimer's patients done in Europe.
Another study found an increased incidence of the infection ***Chlamydia pneumoniae*** in the brains of deceased Alzheimer's patients. This made a team from McMaster University in Canada to treat 101 patients with **Doxycycline** and **Rifampin**, or dummy pills for three months. Those given antibiotics showed significantly less mental decline. The authors conclude that a **three-month course of 200mg Doxycycline and 300mg Rifampin** results in less worsening in cognitive with Alzheimer's disease. These **result likely represents a halt in disease progression**, there was **significantly less worsening in cognitive function at six months in the antibiotic group** than in the placebo group.

A study reported by researchers from the University of Manchester in British Medical Journal, showed **a high number of small strokes happening in Alzheimer's patients in just within an hour**. These can result from inflammation within the small blood vessels in the brain. The observation strengthens the infectious relationship of Alzheimer's disease. We can conclude that the infecting agent ***Chlamydia pneumonia*** by molecular mimicary is turning on the immune system to attack blood vessels. **Recent studies show a role for circulating beta-amyloidal peptide in small blood vessels of the brain causing white matter disease**. White matter consists of axons (wires) connecting the neurons (brain cells) in the grey matter.
Homocysteine, another marker of inflammation has been found to be elevated in patients with AD. The patients with elevated homocysteine were also deficient in vitamin B-12. **Aluminum** has been reported to cause alzheimers like dementia, in a large number of cases which developed in Guam the problem was resolved after changes in the diet of the local people.
Symptom: Memory loss for recent events, names, numbers, are the early symptoms of Alzheimers. People have difficulty recalling recent events, names, and numbers. They can talk slowly, are easily agitated walk slowly and in later disease behavior issues will increase.
Diagnosis: There are no routine tests to confirm Alzheimer's, so it's a clinical diagnosis based upon symptoms of recent memory loss.

Tests

- **FDG PET** scan shows hypometabolism of the parietal and temporal lobes
- **EEG**. In Alzheimer's EEG will show exaggerated photic driving responses. In 60 consecutive patients at NIH with Alzheimer's had these phenomena.
- **Homocysteine, Folic acid & B-12** levels need to be tested for vitamin deficiency.
- **Check IgG** levels and IgG-subclass levels. (to screen for immunodeficiency)
- **MRI** scans of the head, to look for atrophy in the brain, strokes and hydrocephalus.
- **Screen for Celiac disease**. (please see section on Celiac Disease & whipples disease)
- **E.S.R and CRP if elevated suggest inflammation**.

Different conditions which can cause memory problems.

- Forgetfulness happens due to travel, loss of sleep, fatigue, stress or vitamin deficiencies like (thiamine vitamin-B1, Cynocobalamin- B12, Pyridoxine-B6 and Tryptophan).
- If patient presents **with behavior disorder** then they can have Frontal Temporal Dementia.(Multiple family members have this)
- Vascular Dementia which is caused by multiple strokes, patients have hypertension, difficulty walking and weakness.(is a treatable condition by controlling blood pressure)
- Lower consumption of water will cause memory loss. Increase water intake.
- Low testosterone levels will cause memory loss, check & replace testosterone.

Treatment: There are some effective treatments for Alzheimers, seen in small studies.

- Three-month course of 200mg Doxycycline and 300mg rifampin for Chlamydia.
- Take sublingual supplements of B6, B12 and Folic acid.
- Avoid aluminum in medicines (buffered aspirin has aluminum, antacids, deodorants, antiperspirants and TPN feedings may contain aluminum)
- A tablespoon or 200 mg of Curcumin (Turmeric) daily works in reducing the plaques of Alzheimer's. (Research study done at UCLA). Sold in Indian Food stores called Haldi.
- Omega-3 oil or aspirin taken daily to reduce inflammation and prevent recurrent small strokes, which were reported from a study done at University of Kentucky.
- Colostrum is rich in IgG. Colostrum 1000mg in studies has been found helpful.
- Mild physical activity three times a week reduces the risk for alzheimers.
- Calories need to be restricted, and the water intake should be more than 8 glasses of water a day, this intake of water should turn urine color to light yellow.
- If IgG levels are low then treat with IVIG 400mg/kg per month.

Aspirin reduces the risk of developing Alzheimer's by 55%. Aspirin 325mg has to be taken at least once a week to avoid Alzheimers. Use a high fat diet (high in Omega-3 and low in Omega-6) found in **walnuts, almonds, cod liver oil or fish oil, whole wheat, olive oil and flaxseed-oil**. Most patients with Alzheimers will have sun-downing, when they become agitated at night. **Lamotragine** an epilepsy drug is used to control behavior in Alzheimer's patients.

Neuromyelitis optica-Transverse Myelitis: Transverse Myelitis is a inflammation of the spinal cord. Myelitis is sudden onset and is caused by autoimmune process. Cases may have a preceding history of flu, infection or vaccination such as hepatitis.
Neuromyelitis Optica or Devics Disease: These conditions have an association of Transverse Myelitis (TM) with optic nerve inflammation (blindness). The disease may have a relapsing, remitting course and responsd to steroids, sometimes poorly. NMO has a poor prognosis, due to the occurrence of necrosis within lesions. Relapses are commonly treated with corticosteroids and people with recurrent attacks may be managed with chronic immune suppressive treatments. Intravenous gamma globulin (IVIG) and plasma exchange are reasonable treatment options because NMO is believed to be antibody mediated and associated with S.L.E. Case reports of Lymes with optic neuritis in both eyes have responded to **Doxycycline**. The dose is 200mg daily for a week then, 100 mg daily for a week. Use Omega -3 oils to reduce inflammation.

Transverse Myelitis (TM): Myelitis means inflammation of the spinal cord; transverse refers to involvement across one level of the spinal cord. Myelopathy is a general term for a disorder affecting the spinal cord. Infectious agents have a protein which resembles or mimics the structure of myelin in the spinal cord. When the body mounts an immune response to the invading virus proteins, The immune response mistakenly responds against the spinal cord myelin, (which is similar to the virus proteins). This leads to inflammation and injury within the spinal cord. The nerve fibers in the spinal cord carry all the instructions from the brain to the extremities; they also carry back sensory information to the brain like touch, pain and temperature. Inflammation in the spinal cord disrupts the information links and causes symptoms of TM which include limb paralysis, sensory disturbance, and bowel and bladder dysfunction

Triggers of Autoimmune Transverse Myelopathy or Myelitis & NMO:

- **Systemic** lupus erythematosis, Sjogren's syndrome; Sarcoidosis, Multiple Sclerosis, Paraneoplastic syndrome and antiphospholipid syndrome.
- **Bacterial**: Mycoplasma pneumoniae, Lyme borreliosis, syphilis, tuberculosis, Rocky Mountain spotted fever
- **Viral**: herpes simplex, herpes zoster, cytomegalovirus, Epstein-Barr virus, enteroviruses (poliomyelitis, Coxsackie virus, echovirus), human T-cell, leukemia virus, human immunodeficiency virus, influenza, rabies
- **Post-vaccination** : TM has been reported within a few days or few weeks of the following vaccines.(rabies, cowpox, diphtheria-tetanus-pertussis, measles or rubella, Japanese B encephalitis)

Symptoms of Transverse Myelitis & NMO:

- Back pain or a tight band like sensation going around the abdomen is one of the earliest symptoms of transverse Myelitis.
- Leg weakness or paralysis if the myelitis involves the lower spine.

- Inflammation at neck level causes numbness of the face and weakness in the arms.
- Bladder involvement is rare, loss of urinary control and bowel sphincter control.
- Vision problems such as blindness are present in Devics disease.

Tests: MRI scan of the spine or the brain to look at damage in spinal cord areas is usually normal. Spinal tap is done to take a sample of the spinal fluid and check antibodies against appropriate bacteria suspected in the particular case. A vitamin B-12, B-6 and thiamine levels are done to check for deficiency. Antigliadin antibodies are done to check for Celiac disease. R.P.R is done to check for syphilis and testing for HIV can be obtained in suspected cases. Antiphospholipid syndrome can present with optic atrophy and transverse myelitis with positive IgA type antiphospholipid antibodies.

Treatment of Myelitis & NMO:

- I start all patients on Doxycycline 100mg twice a day for two weeks.
- IVIg is effective in all cases of TM at a dose of 500mg/kg for 4 days.
- Antiphospholipid lipid antibodies is present, simply start anticoagulation with heparin, coumadine and high dose of steroids.
- Replace vitamins if any deficiency is found specially B-12. Thiamine
- Prednisone 20 mg daily in adults can be tapered in a week.
- Some patients appear to become steroid (glucocorticoid) dependent and experience relapses when the dosage of prednisone is lowered.
- Plasma exchange (PE) may be tried in patients who do not respond to glucocorticoids. NMO treated with PE showed moderate or marked improvement.

Chronic inflammatory Demyelinating PolyRadiculoNeuropathy or (CIDP): The peripheral nerves, carry information from the spinal cord to the muscles, they also carry sensory signals back to the spinal cord. The nerves, in our body, have an outer covering called Myelin, which is like a roll of toilet paper wrapped around the axon (axon is inner portion of the nerve). The myelin, helps conduct electricity in our body by a process called salutatory conduction (current jumps from one myelin cell to the other). Due to myelin, nerve impulses travel at speeds of 70-100 meters/second. In GBS, CIDP and autoimmune neuropathy the myelin is attacked and gets damaged, resulting in slow and reuced electrical conduction and we see symptoms of numbness, weakness, burning type pain. If this autoimmune attack against the myelin is stopped, then Schwann cell around the nerves will develop more myelin and the person feels back to normal.

CIDP represents about **one third** of all initially undiagnosed neuropathies (nerve disease). Repeated attacks of weakness or numbness are common, in this disease. A relapsing course with partial or complete recovery between recurrences is seen. The periods of worsening and improvement usually last a week or month. Younger patients are said to have a higher frequency of relapsing course as disease improves and worsens again. Relapses can happen after 7-8 years.

Patients with CIDP respond to immunosuppressive therapy.
CIDP usually occurs within a few weeks following an infectious event or vaccination. Both respiratory and gastrointestinal infections have been implicated as a cause. CIDP can be slowly progressive and develops as diabetic neuropathy. Most cases of CIDP get diagnosed as polyneuropathy and are told, nothing can be done for them. Without anti-inflammatory treatment many will develop autoimmune heart disease, skin lesions, inflammation of the blood vessels, thus a correct diagnosis and early intervention is recommended.
Recent research has shown that CIDP not only involves peripheral nerves, it also causes disease of the brain, spinal cord, muscles.

Symptoms of CIDP: People with CIDP have repeated attacks of weakness that last days, weeks or a month or more. Sensory complaints consist of numbness and tingling in hands or feet. Burning type sensation and pain will force the patients to seek medical attention. The peak incidence is 40-60 years of age. This neuropathy is seen in diabetics, and is slowly progressive. The disease may start as back pain going down the legs or a sudden hand weakness. Autonomic dysfunction termed dysautonomia (dysfunction of the autonomic nervous system) can occur. Symptoms of dysautonomia consist of irregular cardiac rhythm, diarrhea, constipation, dizziness on standing up, burning type feeling, feeling of swelling. Increased sweating which could be on one side of the body. Discoloration of skin below the knees may be seen. Loss of consciousness while the person is standing can happen, this type of CIDP is called autonomic small-fiber neuropathy and is discussed with the seven variants or subtypes of CIDP.
Neurological exam in general shows neck flexor weakness distinguishes CIDP from other neuropathies. Facial muscles may be weak. Eye movements can be affected in CIDP causing double vision. Deep tendon reflexes are absent or depressed and rarely increased. Sensory findings are mild and often include impaired touch and vibratory sensation, with less involvement of small-fiber sensation (pain and temperature). It is common to see bilateral or unilateral weakness of shoulders, hips, hands and feet in most patients.

CIDP Variants -1: Lewis-Sumner syndrome: (LSS) causes numbness and weakness of the hands or hips. It is also called **m**ultifocal **a**cquired **d**emyelinating **s**ensory and **m**otor **n**europathy (MADSAM). **There have been case reports with a normal EMG/NCV** in LSS. However with magnetic stimulation the patients were found to have proximal conduction blocks in the arms.
Symptoms LSS: 1) LSS presents frequently with **arm involvement**, mainly involving the **wrists and hands**, causing the little or ring finger to becomes numb and weak or the thumb middle and index fingers are weak and numb. LSS can involve the **whole hand** causing numbness and weakness. **Patients have difficulty opening and closing their hands and fingers**. They have difficulty driving a car as they cannot grip the steering wheel, they cannot open a door or hold a spoon. Cannot flex or extend the fingers due to weakness. Muscles shrink and bones become prominent.
LSS: 2) LSS can also present with sudden onset of hip weakness. Patients note difficulty in

getting out of a chair, difficulty climbing stairs and weakness of the thigh. On examination the patient cannot elevate the affected knee while sitting (Quadriceps weakness). Mild wasting, fasciculation's (muscle twitching), and some numbness in the legs is present. This can be misdiagnosed as femoral neuropathy or Lumbar plexopathy. **Case report**: In a person with hepatitis-C virus (**HCV**) infection developed (LSS). The neuropathy worsened after IVIg, improved after intravenous methylprednisolone, worse with interferon-alpha, responded again to steroids continued for 70 weeks with clinical improvement of hepatitis.
Test for LSS: EMG/NCV shows multiple electrical motor conduction blocks, located in the upper arm, whereas slowing of conduction (demyelinating features) outside the blocked nerves are rare. Prolonged sensory potentials are found in majority of the patients. **Rarely the electrical conduction block or (damaged area) can be in the upper-arm and EMG/NCV usually done in the lower arm looks normal**.
Treatment: LSS responds well to IVIg or **steroids**. (**Pulse steroids recommended**).

CIDP Variants-2: Multifocal Motor Neuropathy: MMF is purely a **motor** or weakness issue. No sensory nerves involvement like numbness is seen. It affects **men** much more than women. Some patients complain of numbness, about 50% patients have IgM antibodies to ganglioside GM1. Diagnosis depends on the demonstration of short areas of partial motor conduction block caused by demyelination at sites not vulnerable to entrapment. Sensory conduction is normal across the same segments. **Even if no definite conduction block is found** in an otherwise typical case, a trial of treatment may be indicated.
Symptoms / examination MMF: A progressive muscle disorder with muscle weakness in the hands, there is asymmetric involvement of the muscles. Muscle wasting, cramping, and twitching of the muscles are seen. The disorder is sometimes mistaken for amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease). Tendon reflexes are often absent or weak. The weakness can spread to involve the legs and feet causing patients to be confined to wheelchairs. In some patients the tendon reflex can be increased.
Tests for MMF: Antibodies against GM1 ganglioside (fat part of the nerve) are present. These antibodies are rare in any other disease. The EMG/NCV characteristic finding is, **conduction block**. Nerve conduction studies show blockade of impulses at sites along the course of motor axons (nerve fiber) providing evidence that the site of disease is in the peripheral nerve. The phenomenon of conduction block has been described in patients with sensory-motor neuropathies (chronic inflammatory demyelinating polyneuropathy (CIDP)).

Treatment: MMF responds best to treatment with IVIg.

CIDP Variants-3: ANTI-MAG (Myelin Associated Glycoprotein) Neuropathy: Patients with MAG polyneuropathy have antibodies to myelin-associated glycoprotein (MAG). A slower, progressive course causing weakness, numbness and atrophy in the legs, associated with poorer response to treatment.

CIDP Variants-4a: MGUS Monoclonal gammopathy of unknown significance, MGUS (or benign monoclonal gammopathy, BMG): Monoclonal gammopathy of unknown significance, MGUS is a part of CIDP. Any neuropathy seen in MGUS is to be considered and treated as CIDP. MGUS usually has (IgA, IgG or IgM) immunoglobulins elevated in the serum. The neuropathy is mainly seen in males. It is a combined sensory/motor neuropathy involving the lower extremities and sparing the cranial nerves. In women this neuropathy advances rapidly from feet to hands and then involves the face. It can cause severe pain. Higher incidence of Myeloma is seen in these patients. The **POEMS** syndrome of **P**olyneuropathy, **O**rganomegaly, **E**ndocrinopathy, **M**onoclonal protein, and **S**kin changes is occasionally seen in some cases.

CIDP Variants-4b: A rare paraproteinaemic neuropathy is (**CANOMAD**) Chronic **a**taxic **n**europathy (drunk like walk), with **o**phthalmoplegia (No eye movements), Ig**M**-paraprotein, cold **a**gglutinins (antibodies precipatate on cold temperatures), and **d**isialoganglioside-antibodies.

Symptoms of MGUS: Patients present with pain and burning, blue toes, to reduce the pain they keep their hands and arms on ice. Pain is severe at night. Case report: 70-year-old man presented with double vision, new onset of relapsing neuropathy, elevated sedimentation rate, IgM monoclonal paraprotein, cold agglutinins, and antidisialosyl IgM antibodies, features of the acronym CANOMAD (**c**hronic **a**taxic **n**europathy with **o**phthalmoplegia, **M** protein, **a**gglutination, and **d**isialosyl antibodies). The patient also had renal failure associated with this syndrome. Treatment with **corticosteroids** improved both the neuropathy and renal failure.
Treatment of MGUS: Is like CIDP with steroids, plasmapheresis and IVIg.

CIDP Variants-5: Small Fiber Neuropathy: Small fiber sensory neuropathy (SFSN) is a disorder in which the tiny sensory superficial nerves of the skin are affected. Patients experience sensory disturbances that start in the feet and progress upwards. Some patients with SFSN experience quick onset **burning pain and numbness over the whole body**, including the face. Patients have other autoimmune diseases, **celiac disease**, amyloidosis, and erythromelalgia or diabetic neuropathy. Nutritional and toxic causes include excessive use of alcohol, amidrone, arsenic, boric-acid, cyanide and hexacarbons (**glue sniffing**). Inherited causes include hereditary sensory neuropathy Type-I (HSN1) with **high arched feet** & hammer toes.
The symptoms of small fiber sensory neuropathy (SFSN) are sensory in nature and include **unusual sensations such as pins-and-needles**, symptoms of **burning sensation** affecting the feet, pricks, tingling and numbness. Some patients may experience pain or coldness and **electric shock-like brief painful sensations**. Since SFSN does not involve large sensory fibers that convey balance information to the brain or the motor nerve fibers that control muscles, these patients do not have balance problems or muscle weakness. In most patients, the symptoms start in the feet and progress upwards. In advanced cases, it may involve the hands. They can also develop **dysautonomia**, with erectile dysfunction, diarrhea or constipation.

Test: EMG/NCV will be normal in small fiber neuropathy. **Skin biopsy** looking at the number of nerve fibers is abnormal. The quantitative sudomotor axon reflex test (QSART) is used to assess the small nerve fibers, which are linked to the sweat glands, is reported as abnormal. Sural nerve biopsy is usually reported as normal .

Treatment: **CIDP treatment guidelines on page 58**. All the patients need to be evaluated for celiac disease. Small fiber neuropathy responds to treatment with Vibramycine or Cipro one tablet twice a day for two weeks and then alternate day treatments for a month.

CIDP Variants-6: Distal acquired demyelinating sensory neuropathy. Present is children as ataxia (walking like a drunk), balance problem, some numbness.
Symptoms / examination: Patients **have unsteady and clumsy way of walking**, and pins and needle feeling in their hands or feet, they have frequent falls. On examination they have reduces vibration and joint position sense, loss of pin prick sensation in the feet or hands. Muscle reflexes are intact.
Test: EMG/NCV can be normal or may show slight slowing of sensory nerves.
Treatment is with IVIg or steroids. Vibramycine & Doxycycline should be tried.

Associated medical Conditions with CIDP: CIDP can be seen together with **Multiple Sclerosis**. Many such cases have been reported showing (White spots on the MRI combined with a neuropathy). **Celiac Disease** will also show a similar involvement of white spots in the brain with a neuropathy. Similar involvement of brain and nerves is also seen in **Lupus**, Inflammatory bowel disease like **ulcerative colitis** and **Crohn's.** In Gastric diseases H-pylori is the main pathogen and antibodies against H-pylori should be tested and H-pylori should be eradicated with the antibiotics protocol described in the stomach chapter. Patients with **diabetes**, SLE, **Sjogrens**, who have a progressive neuropathy it is likely to be CIDP superimposed on their autoimmune disorder. It is better to assume that a new neuropathy developing in patients with arthritis, heart disease and lupus is likely to be CIDP.

Diagnosis of CIDP: CIDP Diagnostic Criteria ALERT American Association of Neurology (AAN): Criteria are only for Research Studies. This should not be used in clinical diagnosis. AAN Electrophysiologic criteria: Require 3 demyelinating range abnormalities (slow conduction velocity, prolonged distal motor latencies or F wave latencies or conduction block) in 2 nerves. These criteria should not be used in Clinical Practice as more then 50% of the patients will not be diagnosed by this criterion. Majority of patients seen in clinical practice fail to meet all of the above criteria.
Laboratory Studies: **CSF Protein level** is increased significantly in 80% of patients usually between 50 and 200 mg/Dl. The CSF Protein is normal in small fiber CIDP.
EMG/NCV test shows findings of a slow nerve conduction (demyelinating pattern) or slightly slow (Axonal pattern) that are usually seen. There are prolonged distal latencies (the time difference measured after shocking a nerve over a segment). Absent or prolonged F-wave

latencies, as the disease progresses, patients tend to develop secondary axonal degeneration. **Patients can have a normal EMG/NCV in small fiber CIDP.** The types of nerve cells that are damaged in painful sensory neuropathies (small, unmyelinated and thinly myelinated axons) are not well studied by EMG and NCS, and these tests give false "normal" results in patients with small-fiber neuropathies. A person with a normal EMG/NCV can still have CIDP.

Peripheral nerve biopsy (**A skin biopsy should be considered in place of a Sural nerve biopsy**) In the past, the best way of getting information about sensory neuropathies that cause pain was surgical removal of a part of the sural nerve at the ankle. This left patients with permanent numbness, and caused other complications in some patients. Skin biopsy, a minor procedure with no serious complications, gives much of the same information. In addition, skin biopsy may even be more sensitive than sural nerve biopsy because it samples the nerves closer to their endings in the skin, where disease starts. Nearly all parts of the body have microscopic nerves running through them to allow sensation and movement. Skin biopsies can be processed in a way that allows us to see and count the number of sensory nerve endings, and to look for any neural abnormalities. Even in Leprosy skin biopsy is equally good when compared with the sural nerve biopsy. Current clinical standards to diagnose CIDP do not recommend a nerve biopsy. As the skip lesions of CIDP may or may not be seen in sural nerve biopsy. After the biopsy the patient usually has a permanent sensory deficit, the sensory loss in the foot accompanied by pain, is worse then the original disease in some patients. I have seen patients who are worse off due to biopsy. Finding of inflammation on the nerve biopsy, although rare, definitely confirms the diagnosis. Findings of predominant demyelination on the nerve biopsy can be used to confirm the clinical presentation and suggest a diagnosis of CIDP. However, the absence of inflammation does not entirely rule it out CIDP. The best technique for a sural nerve biopsy is described by an Austrian team. Where they only remove a 10mm piece of the sural nerve and reattach the stumps by microsurgical repair. They claim none of their patients have any complaints of pain or sensory loss.

Recommended blood tests for neuropathy evaluation: Vitamin levels should be tested in all patients **Cynocobalamine (B12)**, **Pyridoxine (B6)**, **Thiamine**, Niacin, Alpha tocopherol (E), Folic acid, are recommended tests. Thiamine deficiency, in particular, is common among people with alcoholism because they often also have poor dietary habits. Thiamine deficiency can cause a painful neuropathy of the extremities.

- **Thyroid function test** (**TSH & T4**, { rare anti thyroid antibody})
- **Vasculitis evaluation** (**CRP or E.S.R**.) (rare ANA and antiphospholipid antibody).
- **Oral glucose tolerance** test or hemoglobin A1C, to evaluate for diabetes.
- Antibodies (rare anti-MAG, anti-GM1, anti-Sulfatide, anti-GALOP, Anti-GQ1b)
- **Antibodies celiac disease** (Anti gliadin antibody)
- **Lyme disease**, (Borrelia burgdorferi antibodies)
- AIDS testing (HIV antibody test)

- **Syphilis**, (RPR test) it is extremely rare to find this positive unless in San Fransi.
- Hepatitis C (Anti-HCV (antibody to HCV)
- Heavy metals screen for (arsenic, lead, mercury, and thallium).
- Anti-Hu antibody (antibody for a pure sensory neuropathy underlying malignancy)
- SPEP Serum protein Electrophoresis (For Myeloma)
- IgA level, IgG level, IgG-subclass levels (to evaluate for immunodeficiency)
- Antiphospholipid antibodies in CSF (will need heparin, asprin or coumadine)
- Serum Homocysteine levels (B-12 levels are unreliable, homocysteine is a better marker for B-12, B-6 deficiency and suggests inflammation)
- **Sarcoid** causes intense pain and less sensory loss which responds to steroids. Accompanied by joint pains, **weight loss and fatigue**. Angiotensin-converting enzyme level is elevated and chest X-ray is abnormal.
- **Porphyria** will cause a autonomic neuropathy and weakness, abdominal pains, porphyrinogens in blood and urine are elevated. During attacks Urine left in a cup becomes dark on sunlight exposure. Cerebrospinal fluid show elevated protein. Psychological features with **shoulder or hip asymmetric** weakness suggests poprphria.
- **Amyloid** typical affects pain & temperature fibers, but occasionally patients can develop large-fiber neuropathy as well. Carpal tunnel syndrome or painful peripheral neuropathy, sensory or mixed neuropathy is also seen. Initial symptoms of **sexual impotence**, cardiac problems and low blood pressure on standing develop. Urinary proteins are elevated.
- **Celiac** disease causes a neuropathy. Please read the diet or celiac disease section for the Gluten free diet guidelines and for disease evaluation.
- Toxins like botulinum (**Botox**) are linked to development of CIDP, if diagnosed early the neuropathy is reversed by antibiotics or IVIg. Patients getting Botox injections should be alert to any new symptoms of weakness and numbness.

The protocol for CIDP treatment: James Austin first documented the steroid responsiveness of Chronic Inflammatory Demyelinating Polyneuropathy in 1958. Prednisone was used orally; the trend has changed towards intravenous pulse doses. The mean time for initial response to steroid treatment is two months. After attaining maximum benefit (usually in 6-12 months), prednisone is slowly tapered. The tapering of prednisone may result in a relapse of CIDP. Recent studies show that IVIG, prednisone and plasma exchange are all beneficial in autoimmune diseases. Plasma exchange performed twice weekly for 3 weeks generally resulted in transient improvement in progressive and recurrent cases of CIDP. Intravenous immune globulin (IVIG) has been found to be beneficial and is considered the best treatment for CIDP.

Infections: (Try to get rid of any associated infection in autoimmune cases) Autoimmune diseases in general and GBS & CIDP in particular are clinical presentations of many different types of infectious diseases, some of the known etiologies are Borelli, Campylobacter Jejuni, Brucella, Chlamydia pneumonia, Coxiella burnetii, Mycoplasma pneumoniae, Legionella

pneumophila, Listeria monocytogenes, H.I.V and Treponema palladium. **Many patients who were treated with antibiotics not only got better but had no further attacks.** The antibiotics commonly used have been **Doxycycline**, Zithromax, Biaxin **Ciprofloxacin**, and Penicillin, with an excellent response.

- In cases of GBS induced by Coxiella Burnetii, 14 days doxycycline treatment (200 mg daily) induced rapid and complete recovery. Prolonged antibiotic treatment may be required to prevent relapsing infection from the resistant bacterium. In Chlamydia pneumonia treatment with Zithromax, Biaxin, Erythromycin or **Ciprofloxacin**.
- Cases of GBS where Lymes disease is the cause are treated with Ceftriaxone intravenous for two weeks or **Doxycycline** 200mg for two weeks orally.
- People in areas of West Nile Virus (WNV) need to be alert for GBS, CIDP caused by WNV and these cases should be promptly treated by Doxycycline.
- Cases acquired by Mold the use of IVIg with itraconozole results in resolution.
- CIDP/ GBS associated with hepatitis-C virus infection are treated by interferon-alpha-2b and ribavirin. Viral eradication is confirmed during the 4th week of treatment and is followed 3 weeks later by neurologic improvement. The patients have resumed normal activity within a year of this treatment.
- Cytomegalovirus infection use ganciclovir (5 mg/kg BID) for 4 weeks.
- Treatment with antibiotics in the first couple of days of campylobacteriosis is recommended for those with weakened immune systems, pregnant women and people with relatively severe symptoms. The use of antibiotics called fluoroquinolones to treat disease in chickens is creating strains of drug-resistant campylobacter in humans.
- Finding a source of inflammation in a patient with CIDP and then removing it also benefits the patients, after adeno-tonsillectomy, a patient's CIDP went into remission.
- HIV virus and Aids can present with neuropathy which responds to IVIg.

Immunomodulatory treatment for autoimmune diseases including CIDP/GBS.

Immunomodulatory treatment is started after making sure that any infection present in the body has been cleared up. Vitamin, mineral and amino acid deficiency should be corrected. The patient should follow dietary recommendations in the diet section. Those patients with positive antiphospholipid antibodies should be on aspirin or subcutaneous heparin, usually these are elderly men with a sensory-motor neuropathy, and they are at high risk of having strokes.

Emergent or Immediate treatments for Autoimmune disorders & CIDP:

A nanotech magnetic pulsar will reverse the neuropathy within fifteen minutes.

All patients need to take Omega-3 fatty acids 2000mg daily. All the patients need vitamin-B-12, folic acid, Vitamin B-6 tablets taken under the tongue. Omega -3 are present in Flaxseed oil, olive oil, cod liver oil and Fish oil.

The First treatment for **any autoimmune patient** or **acute neuropathy** patients should be a trial of **Ciprofloaxcillin 500mg** twice daily or **Doxycycline 100mg** twice daily for two weeks. Then one tablet, once a day for a week. For long term treatment either drug can be taken on alternate days like Monday, Wednesday & Friday for 4-6 weeks as needed. I recommend taking the drug at night with fluids. Doxycycline can cause yellowish discoloration in children who have growing teeth. Nonreponders to antibiotic should try the next steps below:

There are three short term treatments:

- **1) IVIg:** is the first line treatment in USA it has reached this position due to ease of infusion in the patient's home. IVIG is the only treatment recommended during pregnancy. IVIg is an expensive and needs to be repeated monthly. The earlier IVIg is given in the course of disease the better the disease response. The starting dose is 500mg/kg given on consecutive or alternate days for a four day course. The rate of infusion is controlled to around 100-200 cc per hour. Usually a 5% solution of IVIg is used. I have used one aspirin 325mg daily to prevent thrombosis combined with 8 glasses of water daily. This dose of IVIg is repeated usually up to five months. In the meantime the patient is started on an immunosuppressant. This immunosuppressant is started with the intention that it will become the primary pharmaceutical agent in the long run. The immunosuppressants are listed under (**List A**) **below.** IVIG will lose its efficacy in the long run and it has to be replaced. If the IVIg does not work then it is recommended to use one gram of intravenous steroids with IVIG, and also use an H-Pylori eradication program described in the Gastric section. Combined treatment with steroids is recommended in most cases. For the long run IVIg should only be used in those patients who have exhausted the agents in (**List A).**
- **2a) Steroids:** Some patients only respond to steroids. For long term use it's recommended to use alternate day steroids or intravenous steroid pulses. Intravenous route 1-gram of Solumedrol is infused over an hour. Then the patient can be maintained on a oral dose. Starting with 1-mg/kg/day after 1 to 2 weeks the dose can be tapered to adjust to the clinical response. Once the dose is being tapered a long term immunosuppressant should be started choose from **cyclosporine**, Imuran, cytoxan, Methotrexate, or any of the agents listed under list A.
- **2b) Steroid Pulses:** Initial dose of 1000 mg/ of intravenous- methylprednisolone (IVMP) on every fifth consecutive day, then followed by 1000 mg IVMP every-week for the next month. IVMP is then reduced in frequency and dose over a period of 2 months continuing to 2 years. Patients are maintained with long-term high-dose intermittent IVMP every 2

to 12 weeks for up to 10 years with stable strength. In a few patients, the intermittent high-dose IVMP is changed to intermittent oral corticosteroid if poor veins limit IV line access or difficulty getting to an IV infusion center. Rare adverse effects occurred in only 1 or 2 patients receiving IVMP or oral prednisone, included cataracts, insomnia, pneumonia, ruptured diverticulitis, herpes- zoster, mood changes, and cramps. Lower doses are better tolerated by some patients. High dose of steroids beyond 6 months are not advised and switching to lower doses combined with a second drug from the list below is recommended. Asprin treatment should be given to all patients on long term steroids to prevent avasular necrosis of bone. (Avascular necrosis is a vasculitis in the bone which can lead to fracture of the hip). Gastric bleeding can happen.

- **3) Plasmapheresis:** Helps remove abnormal antibodies circulating in the serum. This procedure is only done in hospitals. During the procedure patients blood is run through a tube to the plasmapheresis unit, which spins the blood at high speeds. During the spinning phase of plasma, antibodies and plasma are removed from the blood. Fresh plasma or fluids are added to the patient's blood cells and returned back to the patient by an intravenous line. Usually three plasma exchanges per week are done for first 2 weeks. If the procedure is available it should be tried on those patients who have not responded to IVIg and steroids. Low blood pressure, allergies to equipment, low potassium and low serum calcium can occur during the procedure.

List A: Agents used for **refractory patients in autoimmune diseases**. Some of the successful immunosuppressive treatments reported are,

- **Cyclosporine A (CyA)** The daily dose of CyA should be 3 mg/kg/day. If patients respond to cyclosporine, remission can be maintained for 2 years, after which the dose can be slowly reduced over one year. Eventual withdrawal should be considered.
- **Methotrexate** gives a rapid onset of benefit within (months). Can be combined with corticosteroids. With routine monitoring, serious side effects are uncommon. Methotrexate dose is started at **2.5 mg once a week**, increased to **7.5** to 25 mg orally. **Taken once a week on weekends**. CBC and liver functions need to be monitored. Cause serious liver disease in presence of alcohol.
- **Azathioprine (Imuran)** is a broad spectrum immunosuppressive agent and has a steroid sparing action, provides long-term immunosuppression with relatively few side effects the dose is 2.5 to 3 mg/kg daily. Imuran is used to reduce needed doses of corticosteroids. However, it can take two to six months to show benefit and some patients do not improve at all. **It works well in patients who have chemical exposures triggered disease.** Azathioprine is metabolised by enzyme and 10% of the population have such enzyme deficiency. Measurement of enzyme values identifies the heterozygotes (different genes), whose dose should be halved, and homozygotes (similar genes), who should probably not be given the drug. It should not be used with allopurinol.

- **Cyclophosphamide** is an alkylating agent, which predominantly depletes B lymphocytes 2.0 to 2.5 mg/kg/day, given as a single dose each morning. Patients who were refractory to conventional treatment have responded to this treatment with high-dose. Women should not get pregnant on this treatment.
- **Etanercept,** 25 mg twice per week. Some patients may have significant improvement on this treatment. Etanercept is an injectable drug that blocks tumor necrosis factor alpha (TNF alpha) and is used for treating rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.
- **Interferon A:** Interferon beta-1a (Avonex) reduces inflammatory responses shows benefit in refractory patients at a dose of 30 microg once weekly for 6 months is used.
- **Mycophenolate mofetil** (MMF) Cellcepth mean dose, 2 g/day given for an average of 14 months). MMF showed a good response in 1/3 of the patients treated.
- **Rituximab** is an intravenous drug that is used to treat B-cell non-Hodgkin's lymphoma. It belongs to a class of drugs called monoclonal antibodies. Monoclonal antibody against CD20 antigen on B-cells. It represents a **successful therapy** in otherwise refractory autoimmune diseases. Initial: 375 mg/M2 intravenous, I/V Twice Weekly Maintenance: 375 mg/M2 IV every 10 weeks. TB if present should be treated before starting treatment with rituximab. Patient who has failed treatment with steroids, IVIg, cyclosporin, plasmapheresis, Rituximab will be effective with just 4 weeks of treatment.
- **Hyperbaric Oxygen Therapy works for polyneuropathy and autoimmune diseases caused by infections.** The theory states that more oxygen enters the body under higher pressure and improves healing. Increased oxygen also helps eliminate infective organisms like Mycoplasma and Borrelia from the body.
- **Magnesium** supplements can help reduce inflammation and relives pain. Dose is 400 mg twice or three times a day. Magnesium supplements used for a year have led to an improvement of nerve function significantly. Vitamin D and calcium supplements are also effective in some cases. In those countries where magnesium supplements are not available please use homeopathic magnesium-phosphate 30-60x 5-7 drops daily.
- **Bovine Colostrum** has been used to reduce muscle stiffness, with good results. The dose needs to start at 400-500 mg of IgG twice a day and go to 1-2 grams a day as needed.
- **Antibiotics like Cipro (ciprofloxin), Vibramycin (Doxycycline), Azithromycin.**
- **Stem-cell-transplant** has been used in autoimmune diseases with success, in the future this last resort treatment will become as simple as giving an injection.
- **DHEA** is a health supplement which builds muscles and improves strength. It also improves osteoporosis. Use on alternate days if you get short temper from DHEA.
- **Sex:** Autoimmune patients may see reduced sexual function, especially men. It is recommended they use a half an inch wide rubber band around the penis shaft. This will improve erectile function. Women need to use lubricants due to vaginal dryness. Both sexes need to practice pelvic floor exercises see last pages of this book.

Prognosis of neuropathy and autoimmune diseases: Good prognosis in Guillain-Barré syndrome & Chronic Inflammatory Demyelinating Polyneuropathy if treated early is completely reversible. Although 95% of patients will show initial improvement following immunosuppressive therapy, the relapse may happen. If left untreated then patient can become severely disabled. Those patients are not responding to above treatments should be checked for a source of infection and to see if they have some other cause of autoimmune disease such as Celiac Disease oe whipple in the gastric chapter.

CIDP in Children: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is rare in children. Children demonstrate many similarities to adults. Events such as a preceding flu, illness or vaccination are seen in fifty percent of the children. Symptoms onset is quick.
Symptoms: Children frequently present with weakness and loss of reflexes accompanied by sensory loss. Pain in the back and cranial nerve involvement is rare. Cerebrospinal fluid protein levels are usually elevated. They usually present with difficulty in walking, tripping, difficulty going upstairs and rarely just one leg is involved. Request a neurology appointment a primary care doctor may not be able to diagnose this. (Suggest the diagnosis Guillian Barre Syndrome).
Testing: On electrodiagnostic testing, children may show a normal or slightly abnormal nerve study thus ENG/NCV. Nerve Biopsy is unreliable in children or adults with CIDP are not recommended. Repeated EMG/NCV testing is not recommended as slowing of nerve conduction can persist for long periods after clinical recovery. Spinal tap can show increased protein. Antibodies for H.pylori, Borrelia need to be checked.
Treatment:

- Tonsils and Adenoid glands need to be checked for infection and treated. Lymes disease should be checked or treated in all patients. The initial response of children with CIDP to immunomodulating therapy is excellent. Intravenous high dose Steroids are contraindicated in children and have been shown to make their condition worse. I.V.I.g and cyclosporine combination has been very effective.
- In resistant chronic inflammatory demyelinating neuropathy, in addition to prednisolone and immunoglobulin, plasma exchange, azathioprine, cyclosporine, methotrexate, and cyclophosphamide can be tried at different times in different patients. Childhood chronic inflammatory demyelinating neuropathy responds to conventional treatment and generally has a favorable long-term outcome.
- I.V.I.g given at a dose of 500mg/kg for 4 days then 500mg/kg every two weeks for two months and then 400mg/kg every four weeks for 4 months. Several studies have indicated clinical improvement after treatment with prednisolone, plasmapheresis and intravenous immunoglobulin. M.R.I. study of the lumbar nerves, can show enlargement, which will respond to prednisone treatment.

Guillain-Barre Syndrome: (GBS) Guillain-Barre syndrome, the most frequent cause of acute neuromuscular paralysis, occurs 1-2 wk after various infections, vaccination in particular, and Campylobacter Jejuni enteritis. Molecular mimicry between the bacteria and human Myelin is seen as having relationship to the autoimmune cause of Guillain-Barre syndrome.
Symptoms: The patient usually presents with back pain and then rapidly develops weakness. In children weakness starts slowly as they tend to trip easily and show difficulty climbing stairs. On examination patients have usually lost their muscle reflexes and are severely weak. Reflexes will be rarely increased in those patients who present with Axonal involvement. Some patients will present with a purely sensory syndrome and this one is usually caused by small fiber involvement, which resolves with steroids (oral prednisone). Purely motor forms of GBS have also been reported named as acute motor axonal neuropathy (AMAN). The pure motor form of GBS usually has Serum anti-GM1b antibodies present, this group of patients respond to IVIg but will not respond to plasmapheresis. GBS can be triggered by many different types of infection. It has been associated with Rocky Mountain spotted fever (RMSF). In RMSF patient initially presented with fever, rash, and an altered mental status, they responded to therapy with **intravenous doxycycline**. Those patients who have an altered mental status, in them a search for an infecting organism should be done by doing a spinal tap. Although Doxycycline is the recommended therapy for children and nonpregnant women, chloramphenicol remains the standard therapy for women during pregnancy. Other infections associated with GBS are, Campylobacter Jejuni (23%), cytomegalovirus (10%), Mycoplasma pneumoniae (6%), and Epstein-Barr virus (3%). In some of these cases there will be a tendency to develop the chronic form of GBS called CIDP, in some there will be a poor recovery when the axon is damaged (axon is the central part of a nerve). Minocycline given early to the patients can help to stop reoccurrence. Patients treated with antibiotics have made an excellent recovery.

Miller Fisher Syndrome: (MFS) is a sub type of GBS in which patients have difficulty in moving their eyes (opthalmopheresis), they have double vision and loss of coordination. Patients tend to complain of dizziness, they notice difficulty in moving their eyes. MFS starts out involving both eyes in most patients, slowly progress to have complete immobilization of the eyeballs. Some patients develop pupillary sphincter paralysis and more than half have bilateral but often asymmetric dropping of eyelids (Ptosis).
Test: Antibodies to the ganglioside GQ1b are associated with Miller Fisher syndrome. Diagnosis is based on clinical findings only. Spinal tap will show a high protein content.
Treatment of GBS is by giving IVIG 500mg/kg per day for 4 days, and then 400mg once every 4 weeks till full recovery. Detailed treatment plans are discussed under CIDP section. The cause of both these disorders is the same, which is an autoimmune attack against the Myelin, Myelin wraps around the peripheral nerves providing electrical insulation. I have written the treatment of GBS, CIDP, Miller Fisher Syndrome and autoimmune neuropathies together in the CIDP chapter. In general antibiotics & IVIg should be the first line agent for treatment of GBS.

Following the diagnosis of an autoimmune disease, a long term anti-inflammatory treatment plan should be made if continued inflammation is seen on tests like ESR. Please read the diet section for tips on reducing inflammation. In some cases the ESR may be normal and if so then there is no need to start a pharmaceutical agent, over the counter supplements like aspirin, **Flax seed oil, Fish-Oil** or Colostrum can be used. Omega-3 Fish Oils are an anti-inflammatory medication and helps to reduce inflammation in all autoimmune disorders. If they are taken at a dose of 3000mg daily for a long term they may help reduce recurrent attacks of the disease. Fish oil and (Cod Liver oil) not only reduce inflammation they also provide the body with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Cod Liver oil should only be used in the winter months especially in countries with reduced sunshine, Cod Liver Oil dosage is reduced in summer months as may cause vitamin-D toxicity. Colostrum is IgG derived from cows, it's the pre milk secreted after pregnancy. Colostrum has powerful anti-inflammatory properties and has shown promise in long term management of autoimmune neuropathies, some have used a dose of 500mg colostrum twice a day minimum, can be adjusted upto 2000mg daily.

Non CIDP-Autoimmune neuropathies: Caused by infections

Leprosy and autoimmune neuropathy: Leprosy (Hansen's disease). Leprosy which is caused by a Mycobacterium lepra initially causes a neuropathy, through a mechanism called molecular mimicry. Autoimmune involvement in Leprosy, involves nearly every organ in the body starting from the scalp, eyes to the feet. In neurological cases it causes bells palsy (dropping of the face), GBS (sudden nerve paralysis), and vasculitis (inflammation of blood vessels). Leprosy can occur with myasthenia (generalized weakness), SLE (lupus) and antiphospholipid syndrome (recurrent thrombosis & infertility). **Leprosy is the oldest autoimmune disease that attacks the nervous system and the most common cause of polyneuropathy worldwide.**

Symptoms: Patients present with cuts or injuries on hands and without feeling any pain. Sensory loss starts at the fingers and toes and may affect a small patch of skin. Loss of sensation can lead to unnoticed injuries which also become infected. A variety of skin lesions are seen like macules (flat), papules (raised). Usually the skin lesion is less pigmented than the surrounding normal skin. Sometimes the lesion is reddish or copper colored, seen on the front and back of the body. Some patients present with a stuffy nose.

Test: Positive skin smears: In some cases, rod-shaped, red-stained leprosy bacilli, which are diagnostic of the disease, may be seen in the smears taken from the affected skin when examined under a microscope after appropriate acid –fast staining.

Treatment: All cases are treated with dapsone, corticosteroids, and rifampin in combination if there is any progression of symptoms the dose of steroid need to be increased. In chronic pain cases CIDP treatment guidelines should be followed.

Syphilis: Tabes dorsalis is a degeneration of the nerve cells and nerve fibers that carry sensory information from the legs back to the brain. The degenerating nerves are in the dorsal (rear)

columns of the spinal cord (the portion closest to the back of the body) and carry information that help maintain a person's sense of position. Tabes dorsalis is the result of an autoimmune response to syphilis infection. Symptoms may take many years to appear after the initial infection. The autoimmune phenomenon called Tabes-dorsalis (TD) is only seen in syphilis, which is described here. Treponema Pallidum the causative agent of syphilis has never been discovered in any biopsy done on the posterior columns. Serum and CSF antibodies have been reported positive in TD against Treponema pallidum. This makes a case for molecular mimicry in TD against the spinal cord.

Symptoms: **Lancinating pain** (lightning like, appearing suddenly, spreading rapidly, and disappearing) often is an early symptom and requires treatment. Neurological presentation is one of ongoing loss of pain sensation, loss of peripheral reflexes, impairment of vibration and position senses, and progressive ataxia. Bladder incontinence and loss of sexual function are common. This constellation of symptoms is described by the mnemonic "**PARESIS**": **P**ersonality disturbances, **A**ffect abnormalities, **R**eflex hyperactivity, **E**ye abnormality, **s**ensorium changes, **I**ntellectual impairment and **s**lurred speech. The ocular abnormality is manifested as **Argyll-Robertson pupils** (small, irregular pupils bilaterally, nonreactive to light but reactive to accommodation). While syphilitic meningitis can develop in tertiary syphilis, it more commonly occurs in earlier stages of the disease.

Diagnostic Test: a screening RPR / VDRL test. Is confirmed by FTA-ABS

Treatment:

- Procaine penicillin 1gm I.M. daily for 21 days (with 1gm probenecid orally daily).
- Doxycycline 100mg three times daily for 21 days.
- Benzyl penicillin 2-4 gm I.V. every 4 hourly for 10 days
- Steroids are effective in controlling pain.
- Chronic cases are treated with treatment guidelines under CIDP.

Facial palsy (Bells Palsy**):** This is a sudden onset of temporary facial droop caused by inflammation and paralysis of the facial nerve. The inflammation in the facial nerve is the result of autoimmune diseases and can involve the other side. A swollen facial nerve can be compressed in the facial canal. Facial palsy can be an early manifestation of lymes disease. Usually the causative factor is herpes virus, cyto megalo virus (CMV) or Borrelia. Facial palsy is triggered by exposure to cold air draft, reported commonly in London Taxi drivers and snow plough drivers around the world.

Symptoms: Symptoms range in severity from mild weakness causing a facial droop to total paralysis and may include twitching, weakness, or paralysis, drooping eyelid or corner of the mouth, drooling, dry eyes, impairment of taste, and excessive tearing in the eye. Facial palsy can occur on both sides when accompanied by Guillian Barre syndrome.

Test: Lyme titer, rheumatoid factor, erythrocyte sedimentation rate, antinuclear antibody, echocardiogram, RPR (syphilis), HIV titer, chest X-ray

Treatment:

- I recommend Minocycline / Doxycycline 100mg daily for two weeks and one week of oral prednisone.
- Prednisone 1mg/kg/day tapered and stopped from one to two weeks
- Administer acyclovir (Zovirax) 800 mg PO 5 times/d for 10 d; 20 mg/kg in patients younger than 2 years. HSV (herpes) is the cause in more than 70% of Bell palsy cases.
- It is recommended that some cotton wool be placed in the affected ear to reduce noise. Finally tinted glasses need to be used in the affected eye. The eye needs to be patched and kept moist. Food may lodge in the mouth and will need manual removal. Rest is recommended until recovery results. Minocycline helps reduce inflammation, and if any Borrelia organism is present minocin will inactivate them.
- (Omega-3) can be used in place of steroids dose of 3000mg daily. (Flaxseed, Olive, fish)

Dystonia: Dystonia is defined as involuntary, sustained muscle contractions that can cause abnormal postures, twisting, or repetitive movements in any part of the body. Dystonias include:

- **Hemifacial Spasm,** (twitching of the face muscles or eye muscles)
- **Blepharspasm (eye closure)**
- **Meiges syndrome (facial spasm)**
- **Spasmodic torticollis (neck twisting)**
- **Writer's cramp (**difficulty writing and cramps with writing)

The above dystonias can be autoimmune and be accompanied by other autoimmune conditions; these patients have elevated sedimentation rate & C-reactive protein and evidence of a preceding streptococcal infection. Antistreptolysin-O titers should be obtained to confirm a recent invasive streptococcal infection. Other important antibody markers include antihyaluronidase, antideoxyribonuclease-B, and antistreptokinase antibodies may be present. In one study 65% of adults with dytonia had Anti-basal ganglia antibodies (ABGA).
Test: Some dystonias can accompany SLE or M.S or Wilson's disease. Thus a MRI and spinal tap and ANGA can help diagnose these conditions.
Treatment: For strep induced dystonia look in PANDAS chapter, Botox is an approved and effective treatment for all dystonias. In MS and SLE induced dystonia steroids can help. Doxycycline 100mg twice daily for two weeks and on alternate days for two months can be used. Epilepsy medication and Valium reduce dystonias. Omega-3 fatty acids are useful.

Diabetic Polyneuropathy & Diabetic Amyotrophy: Multiple studies in the last ten years have shown that diabetic polyneuropathy and amyotrophy are in reality a vasculitis (inflammation). These syndromes respond to anti-inflammatory treatments. Here is a excerpt from Dr. king Engle at USC. "Chronic Immune Dysschwannian/Dysneuronal

Polyneuropathy is an autoimmune peripheral-nerve and/or nerve-root disorder known to usually respond to intravenous immunoglobulin-G treatment. Benefit can involve any combination of motor-nerve fibers and large and small sensory-nerve fibers responsible for a progressively crippling, unbalancing, discomforting or painful disorder. "Diabetic neuropathy" is commonly considered untreatable. However, 80% of my type-2 diabetes patients with polyneuropathy, adequately-treated with intravenous immunoglobulin-G, off-label, were relieved, sometimes completely, of various motor and sensory symptoms, including pain, thereby resembling Chronic Immune Dysschwannian/Dysneuronal Polyneuropathy. Spinal fluid protein in them is often elevated, higher values seeming to auger a better intravenous immunoglobulin-G response. Continuing the improvement requires continuing the intravenous immunoglobulin-G treatment, indicating both intravenous immunoglobulin-G responsiveness and dependency. The intravenous immunoglobulin-G responsive type-2 diabetes polyneuropathy usually is dysschwannian, sometimes mainly dysneuronal IVIG is the most beneficial and safest treatment, is costly, but if intravenous immunoglobulin-G-treatability of a dysimmune component of type-2 diabetes neuropathy is overlooked, dismissed or rejected, as commonly happens, other costs are high regarding the patient's worsening morbidity and disability, and resultant need for increased medical care".

I recommend that all diabetic neuropathy patients be treated according to CIDP guidelines (page 56-57). Doxycycline 100mg twice a day should be tried to see if it helps the neuropathy.

Acute Femoral Neuropathy: This condition is seen in diabetic patients, it starts out with an intense pain in the buttocks. Then the pain moves down the leg. Weakness will be seen when trying to get out of a chair. Weakness will be felt when trying to climb steps and the flexed leg will give away and fall will result. On examination the knee jerk is usually absent. Blood sugar is to be controlled with insulin; all the patients with femoral neuropathy need to be started on Ciprofloxacin 500mg twice a day and should be continued for two weeks. The antibiotic course should be repeated whenever the weakness gets worse. The course of a femoral neuropathy lasts six months. The other side is usually affected within a few months. Patients with femoral neuropathy respond quickly to CIPRO 500 mg twice a day for two weeks and then once a day for two weeks. Omega-3 oils and a good diet will help control symptoms.

Autonomic small fiber neuropathy (pandysautonomia): Very small nerves control the function of the internal organs like the heart, blood vessels, stomach, intestines and the nerves controlling the amount of light entering the eyes. When these nerves are damaged this is called dysautonomia or pan-dysautonomia. This nerve which controls the organ functions is collectively referred to as autonomic nervous system. Hypothalamus is a small area in the brain that controls the autonomic nervous system. Autonomic means these nerves are not under our direct control they are independent. The **a**utonomic **n**ervous **s**ystem (ANS) consists of two parts. **Parasympathetic** (nerves which slow the heart and increase intestinal motility) and

sympathetic systems (nerves that accelerate the heart, constrict the blood vessels, open the airways and enlarge the pupil) are affected. When we get angry the hypothalamus in the brain triggers the sympathetic nerves to raise the blood pressure and increase the hart rate as it prepares the body for a fight. (Remember to stay calm so we do not let the hypothalamus take over our life. A person, who is enraged, is under the control of hypothalamus)
Sympathetic system (SNS) is referred as the "**fight or flight**" system, it has a stimulating effect on organs. The sympathetic nerves constrict blood vessels, in intestinal tract and skin, while increasing muscle and lung blood flow. Bronchioles dilate allowing more oxygen to enter lungs. At the same time, the SNS increases heart rate, increases blood flow to the skeletal muscles and diverts blood away from intestinal tract. Sympathetic nerves enlarge the pupils and relax the lens, allowing more light to enter the eye. **Sympathetic are stimulated by attraction**, thus unconsciously dilating one's pupils makes the person looks more attractive. If you see the other person's pupil dilate that means they are interested in you.
Parasympathetic nerves **slow & relax** the organs thus called the "**rest and digest**" response. Parasympathetic will dilate blood vessels to the intestines which helps in digestion of food, while slowing the heart rate it allows the body to rest. The airways (bronchioles) are tightened as the need for oxygen has diminished, constrict the pupils and less light enter the eye. **Dysautonomia** is seen in CIDP with Involvement of the Autonomic Nervous System.
Symptoms: Burning type pain in legs or arms with loss of hair in extremities. Small fiber loss will cause burning sensations. Localized increased sweating (hyperhydrosis) and eyelid drooping (Horner's syndrome). Upon standing, autonomic failure can lead to loss of consciousness. Sexual dysfunction, hypertension, hypotension, asthma, syncope and heart arrhythmias are seen.
Testing: **Tilt test** has been abnormal most frequently. Check antibodies for Sjogrens, ANA for Lupus, Borrelia-antibodies for Lymes and anti-gliadin antibodies for Celiac-disease. Serum B-12 levels and H-pylori antibodies both these conditions can cause autonomic neuropathy. Voltage gated antibodies need to be checked for Eaton Lambert syndrome. Spinal food protein will be elevated in Guillian Barre and CIDP syndromes. A skin biopsy can be done to look for atrophy of autonomic nerve fibers.
Treatment:

- To prevent syncope (passing out spells) florinef, propranol are used.
- Symptoms resolve slowly after **intravenous immunoglobulins** and prednisone.
- Treatment guidelines given under CIDP should be followed in new onset of AN. This condition has also responded to plasmapheresis.
- Celiac disease can present with similar symptoms and needs to be ruled for treatment look under the gastrointestinal chapter.
- If H-pylori antibodies are positive and B-12 levels are low look under the gastrointestinal chapter for treatment of these conditions.

Holmes-Adie syndrome: **(HAS) Ross syndrome & Harlequin syndrome:** These syndromes are autoimmune disorders resulting from a small fiber autonomic neuropathy involving the feet and a similar neuropathy involving the small autonomic nerve fibers to the eye. These syndromes can be triggered by injury, heat or infections. The disease can spread slowly if left untreated. This condition has been associated with Sjogrens and its antibodies are positive in HAS patients, celiac disease is also an associated condition. In HAS one eye has a pupil that is larger than normal and constricts slowly in bright light (tonic pupil), along with the absence of deep tendon reflexes, in the ankles. HAS begins gradually in one eye, and often progresses to involve the other eye. At first, it may only cause the loss of deep tendon reflexes on one side of the body, but then progress to the other side. The eye and reflex symptoms may not appear at the same time. People with HAS can sweat excessively, usually only on one side of the body. The combination of these 3 symptoms: abnormal pupil size, loss of deep tendon reflexes, and excessive sweating is called **Ross's syndrome**, which is a variant of HAS. Some patients will have cardiovascular abnormalities, liver failure, gall stones due to reduced bladder motility. It is most often seen in young women. HAS is thought to be the result of inflammation and damage to neurons in the *ciliary ganglion*, an area that controls eye movements.

Harlequin syndrome is characterized by excessive sweating (hyperhydrosis) on one side and flushing, which are induced by heat or exercise. Usually, the sympathetic deficits confine to the face causing more sweating. Rarely, the cells in the ciliary ganglia are involved causing a mild eye lid droop. The unilateral facial flushing and sweating is induced by heat and exercise, observed on very close examination.

Symptoms include:

- **dilated pupil** in early stages
- decreased response to direct light reflex
- **tonic pupil**: pupil **slowly** constricts in bright light
- once the pupil has constricted it remains small for a long time (tonic pupil)
- decreased accommodation reflex (takes a long time to focus)
- decreased tendon reflexes, patients are often young women

Tests:

- Antigliadin antibodies to test for Celiac disease.
- CRP and ESR, Borrelia antibodies for Lymes disease.

Treatment: These syndromes can be initial presentations of underlying autoimmune disease, and sometimes develop in poorly treated autoimmune disease patients. If the disease is left untreated, these conditions can progress. New onset of these conditions can be part of an autonomic neuropathy which may respond to steroids. If Lymes disease is suspected then use Doxycycline 100mg twice a day for two weeks.

Reflex sympathetic dystrophy R.S.D or Complex regional pain syndrome:
Complex regional pain syndrome or RSD is essentially inflammation of the autonomic nerves in a localized area. RSD has been associated with injury dating back to the Civil War. We have already described the association of autoimmune disorders with injury. In general, patients who have complex regional pain syndrome suffer from pain, sensory changes, edema, sweating, and temperature disturbance in the afflicted extremity. Chronic changes can involve the skin, nails, and bone. Persistent inflammation, of the sympathetic nervous system and the central nervous system causes this condition. This is usually associated with CIDP.
Symptoms: (1) increased sweating, (2) color changes, (3) skin temperature changes, (4) weakness of the affected area (5) swelling, (6) symptoms outside the affected dermatome.
Treatment: RSD, CRSP are caused by inflammation of the Autonomic nervous system. Many reports show patients improved after steroid and IVIg treatments. Both of these conditions have developed in immunosuppressed patients and promptly returned to baseline after reduction in immunomodulatory treatment. RSD has been reported with Lymes disease, herpes zoster virus, Parvovirus B19 and Campylobacter jejuni. Cipro 500mg twice a day and a trial of Vibramycine 100mg twice a day should be tried for two weeks. Please read the chapters on autonomic neuropathy and small fiber sensory neuropathy in the CIDP section.

Palatal myoclonus (PM) is a rhythmic contraction of the soft palate in the throat. When associated with eye movements, it is called "oculopalatal myoclonus". A **clicking sound** is commonly heard by the patient. The frequency of the jerking is ordinarily 1-2 Hz. PM is the only movement disorder that persists during sleep. The inferior olive enlarges and develops rhythmic discharges when it is denervated by ipsilateral brainstem disease or contra lateral cerebellar disease, and is responsible for the palatal myoclonus. PM may be stopped by neck position, or eliminated on mouth opening. Palatal myoclonus is a clinical diagnosis and since the inferior olive enlarges the possibility of inflammation is raised, in some cases GAD antibodies have been reported positive, which makes a relationship with autoimmune diseases.
Tests:

- MRI scan of the brainstem with thin sections through the medulla.

Treatment:

- A course of Doxycycline 100mg twice a day for two weeks should be used and followed by Ciprofloxacillin 500mg twice a day for a week.
- Tegretol, Baclofen or Valporate may help.

Trigeminal neuralgia (TN) Pain in the cheek or head, also called *tic douloureux*, is a sudden jerk of the head due to pain. The pain causes, sudden burning or shock-like face pain that lasts a second followed by a pain free interval for a few minutes and can continue to reoccur in episodes. The intensity of pain is usually incapacitating. TN pain is typically felt on one side of the jaw or cheek. Episodes last for days, or weeks at a time and then can reoccur later. In the days before an episode begins, some patients may experience a tingling or numbing sensation or a somewhat constant and aching pain. The attacks often worsen over time. The pain can be triggered by vibration or contact with the cheek (such as when shaving, washing the face) brushing teeth, eating, drinking, talking, or being exposed to the wind. TN occurs in people over

age 50, and is more common in women than in men.
TN is a presenting symptom in SLE, mixed connective tissue disorders and multiple sclerosis, with bilateral symptoms. Antibodies against anti-RNP are positive in these patients.
Tests: M.R.I. scans of the head to check for MS, tumor or any abnormal blood vessels around the trigeminal nerve. Anti-RNP antibodies need to be checked.
Treatment: If the MRI has ruled out vascular lesions then steroids are used which usually resolve the condition. Gabapentine or Valporate can be used for long term pain control. In early cases steroids need to be tried to suppress inflammation especially if GAD antibodies are present. Valporate can be used for long term but success is low. A course of Cipro 500 mg twice a day or Vibramycine 100mg twice a day should be tried early in the course. Magnetic pulser stops the pain in 15 minutes. Turmeric and Flax seed oil are of benefit.

Amyotrophic lateral sclerosis (ALS) Autoimmune ALS: Also named Lou Gehrig's disease after the famous Baseball player who died due to this ALS. It is a progressive, fatal neurological disease that attacks the nerve cells (neurons) responsible for controlling muscles. In ALS, both the brain and the spinal neurons degenerate or die. ALS is triggered by diverse causes, some are toxic exposures, injuries and infections. Anti-Fas antibodies have been found in ALS patients, increased titer against GM1-gangliosides, (AGM1-gangliosides) is seen in 20% of ALS patients' serum. Many other inflammation markers are increased in the disease. In one series 25 patients with ALS were reported with **IgG-subclass deficiency** and T-cell deficiency. A study in Guam looking at pathogeneses of the diseases, showed intake of **low calcium** (Ca) and **magnesium** (Mg) and **high aluminum** water and a plant excitatory neurotoxin as possible causes. In Italy increasing **numbers of soccer players** have developed ALS, could be related to, use of illegal toxic substances or exposure to pesticides used on playing fields. Young patients with HIV develop ALS which promptly responds to antiviral treatment.
Another theory is that ALS is caused by toxic levels of **glutamate (MSG or fast food salt**) in the brain. Glutamate is a part of protein that cells in the body use to help break down food and build up body tissues. In the central nervous system, nerve cells (neurons) use glutamate to communicate with one another. Because too much glutamate can be toxic, the brain usually regulates the substance, keeping levels to those needed for body functioning. Abnormally high levels of glutamate have been found in the cerebrospinal fluid (the clear watery fluid that surrounds the brain and the spinal cord) of some patients with ALS. In experiments, scientists have found that a protein responsible for removing excess glutamate from the brain appears not to work properly in people with ALS. They theorize that toxicity resulting from excessive glutamate might be killing motor neurons. The death of these cells leads to progressive muscle wasting in patients with ALS.
Symptoms: The muscles gradually weakens, muscles waste away and twitch (fasciculation's). Patients with ALS lose their strength and the ability to move their arms, legs, and body. Muscles in the diaphragm and chest wall fail, and then patients lose the ability to breathe. In most cases the disease does not impair a person's mind, a small percentage of patients may experience problems with memory or decision-making, and there is growing evidence that some may even

develop dementia. They have emotional liability and tend to cry easily. There are no sensory symptoms.
Tests: A.L.S. patients have been shown to have immunoglobulin sub class deficiency. Low levels of IgG subclass1 & 3. Thus check for IgA levels, IgG levels and IgG-subclass levels.
Treatment:

- Many small studies have been reported where the use of **Minocycline** has shown some benefit in ALS patients. A trail of Minocycline should be given to all patients to reduce oligodendrocyte apoptosis (cell death), microglial/macrophage activation, improve functional outcome. Research studies with Minocycline and Riluzole shows benefits. Treatment with the neuroprotective drug Riluzole has previously been shown to increase the probability of survival in patients.
- If IgG-subclass levels are low then they have immune deficiency and then IVIG should be tried if available. Rarely a M.M.F. case can present and look like ALS. There is the case of a patient in Massachusetts General Hospital who has a diagnosis of ALS and improved with IVIg. We have seen another patient who had an ALS diagnosis after receiving IVIg; he was able to get out of the wheelchair. Three studies have been reported on IVIg and ALS, none of the patients improved in any of these studies.
- Stop all foods with Glutamate and increase the Magnesium in the diet. Please see the diet chapter for more information.

Chronic Lyme disease and autoimmune dysfunction: Lyme disease was first recognized in 1975 after a number of cases occurred in the same town in North America. It subsequently took its name from this town, which was called Old Lyme, in Connecticut. Lymes disease which is spread to humans by a small bug called the deer tick. This bug passes a spirochete called Treponema Pallidum to the human. Lyme borreliosis is due to infection with the spirochete Borrelia burgdorferi, and is associated with persistent infection unless treated with antibiotics. The persistent nature of infection by B. burgdorferi can lead to development of chronic autoimmune disease. Lymes transforms into multiple autoimmune conditions. Klempner did a study in chronic Lymes and found that chronic antibiotics did not change the course of chronic disease. Then NIH (National Institutes of Health) recommended that autoimmune basis of Lymes disease needs to be explored. Early cases which were treated with IVIg have had good success. A study by Recvhes showed that B. burgdorferi may share common epitopes which mimic self-proteins. Currently Borrelia antibodies have been associated with remitting relapsing Multiple sclerosis, Thyroiditis, carotid artery disease, epilepsy and arthritis.
Symptoms: Usually the first sign of Lymes infection is a circular skin rash at the point of entry. This can easily be overlooked. Followed by symptoms of tiredness, headache, joint pains, and flu-like symptoms may also occur. If not treated these symptoms may last for weeks, even months. As the disease progresses then shortness of breath, chest pains, weakness, and tingling numbness in the legs and arms starts. Some may start to notice memory problems, difficulty

concentrating and fatigue.
Treatment: Acute Lymes is an infection. If multiple organs or the nervous system are involved then Lymes is an autoimmune disease and immune suppressive treatments are required.

- Oral agents such as doxycycline or amoxicillin are successful among more than 90% of patients. The intravenous Ceftriaxone is the drug of choice for severe acute and chronic infections and especially if neurological involvement is seen. Regardless of therapeutic agent, there appears to a small minority of patients (<10%) who do not respond; such cases may be due to long-term persistence of Borrelia cysts. Austin was the first to report that Borrelia loses its infectivity at higher oxygen concentrations setting up the hyperbaric oxygen chamber treatments. Patient report that hyperbaric chambers do help cerebral and cortical symptoms.
- Steroids can also be used for immunomodulation, see the celiac diet section which should be tried in all patients.
- Chronic Lyme patient who does not show any response to antibiotics should be treated with IVIg. If there is no response to IVIg then steroids and IVIg combination can be used. In resistant cases plasmapheresis can be tried. Please see the CIDP treatment section for all treatment options.

Multiple Sclerosis: Multiple sclerosis (MS) is a chronic, autoimmune disease in which immune system attacks the Myelin covering the nerves in the brain and spinal cord. This is similar to CIDP neuropathy where the attack is against peripheral myelin. The Myelin in the Brain and spinal cord is made by cells called oligodendrocyte and in the peripheral nerves by Schwann cells.
Multiple sclerosis, can develop after exposure to (Epstein-Barr virus (EBV), Chlamydia pneumoniae, Borrelia), the body then incorrectly directs antibodies and white blood cells against the myelin sheath, which surrounds nerves in the brain and spinal cord. This causes inflammation and injury to the myelin-sheath. This damage results in multiple areas of scarring (sclerosis). Eventually, this damage can slow or block the nerve signals that control muscle coordination, strength, sensation and vision. This damage can be visualized by a M.R.I. scan as multiple white spots in the brain. There are some high risk areas in the world where the incidence of M.S. is higher. These areas include Northern United States, United Kingdom, Finland, Canada and New Zealand. The high risk areas, on the world map, lie between 45 degree North and 60 degree north. The area of the world below 45 degree south also has a higher incidence of MS. Children born in high risk areas show a higher incidence of MS. Lower amount of Sun light in the high risk areas may result in lower amount of Vitamin-D in people and animals living in these areas.
A historic study was published by workers at the Vanderbilt School of Medicine showing CSF samples from patients with relapsing-remitting MS, having increased antibodies to C-pneumoniae.
Types of M.S

- **Relapsing remitting** type of MS is seen in 90% of the cases characterized by relapses (disease flare-ups), followed by periods of remission. This is the most common type. I

have seen many cases where the patient was labeled as progressive MS only to find they had clear history of remissions and relapses.

- **Primary progressive** form of MS, which shows a gradual decline, without periods of remission. People with this form of MS are usually older than 40 when symptoms begin.
- **Secondary progressive.** About half the people with relapsing remitting MS eventually enter a stage of continuous deterioration referred to as secondary progressive MS.
- **Progressive M.S.** Progressive downhill course.

Symptoms of M.S. are:

- Numbness or weakness which typically occurs on one side of the body.
- Double vision, blurring of vision or sudden loss of vision (optic neuritis).
- Tingling numbness or pain one half of the body.
- Electric-shock sensations that occur with certain head movements
- Tremor, lack of coordination or unsteady gait and weakness.
- Fatigue specially after exposure to heat, or exercise.
- Dizziness or feeling of spinning.

Tests:

- **M.R.I.** Scan can confirm the diagnosis of M.S. which shows multiple white spots.
- **Spinal tap**: increased white cells and increased proteins with oligoclonal bands.
- CSF antibodies to ***C pneumoniae***. **Borrelia, Chlamydia, H, Pylori, Acinetobacter , Pseudomonas and Gluten.(**antgliadin antibody)
- **Plasma homocysteine** levels can be elevated. Serum calcium & vitamin D levels reduced. Serum Vitamin B-12 low, thiamine and B-6 levels may be low.

Treatment:

- **Minocycline** is a therapy for M.S it has been shown to reduce lesions on the MRI scan. Minocycline is a tetracycline antibiotic given 100 mg at night (Monday, Wednesday, and Friday). Minocycline treatment should be tried for at least two months at least to get rid of Chlamydia, Borrelia if this helps try for 2-3 months. Treat according to antibody results. Please see the antibiotic section for details on all antibiotics which will help MS.
- **Diet:** If antigliadin antibodies are present then a two to three month trail of a diet on milk, rice, meat, chicken, fish, vegetables and fruits need to be tried to se if any benefits result. Please read the diet section for more information. Vitamin-D replacement with cod liver oil benefits all patients. Vitamin B12 sublingual supplements are beneficial.
- **Methylprednisolone (Solumedrol): Is used to reduce inflammation in a new attack of M.S.** Mix 1 gram of methylprednisolone in 16 cc of sterile water and add to 150cc of 0.9% NS. Infuse over 1.5 hours. If Methylprednisolone is not available: Then use Decadron 20mg plus 50 cc of 0.9% NS. Infuse over 30 minutes.
- **Beta interferons**. Interferon beta-1b (Betaseron) and interferon beta-1a (Avonex, Rebif) are genetically engineered copies of proteins that occur naturally in the body. They help fight viral infection and regulate your immune system. Betaseron is injected under your skin (subcutaneously) every other day. Rebif is injected subcutaneously three times a

week. Avonex is self-injected into the muscle (intramuscularly) once a week. These medications reduce flare-ups of MS. Beta interferons should never be used in combination with one another. Only one of these medications should be used at a time.

- **Intravenous Immunoglobulin (IVIg)** some new studies have shown that IVIg given early in the treatment of M.S will help delay the disease onset and provide a long term remission. The dose is 500mg/kg/day for four days. Has to be repeated for 5-6 months.
- **Muscle relaxants.** Baclofen and tizanidine (Zanaflex) are oral treatments for muscle spasticity. Zanaflex appears to control muscle spasms without leaving your legs feeling weak but can be associated with drowsiness or a dry mouth.
- **Medications to reduce fatigue.** To help combat fatigue, the antiviral drug amantadine (Symmetrel) 100mg once a day has been used. B-12 sublingual tablets help fatigue.
- **Plasma exchange (plasmapheresis).** Plasma exchange help restore neurological function in people with sudden severe attacks of MS who don't respond to high doses of steroid or IVIg treatments. For a list of all other drugs please see the CIDP treatment section.

Lambert-Eaton Myasthenic Syndrome: Lambert-Eaton myasthenic syndrome (LEMS) is a paraneoplastic syndrome producing antibodies against presynaptic voltage calcium channels**.** Some of the patients have a cancer, particularly a small cell carcinoma of the lung. A search for chest cancer should, therefore, be made in patients with newly diagnosed Lambert-Eaton syndrome, and should be repeated at intervals during the first years after the onset of symptoms.
Symptoms in LEMS: The patient complains of weakness and pain, initial short increase of the muscle strength after exercise is seen followed by weakness and fatigability. The proximal muscles, especially the (thigh, pelvis, shoulders, arms) appear weak and unsteady gait are commonly observed, early in early disease. Rarely, mild degree of ptosis, weakness of facial muscles difficulty is swallowing and talking (Bulbar weakness). **Some patients can have reduced Muscle tendon reflexes, which may increase after activity or exercise**. Dysfunction of the autonomic nervous system is also common, which may be manifest as visual disorder (**blurred vision** due to impairment of accommodation in the pupil), dry mouth, sexual impotence due to erectile dysfunction or constipation are all due to autonomic dysfunction.
Test for LEMS: X-Ray chest, CT or MRI imaging scan of the chest may be supplemented by sputum analysis and bronchoscopy (all these tests are done to search for a tumor). A serum test for voltage-gated calcium channel antibodies (anti VGCA antibodies). Electrophysiological testing shows a small compound muscle action potential and improvement in size of the action potential with exercise.
Treatment in LEMS:

- Patient improves after removal of the cancer. If no improvement is seen, then immunosuppressive therapy with prednisolone and Azathioprine will usually help control symptoms. In some cases even remissions have been reported.
- IVIG and Plasmapheresis are an effective treatment for patients with severe symptoms. 4-Diaminopyridine (possibly in combination with pyridostigmine) seems to be ideally

suited for the symptomatic treatment of the Lambert-Eaton syndrome. It enhances the release of acetylcholine from the presynaptic nerve terminals.

Myasthenia Gravis: Grave means serious: Myasthenia gravis is a chronic autoimmune neuromuscular disease characterized by weakness of the voluntary (skeletal) muscles of the body. The name myasthenia gravis, means "grave muscle weakness." The hallmark of myasthenia gravis is muscle weakness that **increases during activity** and improves after of rest. Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often, involved in the disorder. The muscles that control breathing, neck movements and limb movements may also be affected when a nerve impulse travels down the nerve, a chemical neurotransmitter called acetylcholine is released in the nerve ending and travels to acetylcholine (Ach) receptors located on the muscle side of the synapse, causing the muscle to contract. Among people with myasthenia gravis, this normal impulse transmission of Ach is disrupted by autoantibodies that target the body's own Ach- receptors and block them. If enough receptors are blocked by autoantibodies, then the muscle contraction will be weak, causing the symptoms of myasthenia gravis.

Many pesticides contain organophosphorus chemicals that can inhibit the acetyl cholinesterase enzyme and make myasthenia worse. Halides (like **chlorine** and **fluorine**) may pose additional risk for myasthenia gravis patients. In one case report, a patient was exposed to chlorine gas and subsequently developed generalized myasthenia gravis). Fluoride is also implicated, and fluoridated water may trigger a myasthenia gravis crisis or contribute to long-term deterioration, with extreme exhaustion and muscle weakness, so please avoid fluoride containing toothpaste. You can make your own by using baking soda**.**

Symptoms: **Dropping eyelid** or **double vision**, are the initial symptom of myasthenia gravis in two-thirds of patients. If both the eyelids are drooping it is difficult for the physician to notice this. Difficulty chewing, swallowing, or talking, is the initial symptom in some patients, and limb weakness in rare. Initial weakness is rarely limited to single muscle groups such as neck or finger extensors or hip flexors. The severity of weakness fluctuates during the day, usually being least severe in the morning and worse as the day progresses, especially after prolonged use of affected muscles. Patients just have ocular Myasthenia, they can present with double vision.

- **Diagnosis of Myasthenia**
  Ice test. After covering the patient's eye with an icepack for a couple of minutes, the physician will look for improvement in the drooping eyelid. Any improvement may point toward a myasthenia gravis diagnosis.
- **Tensilon Test.** As acetylcholine receptors are blocked in myasthenia gravis, drugs that increase the amount of acetylcholine can be used, to test for the disease. **Edrophonium** is a fast-acting acetyl cholinesterase inhibitor that, when administered intravenously, will produce immediate and temporary relief of muscle weakness in myasthenia gravis patients by sparing existing acetylcholine. Edrophonium onsets quickly (30 seconds) and

lasts for only about five minutes. If the patient has an eyelid droop, then you give 8mg of Edrophonium, in a positive test the eyelid will rise up to its normal position.

- **Antibodies**: Antiacetylcholine receptor antibodies are detectable in the serum of about 80 percent of people with myasthenia gravis. However, they are present in only about 60 percent of people with symptoms that are confined to the eye muscles. Cases that involve swallowing (bulbar muscles) muscle specific kinase (MuSK) antibodies are seen.
- **Electrophysiological studies**. The amplitude of the **c**ompound **m**uscle **a**ction **p**otential (CMAP) obtained by **r**epetitive **n**erve **s**timulation (RNS) is normal or slightly reduced in patients without MG. The amplitude of the fourth or fifth response to a train of low frequency nerve stimuli falls at least 10% less from the initial value in myasthenic patients. This decrementing response to RNS is seen in proximal muscles, such as the facial muscles, biceps, deltoid, and trapezius than in hand muscles. A significant decrement to RNS in either a hand or shoulder muscle is found in about 60% of patients with myasthenia gravis.
- **Thymus Tests:** An X-ray of the thymus can be done to look for enlargement. A C.T scan or MRI scan can show a tumor within the thymus. Some people with myasthenia gravis suffer from some form of abnormality in the thymus gland. The thymus gland is where T-cells the chief immune cell involved in myasthenia gravis are produced. About 70 percent of people with myasthenia gravis have an enlarged thymus gland (hyperplasia), and 20 percent have (usually benign) thymic tumors called thymomas
- **Thyroid Tests:** Hyperthyroidism and hypothyroidism can be associated with increasing myasthenic weakness (Need to test TSH, T3-T4)

Treatment of Myasthenia:

- **Acetyl cholinesterase inhibitors**: These drugs work by blocking the enzyme that normally destroys acetylcholine in the synapse; this allows the existing acetylcholine more time to interact with the available receptors. (**Pyridostigmine 60mg three times** a day or neostigmine).
- **Thymectomy**: Surgical removal of the thymus gland, following a thymectomy, patients often report that symptoms lessen and, in many cases the disease disappears completely. **A new simpler way of doing Thymectomy** has been reported. CT-guided percutaneous ethanol injection is a minimally invasive alternative treatment for myasthenia gravis. 22-gauge needle is inserted into the thymus under CT guidance, and then ethanol is injected step by step until it is distributed throughout the whole thymoma, the normal thymus. The amount of ethanol injected ranges from 2 to 13 mL, with a mean of 7 Ml. Follow-up at 3-4 weeks shows that the thymus or thymoma has completely necrotized. (A 5-year follow up study showed that the condition markedly improved in 35 patients.) (AJR Am J Roentgenol. 2003 Sep; 181(3):721-4.Wang P)
- **Plasmapheresis**: Plasmapheresis separates plasma, which contains the autoantibodies, from red blood cells, which are then returned to the body. This treatment improves symptoms temporarily and is especially valuable in preparation for surgical removal of the thymus. The most common side effects are reversible hypotension (low blood pressure) and mild tremor.

- **Intravenous immunoglobulin**: High-dose intravenous human immunoglobulin (IVIg) has emerged as a therapy for various neurologic diseases, including myasthenia gravis. Studies that compared plasmapheresis and IVIg found that the improvement had a more rapid onset after plasmapheresis than after IVIg. During pregnancy only IVIg is the only drug to be used.
- **Immunosuppressants**: Please see treatment guidelines under CIDP. High-dose cyclophosphamide is an effective alternative in patients with refractory disease.

Drugs to be avoided in Myasthenia: Some of the medications reported to cause exacerbations of MG include the following:

1. **Antibiotics** – Macrolides (erythromycin, Zithromax), fluoroquinolones, amino glycosides, **tetracycline**, and chloroquine
2. **Antidysrhythmic agents** - Beta-blockers, calcium channel blockers, quinidine, lidocaine, procainamide, and trimethaphan
3. **Miscellaneous** – Diphenylhydantoin (Dilantin), Lithium, chlorpromazine, muscle relaxants, Penicillamine, levothyroxine, adrenocorticotropic hormone (ACTH), and, paradoxically, corticosteroids. Riluzole, intravenous iodinated contrast, Amitriptyline, Artane & Timolol. Avoid Fluoride in toothpaste and water.

Stiff-Person Syndrome: Stiff person syndrome (SPS) shows fluctuating muscle stiffness in the back, arms and legs. The first symptom is a persistent stiffening of the back or a limb which may is worse under stress. A sensation of aching or stiffness may be noted. This progresses with time and is described as stiffness. Additionally patients experience spasms of the involved muscles which are severe, and painful. People develop startle, a heightened sensitivity to stimuli such as noise, touch, and emotional distress. Startle, can set off muscle spasms, sudden jerking or falls. Abnormal hyperextended posture is characteristic in SPS also called the lordotic posture and rarely a flexed hunchback type posture is seen. Some SPS patients have difficulty walking and walk with small stiff, steps and tend to trip easily, loud sound can cause spasms. Many people are kept awake and in pain by dogs barking in the night. Some people arch over in an opisthotonic (backward bending attack with the head and heels touching the bed and rest of the body arched above the bed) this posture is very painful and can last hours at a time, relived by sleep. SPS affects **twice as many women** as men. It is frequently associated with other autoimmune diseases such as diabetes mellitus (DM), thyroid disease, Vitiligo, pernicious anemia, adrenal insufficiency. Glutamic-acid decarboxylase antibodies are present in one quarter of the patients. Half of the patients will become wheel chair bound, despite treatment.
Symptoms: There are painful muscle spasms and the patient is sensitive to sudden movement or stimulation. The stiffness of the muscles subsides during normal sleep.

- Constant painful muscle spasms in back, abdomen, legs arms and neck.
- Stiff-legged gait, short steps, trips easily
- Slow eye movements, Shortness of breath , muscles feel like rocks
- Hunched posture or a hyper extended posture (lumbar hyperlordosis).

- Difficulty making sudden movements, loud sounds irritate

Tests:

- Positive anti-GAD (glutamic-acid decarboxylase antibodies)
- Borrelia antibody in CSF (may be positive)
- Electromyography (EMG) - Continuous muscle unit activity at rest is prominent in the paraspinal muscles. Muscle activity disappears with diazepam and in sleep.

Misdiagnosed as: Parkinsons, multiple sclerosis, fibromyalgia, anxiety disorder.

- **Treatment**: These patients respond to Vibramycine, prednisone, Azathioprine, with long acting benzodiazepines (Ativan, clonazepam, Valium), Baclofen, Some patients show a good response **IVIG** and rarely plasmapheresis. **Physical therapy** is very important to try to stretch the joints and improve the range of motion. In those patients who show no response to any treatment an intraspinal **Baclofen pump** helps control muscle spasms. Antibiotic treatment with Minocin or doxycycline needs to be tried, as some cases can be secondary to Borrelia infections.
- SPS with Thymoma has been reported which resolved after Thymus removal.
- If you see that the usual treatments are not helping the patient then it is time try Magnesium supplement at 400 mg three times a day. Celiac diet should also be tried. See the diet section. Fish oil up to 1 gram daily with an Asprin should be used by all patients unless there are contraindications like stomach ulcers or bleeding disorders which can get worse by using Asprin.

Cramp Fasciculation Syndrome (CFS): This condition is a focal form of SPS & Myotonia. CFS is seen in young asthmatic patients. The symptoms are worse in cold weather and with exercise. Rippling type irregular movements of affected muscles are visible at rest with the naked eye; there is hypertrophy (enlargement) of the affected muscles as compared to the opposite side. The condition responds to Vibramycine 200mg twice a day for two weeks and then on alternate days for a month. Omega-3 Fatty acids are helpful and in resistant cases a course of IVIg helps. These are long term conditions requiring long term treatments, CFS is associated with other autoimmune disorders like asthma.

Sydenham Chorea. Sydenham's chorea is generally regarded as an inflammatory complication of Group-A beta hemolytic streptococcal infection, the disease is more common in females than in males and in childhood. In adolescence, the affected populations are composed almost entirely of females. Sydenham's chorea has a post-streptococcal autoimmune etiology appear to arise from targeted dysfunction of the basal ganglia. PANDAS (**p**ediatric **a**utoimmune **d**isorders **a**ssociated with **s**treptococcal **i**nfections) are the acronym applied to a subgroup of

children with obsessive-compulsive disorder or tic disorders occurring in association with streptococcal infections. Recent reports show dystonia, chorea encephalopathy, and dystonic choreoathetosis occurring as squeal of streptococcal infections.
Symptoms: After streptococcal infection, within a few months, chorea, arthritis or carditis is seen. The patient develops fast (jerky), purposeless, nonrepetitive, involuntary movements that disappear with sleep and can involve all muscles except the eye muscles. Voluntary movements are abrupt and jerky, with impaired coordination. Facial grimacing is common.
Test: Throat culture is done, anti-deoxyribonuclease B (anti-DNase B) and anti-streptolysin O (ASO) titers. Antibasal ganglia antibodies (ABGA) are associated with Sydenham's chorea and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.

Treatment of chorea:

- Benzathine penicillin G in a monthly IM injection of 1.2 million U is effective, including penicillin G 400,000 U divided bid (twice a day) or penicillin V 250 mg divided bid. Sulfadiazine, in a single oral dose of 1g/day or 500 mg/day in patients who have weight less then 50 lbs., Sulphadiazine is as effective as other oral regimens.
- To suppress inflammation aspirin or prednisone should be used. In nine patients with severe chorea and two with neuroleptic-induced Parkinsonism were treated with pulse steroids and oral prednisone for two- seven months with major improvements.
- The National Institutes of Health reported using IVIg in chorea patients with 70% reduction in the symptoms. With plasmapheresis the reduction in symptoms of chorea was 50%; with steroids 30% reduction in chorea symptoms was seen.

Parkinson has an autoimmune etiology and responds to immunomodulation: Parkinson's disease (PD) is a progressive disorder that affects nerve cells (neurons) in the brain that help controls muscle movement. This group of nerve cells located in (substantia nigra) produce dopamine, a chemical which is used for transmitting signals from brain cells to facilitate movements. By the time PD symptoms appear, 70 to 90 percent of dopamine producing cells have been destroyed. This disease is caused by diverse causes, some of which are immune mediated. Recently increased iron levels in the substantia nigra have been reported. Pesticides exposure has been associated with development of Parkinsonism. Amateur gardeners were 9 percent more likely to suffer from the disease than non-pesticide users. **Farmers were 43 percent** more likely to develop Parkinsons. **Rotenone** (pesticide) has been associated with an effect on dopamine neurons that are located in the brain stem. In rural Fairfield, Montana Parkinson's disease occurrences is much higher than the national average of 1 in 1000, at least 12 people living around the Fairfield area, with a population of 650, have contracted the disease. University of Calgary and the University of Saskatchewan tested the hypothesis that the occupational use of herbicides is associated with an increased risk for Parkinson's disease. M.P.T.P is a toxin found in synthetic street drugs and has caused Parkinsons in many prominent

music players. Recently a number of studies have also shown that **H-pylori infection is common in Parkinson** patients. Some of these cases in late stages were treated with H-pylori eradication and a U-turn of the disease was seen. In another group the treatment was stopped as they did not see improvement. A benefit in Parkinson's sufferers is that they do not get any wrinkles as they cannot smile. Several autoantibodies and disturbances in T-cell function have been found in PD, and are considered important in the pathogenesis of idiopathic PD. The autoimmune destruction of the substantia nigra input leads to a secondary loss of the dopaminergic system and hence PD. Autoimmune Parkinsons is seen following transplant surgery, after immunosuppression and following exposure to infections, with SLE. In three case reports the PD reversed with the use of IVIg treatment. Half the patients with PD have abnormal levels of anti-Fas antibodies and Anti-GAD antibodies

Causes of Parkinsonism include:

- Lacunar strokes can be vasculitis. (Inflammation)
- Encephalitis, inflammation of the brain usually triggered by infection
- Lymes disease, Epstein Barr Virus (Inflammation)
- Progressive supranuclear palsy, (eyes may not go up or down)
- Multiple systems atrophy, a disorder that destroys the nervous system
- Corticobasal degeneration, a rare neurological disease
- Chemical exposure and medications, such as some antipsychotics or MPTP
- Autoimmune diseases like SLE. (Inflammation)

Signs and symptoms of Parkinsonism include:

- Tremors at rest, pill rolling type. (Tremor disappears while eating or working)
- Flexed posture, the person is bent slightly forward, Slowed movements
- Impaired soft speech , small handwriting
- Muscle stiffness, reduced smiling, **no wrinkles** (khans sign)
- Loss of automatic movements such as blinking

Tests: There are no tests for Parkinson's disease. CT scan of the head can be done to look for strokes. H-pylori antibodies, Borrelia antibodies checked in patients to see if they are carriers of the infection. ANA and CRP can be checked specially in women to look for Lupus.

Treatment:

- **Sinemet** 25/100 three times a day and amantadine 100mg a day.
- Two girls with SLE, developed Parkinsonism, who recovered with IVIg.
- In post Viral infections induced Parkinsonism, steroids and IVIg work well. In Lymes disease associated Parkinsonism steroids are effective.
- **Doxycycline 100 mg** twice a day for two weeks and then 100mg on alternate days for a month is helpful and can be continued for three to four months.
- Omega -3 Fish oil and Flaxseed oil supplemts work well at 2000mg daily.

Parkinson Plus is a form of Parkinsons which does not respond to any treatment, we have seen a response in one patient with micro-electrical frequency and Vibramycine 100mg twice a day. If you need the micro electrical device please contact www.cidpusa.org.

Paraneoplastic Disorders: Cancer patients may develop neurological problems, many years before their cancer gets diagnosed. Paraneoplastic syndromes are a group of autoimmune disorders that are triggered by a person's immune systems response to cancerous cells. Paraneoplastic syndromes occur when cancer-fighting antibodies or white blood cells known as T cells mistakenly attack normal cells in the nervous system. These disorders typically affect middle-aged to older persons and are most common in persons with lung, ovarian, lymphatic, thymus, testicular and breast cancer. Following twelve types of syndromes are usually seen.

- **Autonomic dysfunction:** Abnormal pupil response (cannot focus), Constipation, Impotence, Orthostatic hypotension (dizzy feeling on standing up), Sweating abnormalities
- **Brainstem encephalitis:** Dizziness, spinning feeling (Vertigo), difficulty swallowing, No eye movements (Opthalmopelgia), eyes move back and forth (Oscillopsia), slurred speech (Dysarthria)
- **Cerebellar degeneration:** Dysarthria, Clumsy Gait (ataxia), jerky eyes (Nystagmus). Anti-Yo or anti-Purkinje cell antibody may be present.
- **Focal cortical encephalitis:** Depression, Anxiety, Seizures, Confusion, poor memory
- **Lambert Eaton Myasthenic Syndrome:** (LEMS) Shoulder, hip and neck weakness fatigue, Strength improves as by afternoon, Reduced or absent muscle reflexes.
- **Limbic encephalitis:** confusion, recent memory loss, depression, hallucinations, Seizures (non convulsive, PLEDS seen in EEG). Anti-Hu antibodies are present.
- **Myelitis:** Inflammation of the spinal cord causing weakness, numbness in limbs.
- **Opsoclonus/myoclonus:** Myoclonic (brief, shock-like muscle spasms), and Opsoclonus (irregular, rapid eye movements). Anti-Ri antibodies may be present.
- **Retinopathy** Night vision problems, Photosensitivity, Visual loss,
- **Sensory neuropathy:** Numbness in the feet, ankles & knees, deafness, pain similar to described under tabes-dorsalis, altered taste and smell. Anti-Hu antibodies present.
- **Morvan's chorea :** Neuromyotonia (muscle **cramps**), myokymia (muscle **twitching**), dysautonomia (**dizzy** feeling, **constipation**, and urinary incontinence), hyperhidrosis (excessive **sweating**) in chest and limbs, weight loss, impaired recent memory, anxiety, restlessness, no sleep, visual hallucinations, itching with dry skin.
- **Stiff person syndrome:** Muscle stiffness (look under Stiff person syndrome chapter for details and Antibodies directed against amphiphysin)
- **Lateral amyotrophic syndrome** (LAS) weakness in muscles and atrophy and hyperreflexia with fasciculation's (**muscle twitching**). This form of LAS differs from the

nonparaneoplastic form as **it includes sensory loss involving (loss of joint position sense or inability to feel vibration or pallesthesia). {no feeling in legs**}

Tests:

- ESR & CRP are elevated,
- Tests for paraneoplastic antibodies may show their presence (anti Hu, antiRi, GAD)
- MRI scans of chest and abdomen and endoscopies of the stomach and intestines are recommended looking for lung, abdominal, thymus tumor or breast cancer.
- Tumor markers. For example, **CEA** (carcinoembryonic antigen) is increased in patients with tumors of the breast, lung, and digestive tract, as well as in patients who are heavy smokers. On the other hand, prostate-specific antigen (**PSA**) is increased only in patients with prostatic disorders, benign (including inflammatory diseases) or malignant.

Treatment of Paraneoplastic Syndromes: Treatment with plasmapheresis, IVIG of 500mg/kg given daily for four days or steroids is initial treatment which may help control the symptoms. If a tumor is found then removal of the tumor will cure these syndromes. If autoantibodies are detected, the best drug to use may be cyclosporine. For long term use Azathioprine is effective.

Neuro-Myotonia: Isaac's syndrome or continuous muscle fiber activity syndrome:
NeuroMyotonia is a rare disorder in which continuous fine repetitive muscle movements called (myokymia) are seen. Muscle weakness can be present. Muscle relaxation may be difficult especially after physical activity involving the particular muscle. Continuous activity in the motor neurons activates the peripheral nerve fibers that activate these fine muscle movements.
Symptoms of NeuroMyotonia: Which include progressive muscle stiffness, continuous vibrating or twitching muscles, cramping, increased sweating, and delayed muscle relaxation, occurs even during sleep or when patients are under general anesthesia. Many patients develop reduced reflexes and muscle pain, but numbness is relatively uncommon. Symptoms can be limited to twitching of eyelids, facial muscle spasms. In most patients stiffness is most prominent in limb and trunk muscles, they have difficulty walking and continuous rippling in muscles of upper and lower limbs is seen. Speech and breathing may be affected if pharyngeal or laryngeal muscles are involved. Involuntary flexion of ring and little finger with associated pain in the elbows is also seen.
Tests in NeuroMyotonia: EMG test shows, Myokymic discharges in involved muscles (spontaneous firing of single motor units as doublet, triplet or multiple discharges at irregular intervals) sounds like marching soldiers. Nerve conduction study can show neuropathy. Blood counts, chemistry, thyroid profile, Rh factor need to be checked and are usually normal. CPK is raised. CSF shows elevated protein and lymphocytes. Voltage-gated K+ channel antibodies can be present.

Treatment of NeuroMyotonia: Steroids with Doxycycline are first line of treatment. Plasmapheresis, IVIg and immusuppressive drugs can be used. See guidelines in CIDP section.

Moyamoya disease (MMD): It's a rare, progressive cerebrovascular disorder caused by blocked main arteries at the base of the brain. The name "Moyamoya" means "puff of smoke" in Japanese and describes the tiny vessels formed to compensate for the blocked arteries. Patients suffer from recurrent mini strokes. MMD can occur in any age, in some patients it is associated with the antiphospholipid-antibody; in these cases if early anticoagulation or asprin treatment is given there is complete remission. MMD is also associated with Downs's syndrome.
Symptoms of Moyamoya: Visual problems, weakness, numbness and difficulty speaking, seizures and paralysis.
Tests for Moyamoya: Cerebral angiography shows the typical findings of MMD, with occlusion of both internal carotid arteries at the base of the brain, coupled with development of small new blood vessels. **Antiphospholipid antibodies** can be present**,** Vitamin B1, B6, B12, and Homocysteine levels should be checked, and vitamin levels can be low with high homocysteine levels suggesting inflammation. CRP levels are elevated showing inflammation. Protein-C and its cofactor, protein-S need to be checked as they can be low and cause excessive blood clotting.
Treatment of Moyamoya:

- Warfarin and Heparin anticoagulation helps reverse disease progression if anticardiolipin antibodies are found. A case has been reported with Mycoplasma Pneumonia infection.
- Patients with progressive disease are helped by superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis. In patients with Moyamoya disease, nicardipine has a beneficial effect on cerebral blood flow and may prevent mini strokes by increasing blood circulation in postoperative patients.

Autoimmune Migraine: Migraine affects 35 million Americans, most of whom are women. Migraine is preceded or accompanied by a sensory warning signs called a (aura), such as flashes of light, blind spots, smell or tingling in your arm or leg. A migraine headache can follow with signs and symptoms, such as nausea, vomiting and sensitivity to light and sound. Migraine pain is usually throbbing and can last for hours or even days.
Inflammatory markers go up rapidly in an attack of Migraines, CRP is elevated, the spinal fluid protein becomes elevated and more white cells are seen in the spinal fluid during a migraine attack. Migraine and epileptic seizure disorders are interrelated and like other autoimmune diseases migraines happen more in women. There may be associated epilepsy with migraine. Migraine often comes in remissions and relapses just like autoimmune disease. Migraine is associated with women just like autoimmune disorders. Some women with Takayasu-disease "pulseless disease" and Lupus present with migraine, as their first symptom. Following anti-inflammatory treatment their migraine attacks usually resolve. Many patients with lupus present with migraines secondary to severe vasospasm. These patients have anti-phospholipids

antibodies and at times the migraine will only respond to steroids or cyclophosphamide. MRI scans obtained during a migraine have shown dramatic thickening of brain folds called (gyral) with enhancement which suggests inflammation.

General symptoms of Migraine:

- One sided throbbing head pain which worsens with physical movement.
- Nausea, Vomiting
- Twisted shining lines in front of the eye sometimes without a headache.
- Weakness or numbness in a hand or leg
- **Sensitivity to light** (Photosensitive headaches respond to magnesium)
- Sensitivity to sound, smell, and light, (patients prefers a dark room)

Tests: CRP or E.S.R. can be elevated. Magnesium levels, B6, B1, B12, Folic acid levels. Anti nuclear antibodies and antiphospholipid antibodies are checked to look for lupus.

Treatment:

- Prednisone 100mg I/V is given in severe cases, oral treatment from 40 mg a day can be started and tapered over two weeks. In resistant case cyclophosphamide pulses are used.
- **Take magnesium supplements total of 400 mg twice a day, and one vitamin B-complex sub lingual formula, to reduce inflammation.**
- If the migraine is related to sleep cycles or photophobia add **Melatonin** at 6mg 30 minutes before bedtime daily to help stop the pain cycle
- All the patients need to be on one **asprin** tablet a day helps control thrombosis associated with anticardiolipin syndrome. In difficult patients coumadine or heparin can be used and both of these will control the headaches also.
- In cluster headache patients one cc of lidocaine placed in the nose on cotton wool will stop the headache. Oxygen inhalations will also stop an attack.
- Other drugs that are used for migraine are propranolol, timolol, amitriptyline (avoid in autoimmune patients), sodium valproate, and lisinopril, atenolol, metoprolol, nadolol, fluoxetine, magnesium, vitamin B2 (riboflavin), coenzyme Q10, and hormone therapy. Colostrum supplement and
- External electrical stimulator (PULSER) are very useful in stopping migraine , if you need these please contact us at www.cidpusa.org

Autoimmune Cluster Headache: Cluster headache is usually seen in men from ages 20-50. The headache tends to occur usually at the same time of the day/night as it is tied to the biological clock. The biological clock is a pacemaking mechanism in mammalian brain that controls circadian rhythms (Latin *circa "**diem***, 1 day"), which are endogenous daily cycles. Dampening of secretory circadian rhythms has been shown after using melatonin, cortisol,

testosterone, endorphin, and prolactin during bouts of cluster headaches; most of these rhythms revert to normal during remissions. The headache happens in a cluster of days with pain free interval lasting months. These headaches are associated with autoimmune diseases and anticardiolipin antibodies have been found in these patients.
Symptoms of Cluster: Swelling of the eye, redness, sweating on one side of the face, nasal stuffiness and severe pain the eye or head, usually lasts a few hours. Pain occurs in a cluster of days, happening every day at the same time.
Tests for Cluster: antiphospholipid antibodies can be present, E.S.R. can be elevated.
Treatment of Cluster headache: Is the same as migraine headaches described above.

Autoimmune Disc Herniation (ADH) & Sciatica: Spinal discs are cushioning material located between each of the vertebrae. The vertebrae are the interlocking bones in the spine that are stacked on top of each other. The discs act as shock absorbers for the spine and allow it to flex, bend, and twist. There are many different terms used to describe spinal disc pathology and associated pain, such as, herniated disc, pinched nerve, or bulging disc. These conditions can result from autoimmune sciatica (AS). The presence of glycosphingolipid antibodies in patients with sciatica and disc herniation suggests an activation of the immune system; which suggests an inflammatory process as the cause of sciatica. Usually injuries are associated with herniation, however in recent studies patients developed back and neck problems without any injury. Patients had multiple disc lesions, associated with spondylodiscitis (inflammation in disc space). None of these cases had a history of even a minor trauma. Prognosis was good with conservative treatment including NSAID (nonsteroidal anti-inflammatory medications, example aspirin), rest, and physical therapy. Biopsy suggested inflammation as the main etiologic factor.

Increased levels of circulating antibodies against one or more glycosphingolipids were detected in **70% of patients with acute sciatica**. **In 50% of the patients undergoing surgery** glycosphingolipids antibodies were seen. During a new attack of pain in sciatica patients, positive neurologic findings were associated with increased levels of these antibodies.
In patients suffering from herniation-induced sciatica, a single infusion of 3 mg/kg of infliximab resolved all symptoms for over a 1-year follow-up period. Furthermore, infliximab does not seem to interfere with the spontaneous resorption of disc herniations.

Symptoms of ADH:

- Pain from neck or back going down the extremity, pain is reduced when lying down.
- Without any history of trauma.
- Numbness and weakness in the extremity.
- Coughing and sneezing aggravates the symptoms.
- Some people may have difficulty in controlling their urine.

Tests for ADH:

- MRI scan of the neck/back will show disc herniation,

- E.S.R. is elevated; anti-glycosphingolipid autoantibodies (anti-GM1) may be present.
- Infection is ruled out as a cause by blood tests.

Treatment of ADH: Treatment should be conservative with rest in all cases of autoimmune sciatica without any need for surgery. Primary drug should be ciprofloxacin taken at 500mg twice a day for two weeks and then once a day for two weeks. If the pain continues then it can be taken on alternate days Monday, Wednesday and Friday for an extra two to three weeks. Anti-inflammatory drugs can be used either omega-3 fatty acids at 2-3 gram a day. High dose pulse steroids, NSAID or other immunomodulatory drugs can be used. Intramuscular 100 mg of steroids are also helpful and can be slowly tapered over two weeks. Please see the list of drugs under the CIDP treatment section. Back surgery can be avoided in these patients and disc swelling will resolve completely with time.

Narcolepsy: Narcolepsy is a disorder characterized by excessive daytime sleepiness. It is caused by the progressive loss of protein called hypocretin present in the brain neurons. Hypocretin neuronal cell bodies are located exclusively in the **lateral hypothalamus**, hypocretin peptides called orexin-A and B appear to affect feeding behavior, energy expenditure, arousal, autonomic outflow, which besides regulating body weight also controls water balance, body temperature and a variety of neuroendocrine pituitary functions. An autoimmune process targets hypocretin neurons in response to yet unknown environmental factor. Narcolepsy consists of three main symptoms:

- **Cataplexy** (laughter, anger causing the person to **collapse**),
- **Hypnagogic hallucinations** (vivid hallucinations during sleeping or awakening),
- **Sleep paralysis** (person wakes up from sleep but cannot move any muscles).

Cataplexy is the loss of skeletal muscle tone without any loss of consciousness. The cataplectic attacks are triggered by laughter; embarrassment, anger, athletic exertion or sexual intercourse. During the attack the body becomes limp but the person is awake.
Sleep paralysis is an inability to move when falling asleep or awakening. Normal patients experience sleep paralysis in the second decade of life for a few times. Sleep paralysis is a daily occurrence for narcoleptics; usually the feeling in sleep paralysis is that a demon is holding the person so that they cannot move. Hypnagogic hallucinations are dreamlike experiences while the person is awake. Examples are a patient saw an airplane land in the middle of a desert, another one saw a bus accident while driving when he stopped his car the road was all clear.
Another symptom of narcolepsy is persistent daytime sleepiness. The narcoleptics fall asleep at inappropriate times, such as driving or flying a plane. Untreated, they are at high risk for motor vehicle accidents and often have trouble at school and the workplace.

Test for narcolepsy: The disease is tested by a sleep test called (MSLT) Multiple sleep latency tests. The test measures the time a person takes to enter the dreaming stages of sleep called REM-sleep. Narcolepsy patients show a short time (latency) to enter REM stage of sleep.
REM means **R**apid **E**ye **M**ovements, which only occur while dreaming in deep stages of sleep.
Treatment for narcolepsy: Treatments include stimulants for reducing daytime sleep, with the recent widespread use of **modafinil**, **antidepressants** are used for cataplexy, and gamma-hydroxybutyrate for both symptoms. Recently intravenous immunoglobulins appear an effective

treatment of cataplexy if applied at early stages of narcolepsy. Prednisone is also effective in treating all the symptoms of narcolepsy. Finally, the discovery of hypocretin deficiency can be addressed with appropriate supplements in the future. Omega -3 fatty acids taken at a dose of 2-3 grams a day in the diet are helpful.

Restless Leg Syndrome:

People with restless leg syndrome, or RLS, have a creepy-crawly feeling in their legs. This causes an irresistible urge to move the legs. It's a major cause of sleep loss, as the symptoms are most likely to occur at night. It has been found that brain cells need iron. They get it from transport molecules that carry iron from the blood. Normal brain cells have doorways that let these transport molecules into the cell. Patients with restless leg syndrome lacked these portals, known as transferrin receptors. This means inspite of adequate amounts of iron in the blood not enough of it can enter the brain to prevent molecular damage.
Previous studies have shown that bacterial overgrowth in the small intestine causes inflammatory cells to increase production of IL-6. This cytokine, in turn, is known to boost levels of hepcidin, a protein that decreases iron absorption and transport. Bacterial overgrowth in the gut could be causing the problems and antibiotic therapy targeting the small intestine might be the solution. RLS behaves differently from other autoimmune diseases, as this condition will increase during pregnancy. RLS is seen commonly, in patients with Fibromyalgia and Irritable Bowel syndrome.

Diagnosis: People who cannot sleep at night due to continuous movements in the legs and odd sensations in the legs. They will often say “I have cramps in my legs”.

Tests: This condition can easily be diagnosed clinically.

Treatment: Any antibiotic which reduces bacterial overgrowth in the intestines will help reduce the symptoms of RLS. A researcher has used a 10-day course of rifaximin (1,200 mg/day), which specifically destroys bacterial overgrowth in the small intestine. Burning type pain associated with RLS can be taken care of by using a course of Ciprofloaxcillin 500mg twice a day for two weeks and then reduce to once a day for the third week and on alternate days for the fourth week.

Central Pontine Myelinolysis: Central pontine myelinolysis (CPM) is a disease affecting the stalk of the brain called Pons. All the neural impulses coming from both sides of the brain to move the legs, arms and body pass through the Pons. In CPM the myelin covering in the pons is destroyed, often associated with demyelination of other areas of the brain. Sometimes the term 'osmotic demyelinization syndrome' is used for pontine and extrapontine myelinolysis. CPM is seen in post transplant cases and autoimmune disorders like SLE, Sjogrens and Porphyria. Chronic alcoholism is a common underlying condition of CPM. In one case report complete reversal of CPM was reported after avoiding alcohol. CPM commonly occurs after the rapid correction of serum hyponatremia (low sodium). CPM is seen in liver transplant patients where the development of CPM is wrongly attributed to the immunosuppressive agent cyclosporine.

Symptoms of CPM: Paralysis is all extremities are usually seen. Also termed man in barrel syndrome as the arms and legs are paralyzed, the person can only move their **eyes**. They also

have head and neck weakness, dysphagia (difficulty swallowing), and dysarthria. (Slurred speech). Sensation is usually intact.

Treatment of CPM: Two cases have been reported where IVIg use led to improvement. In other cases use of steroids has helped reverse the disease. I would also recommend the use of Doxycycline and Omega -3 fatty acids 2-3 grams daily.

Autoimmune Stroke & Transient Ischemic Attacks (TIA): The American Heart Association and the Centers for Disease Control and Prevention recently published a joint scientific statement about using inflammatory markers in clinical and public health practice. This statement was developed after systematically reviewing the evidence of association between inflammatory markers (mainly CRP) and coronary heart disease and stroke. Both of these organizations have admitted to an association between **infections and inflammation**. Infections have long been recognized as a cause of vascular brain disease. Currently, there has been renewed interest in the possibility that common infections may participate in the atherosclerotic process or lead to stroke through autoimmune mechanisms. Specific organisms that have been implicated include **Chlamydia pneumoniae**, herpes viruses, human immunodeficiency virus, and **Helicobacter pylori**. **FHAT** trial showed an association of *h-pylori* infection with ischemic stroke. Commonly many patients have no risk factors such as smoking, hypertension or high cholesterol yet they have ischemic brain disease. The Northern Manhattan Stroke Study "N.M.S.S." showed an association between C-pneumoniae (C-p) and first stroke in multi-ethnic population. Ischemic inflammatory stoke is commonly seen in younger patients. The elevated inflammation can easily be measured by doing a CRP test. Antibodies to C-p IgG and IgA were measured in the N.M.S.S. study; they found elevated IgA antibodies to C-p after the stroke. Another study done in London reported 80 % of their stroke patients were positive for IgA antibodies to Mycoplasma Pneumonia. **These findings help to simplify prevention of a stroke before it happens.** C-pneumonia positive patients need treatment with Minocin or Vibramycine.

Tests for stroke risk:

- Screening with IgA and IgG antibodies against *C pneumoniae*.
- Test all patients either with **E.S.R.** or **CRP** test to see if they are elevated.
- Plasma homocysteine levels to see if the are elevated.

Treatment to target the source of inflammation in cholesterol: If CRP, E.S.R. and IgA antibodies against C-p are elevated antibiotic should be used to lower the CRP value.

- If H-pylori antibodies are found in the patient then triple combination should be used. **Azithromycin** (500 mg once daily), **metronidazole** (400 mg twice daily), and **Amoxicillin** (500 mg twice daily) for two weeks. Along with a lacto vegetarian diet, high fluid intake with milk, green tea and water, reduced carbohydrates are recommended.

- Use Vibramycine 100mg twice a day for two weeks in all other patients, then 100mg daily for two weeks. Treatment then can be continued for alternate days for a month.
- For the long term use Fish oil up to 2 gram daily with an **Aspirin** 32mg daily by all patients unless aspirin is contraindications in stomach ulcers or bleeding disorders.
- If homocysteine levels are elevated then treat with vitamin **B12**, B6 and Folic acid supplements taken sublingually or intramuscular injections.
- Please see whipples disease and Celiac disease chapters.

Chapter 7 Cardiovascular Autoimmune Diseases: Evidence suggests that the leading cause of death in the world is due to infections that common antibiotics can be used to control. In the following section I have not described **celiac disease myocarditis**, which accounts for less then 2% of the reported cases. However it is a treatable condition and antgliadin antibodies can be checked in patients who are unresponsive to conventional treatments. These patents respond to dietary management and short term steroids, diet guidelines are in the Celiac disease section.

Kawasaki disease and acute rheumatic fever are the two leading causes of acquired heart disease in children. Rarely adults will be affected. Reoccurrence can happen in later life. Children with Kawasaki disease are between the ages of 5-8 Majority of the patients affected are of Asian decedent. But it can occur in every racial and ethnic group. Over 4,000 cases of Kawasaki disease are being diagnosed annually in the United States. Less than 1 percent of those who get Kawasaki will die. **Yersinia pseudotuberculosis** (Y-p) infection has been reported in many patients with Kawasaki from Japan, which is easily treatable. Y-p is a Gram-negative coccobacillus and a primary pathogen of wild and domestic animals and birds in the tropics. In the human, Yersinia-p causes varying degrees of illnesses from diarrhea and abdominal pain to fever, red colored (scarlatiniform) skin rash, red inflamed eye (conjunctivitis), red bumps on the shin (erythema nodosum) , and swelling of lymph nodes (lymphadenopathy). The clinical findings described above are similar to Kawasaki disease presentation. Yersinia-p triggered reactive arthritis, eye inflammation, coronary aneurysms, and acute renal failure are an autoimmune response.

Treatment with **ampicillin and tetracycline** is usually effective if stool cultures are positive for the infection. This infection is generally seen in Japan among children exposed to non treated water. The antibiotic will not help the arthritis or Vasculitis for which immunomodulatory treatments are recommended. Part of a coronary artery wall can be weakened and bulge forming an aneurysm. A blood clot can form in this weakened area and block the artery, sometimes leading to a heart attack. Usually all the heart problems go away in five or six weeks, and there's no lasting damage with treatment.

The **symptoms** of Kawasaki disease are,

- Fever
- Red Rash all over the body
- Peeling skin and swollen red hands and feet
- Red Eyes
- Swollen lymph glands in the neck
- Inflammation of the mouth, lips and throat

Diagnosis is made by elevated CRP and **sedimentation rate** with classic clinical findings. Yersinia pseudotuberculosis antibodies can be tested is the stool samples.

Treatment: IVIG is the gold standard, if IVIg is not available use steroids 1mg/kg daily and aspirin combination is used. Omega-3 fatty acids at one gram daily will also help reduce inflammation

- 2g/kg Intravenous gamma globulin **IVIg** dose given as a single infusion can decrease the risk of developing coronary artery abnormalities when given early in the illness
- Cases not responding to IVIg get prednisone plus aspirin and IVIg for a second time.
- Several studies have shown successful treatment with high dose **aspirin** and **prednisone**.
- Aspirin is used to reduce fever, rash, joint inflammation and pain, and to prevent blood clots from forming. Omega- 3 fatty acids and Vitamins can help reduce inflammation.
- Vibramycine or Ampicillin used twice daily for two weeks in cases where positive stool cultures to Yersenia are seen.

Autoimmune Myocarditis:

Introduction to autoimmune Myocarditis: Heart failure is caused by **Cardiomyopathy** (**enlargement of the heart muscles**). The heart walls (muscles) become big and large in size and weak which cause difficulty in pumping blood. Reduced cardiac pumping, results in congestion of blood within lungs and swelling of the feet. Cardiomyopathy is usually triggered by a viral infection mainly C.M.V. (Cyto Megalo Virus). In the past these patients with cardiomyopathy have been treated with cardiac transplantation. A single heart transplant, costs anywhere from one to four million dollars. Patients generally do not improve after a cardiac transplant and most will die within the first year of the transplant. Survivors of transplants develop autoimmune diseases which go unrecognized, they can also have immunodeficiency and cancers. In the last ten years multiple studies have been done which have shown that cardiac transplants can be avoided in the cardiomyopathy patients, and they can easily be treated simply with IVIG or antibiotics. In one study ten patients were treated with IVIG who had end stage cardiac failure. One patient died before the completion of the study but nine others walked out of the hospital after completing IVIg treatment. A year after the treatment they were still doing well. In another study done in Japan nine patients suffering from Cardiomyopathy were treated with IVIg at a dose of 2g/kg. All of them improved and were doing well even four years after the treatment was given. C-reactive protein was measured before and after IVIg treatment and went down considerably with treatment.

Lymes disease results from exposure to Borrelia burgdorferi causes dilated **cardiomyopathy which promptly resolves after antibiotic treatment**. Serological tests for Lyme Borreliosis are positive in 26% of Cardiomyopathy patients. **Cardiomyopathy has disappeared after high-doses of penicillin therapy.**

Following are some subtypes of Myocarditis based upon etiology

A)-Rheumatic Autoimmune Myocarditis: Acute Myocarditis is seen in autoimmune disease. Patients with Rheumatic fever usually present after dental or tonsillar surgery, with shortness of breath, swelling of joints and elevated **a**nti-**s**trept**o**lysin titer (ASO). The cardiac enzymes are elevated and ECG is abnormal. Cardiomyopathy responds promptly to intravenous antibiotics.

An interesting case was reported of a 38 year old ICU nurse who presented with acute myopericarditis, mimicking a new heart attack, confirmed by abnormal E.C.G. and elevated cardiac enzymes, group A beta-hemolytic streptococcal tonsillitis was noted. **After receiving oral penicillin, the clinical recovery was complete, fever, chest discomfort resolved within a few days of treatment. Furthermore, enzyme levels and C-reactive protein returned to normal within eight days.**
Rheumatic fever affects the heart usually involves all three layers endocardium, myocardium, and pericardium to varying degrees. Rheumatic myocarditis does not cause any severe valvular damage in the initial attacks, in chronic untreated disease severe mitral valve and aortic valve failure with regurgitation (blood leaking from insufficient valve closure) may be seen. The main cause of cardiac failure is left ventricular dysfunction resulting from myocarditis in rheumatic fever. Aschoff-nodules are cells seen under the microscope which are a hallmark of rheumatic fever, and have been seen in left side of the heart chambers.

Symptoms: Tiredness, shortness of breath, fatigue, coughing and blue discoloration of face and hands. Swelling of the feet may be visible.
Tests:

- Blood test for ASO titer which is elevated,
- Echocardiogram of the heart to check the valves and the left ventricle for damage.
- CRP and SED rate are elevated showing inflammation.

Treatment:

- Penicillin (either oral penicillin V or injectable Benzathine penicillin) remains the treatment of choice, because it is cost effective, and has long-standing proven efficacy.
- Macrolides (clindamycin), oral cephalosporin's ,
- Oral amoxicillin is mainly used for penicillin-allergic patients; alternatives are clindamycin, Azithromycin, or Clarithromycin.

Patients with autoimmune diseases need antibiotics before they have dental or medical procedures. These are as follows.

- Prosthetic cardiac valves, Previous bacterial endocarditis
- Complex cyanotic congenital heart disease

- Surgically constructed systemic-pulmonary shunts or conduits
- Congenital cardiac defects
- Acquired valvular dysfunction (e.g., rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvular regurgitation and/or thickened leaflets1

B- Chronic Lyme Myocarditis is the least well documented complication of Lyme disease. Cardiac involvement usually occurs within weeks of the infecting tick bite and includes varying degrees of atrioventricular block (impaired electrical activity in the heart) as the commonest manifestation and tachyarrhythmia's (fast heartbeat) and myopericarditis (heart muscle dysfunction). There has been evidence that cardiomyopathy is associated with long term Borrelia burgdorferi infection. Patients with **atrioventricular block** have good prognosis and this is the leading presentation in Lymes Carditis. **Progressive arrhythmia** (increase in irregular heartbeat) and heart failure combined with neurological symptoms (weakness, confusion, & numbness) are common presentations of Lymes disease; most cases are confirmed by positive antibodies to Borrelia. Transient atrioventricular block (irregular heart beat) is the most frequent manifestation of Lyme carditis, sometimes there is complete atrioventricular block which means that electrical impulses from the small chambers do not proceed to the big chambers of the heart.
Symptoms:

- Shortness of breath with activity (exertional dyspnea).
- Rapid heart beats (palpitations).
- Dizziness and tendency to lose consciousness (syncope).
- Repeated attacks of passing out spells and falls with irregular heart beats.

Test:

- Blood test done to check for Lyme antibodies.
- EKG shows irregular rhythm, or blocked AV conduction of the heart.
- ECHO & CT scan, X-RAY of heart will all show cardiac enlargement.

Treatment: There is no need to place permanent pacemakers for Lyme carditis.

- Antibiotic treatment with **intravenous doxycycline** results in **complete remission** of all cardiological symptoms. Continue 100mg alternate day oral treatment for 6 months.
- According to the severity of the disorder, antibiotics are administered orally (penicillin or derivatives) or parenterally with penicillin or cephalosporin's. Standard antibiotic treatment with intravenous Ceftriaxone 2 g twice a day for 14 days.
- Fish oil up to 2 gram daily with an Aspirin 32 mg should be used by all patients unless there are stomach ulcers or bleeding disorders which can get worse by using Asprin.

C- Autoimmune Viral Myocarditis caused by, **(**Human Parvovirus B19, Varicella Zoster, Coxsackie, Influenza-A, Hepatitis-C and Epstein-Barr virus)**:** Viral Myocarditis can occur in children or adults and usually causes chest pain and fever, with heart failure. These patients have a recent history of viral illness and there is no past history of cardiac failure.

Influenza Myocarditis history: Influenza-A virus is well known for its capability for genetic changes. As we trace backwards through history of influenza pandemics, a repeating pattern can be observed**, usually a limited wave of infections in the first year followed by global spread in the following year.** In the 20th century alone, there were three overwhelming pandemics, in **1918**, **1957** and **1968**. During the pandemics high mortality was seen in infants, elderly and sick. **In 1918, there was one distinct peak of excess death in young adults aged between 20 and 40 years old.** Autopsies show multiple-organ involvement, including pericarditis, Myocarditis, hepatitis and splenomegaly. Influenza Myocarditis is an autoimmune disease due to multi organ involvement. Influenza will strike again we need to be prepared to stop autoimmune reactions. The answer will be silver colloid, **cod-liver oil** or electronic pulsars. Contact us to obtain these electronic pulsars which kill organism by electrons to which no bugs can get immunity.

Tests for Viral Myocarditis:

- ECG shows elevation of the S & T waves suggesting a heart attack pattern.
- Creatine kinase (CPK) is elevated suggesting heart attack or varicella infection.
- The left side of the heart is enlarged and left ventricular pump volume or ejection fraction is globally reduced by 45%.
- Myocarditis is confirmed by a biopsy showing lymphocytic inflammatory cells.
- CRP & Sed rate are elevated showing inflammation.

Treatment

- Acyclovir, or Valacyclovir 1-gram three times daily as a antiviral
- Prednisone and Azithromycin for 6 months for immunosuppression.
- IVIg or varicella hyperimmunoglobulins.
- Early treatment can avoid a transplant.
- Omega-3 oils, cod liver oil, curcumin will reduce inflammation
- Aspirin used daily. During one to two months the patient recovery is usually complete

D-) Giant cell Myocarditis (GCM) the most fatal Disease: GCM is a rare, **frequently fatal** inflammatory disorder of cardiac muscle. It occurs in children, teenagers and adults after flu like illness. There maybe an association of GCM in Myasthenia gravis and malignant thymoma developing after patients are placed on immunosuppressive treatment, or after thymoma surgery. Rarely SLE patients may develop GCM in the course of their treatment. **Majority of the people getting this disease are healthy**. **There has been a high mortality reported in this disorder of 90% with and without heart transplant**. **It can reoccur in transplanted heart tissue.** IVIg treatments have not been reported in this disease. **Double vision with orbital Myositis can be an early presentation with GCM.**

Symptoms of GCM:

- Most present with shortness of breath,
- Irregular heart beats, chest pain.
- **Eyes, swelling up and bulge due to Myositis a week before the heart gets involved**.

Test: Erythrocyte sedimentation rate usually 100-108 mm/h at the first hour. C-reactive protein elevated 150 mg/L (normal value, < 5 mg/L. **In early stages the Cardiac ECHO and angiogram can be normal. The tests can rapidly become abnormal within a day**. The biopsy will show classic inflammation and giant cells (extensive inflammatory infiltrates mainly represented by lymphocytes, histiocytes, eosinophils, and multinucleated giant cells).

Treatment of GCM:

- IV prednisolone, **7 mg/kg for 3 days**, followed by1.5 mg/kg/d orally for 2 weeks. This is reduced to 1 mg/kg/d for 4 weeks. Then prednisone is reduced to 0.33 mg/kg/d and **Azathioprine, 2 mg/kg/d** is started. After 6 months, steroids tapered and withdrawn. Azathioprine from the sixth month was reduced to 1 mg/kg/d. At 16 months of follow-up, the patient should receive maintenance low doses of Azathioprine.
- Two cases have been reported one of a teenage girl and a boy who **developed GCM while on IVIg treatment for Guillian Barre Syndrome. Both cases responded to Azathioprine and steroids. Also use Omega-3 oils, aspirin, curcumin and honey.**

E-) Autoimmune Myocarditis in Athletes-**There is an increased incidence of deaths in athletes due to Myocarditis:** The athlete represents the healthiest segment of our society. Yet, there are still reports of sudden death in athletes occurring while on the athletic field. Any athlete who 'goes to the ground' temporarily (syncope), should be treated for myocarditis. Myocarditis should be suspected in athletes with unexplained cardiac arrhythmias (irregular heartbeat) and dysfunction, especially after a flu-like illness. An early diagnosis is desirable in order to avoid the risk of fatal consequences, since physical activity can enhance the inflammatory process. In the presence of life-threatening arrhythmias or rapidly progressive cardiac dysfunction an antiviral or an immunosuppressive treatment should be considered depending on whether a viral agent is present or absent, respectively, in the myocardium.

Symptoms:

- **Some athletes have no symptoms**,
- Some complained of nausea and vomiting, dizziness, weakness, stomach pain.
- Shortness of breath (dyspnea), Backache and awareness of fast heat beats (palpitation).
- Chest pain with activity (angina pectoris symptoms), nausea. .

Tests:

- Cardiac enzymes (CPK) are elevated. ESR and CRP are elevated.
- ECG, stress ECG, echocardiography and stress-echocardiography are abnormal.
- Endomyocardial biopsy showing inflammation is still the gold standard TEST.

Treatment:

- Athletes recovering from acute myocarditis should abstain from moderate exercise. **Rest is the most effective strategies in myocarditis management**. **Athletes need to be on a normal fat diet.** Good hydration and use Cod-liver oil as an anti inflammatory.

- Physical exercise is contraindicated in acute respiratory infection. Athletes with myocarditis should **be withdrawn from all competitive sports for at least 6 months** and resume training when ventricular function and cardiac dimensions return to normal and the clinically relevant arrhythmias disappear.

- Preventive medical examinations are essential, especially in athletes before physical exercise, as are other investigations in every case suspicious of heart disease, including electrocardiogram (ECG), stress ECG, echocardiography and stress-echocardiography. To prevent Myocarditis use omega-3 oils, cod liver oil supplements, see diet section.

Autoimmune Atherosclerosis: In the April 15, 2005 issue of Clinical Infectious Diseases, a study was reported showing a link between **Chlamydia pneumoniae (Cp)** and Heart Attacks, in young people. Researchers in Wisconsin and Maryland conducted a study of young men in the military to determine whether there was a link between Cp infection and heart attack (myocardial infarction). They examined the blood of 600 men in this study. Among them 300 men between the ages of 30 and 50 years old had previously been hospitalized for a heart attack. Because the subjects were in the military, the researchers could examine blood samples that were collected and stored in the Department of Defense's serum repository before the men had their heart attacks. They found that high levels of Cp antibodies in blood were associated with the occurrence of heart attack. This association was particularly strong in blood collected one to five years before the men's first heart attacks.

Today evidence supports an autoimmune mechanism as one of the prime pathogenic processes involved in the development of atherosclerosis and heart attack. About 50% of people having myocardial infarction (MI) or strokes are not exposed to any of the risk factors like lipids and smoking. Yet these individuals with no risk factors go on to develop arteriosclerosis. Many viruses, bacteria and even parasites are claimed to affect plaque deposition. Among them, Chlamydia pneumoniae probably has the strongest association with atherosclerosis.

Recently several viruses, including herpes simplex, cytomegalovirus, and coxsackie B virus, have been implicated in heart disease. **Chlamydia pneumoniae (Cp)** is among the new emerging infections which have been linked to atherosclerosis.

Cp usually causes respiratory conditions that can progresses to pneumonia. Chances are most of us are already carrying this bug. Anti Chlamydia antibodies are found in people all over the world. Cp makes its way into the walls of various blood vessels, where it induces the inflammation and immune reaction that causes heart attacks and strokes.

Seroepidemiologic studies have associated *Cp* antibody with heart diseases and stroke. The association of *Cp* with atherosclerosis is corroborated by the presence of the organism in **atherosclerotic lesions throughout the blood vessels** and the **near absence of the organism in healthy arterial tissue.** *Cp* has also been isolated from heart and neck plaques.

American heart Association and Centers for Disease Control have issued joint statements stating that low level inflammation caused by, **Chlamydia pneumoniae & Helicobacter pylori**, **are possible causes of heart disease and stroke**. There are more then two hundred reported studies showing the relationship of C-Pneumonia to Atherosclerosis. Many studies tried treating these patients with a single antibiotic, some succeeded but majority did not. The answer is simple; we need a combination of antibiotics as there are multiple microorganisms involved, this was successfully done in the study reported below.

For treatment of Cardiac problems and autoimmune arteriosclerosis it is recommended that **Doxycycline, erythromycin or ciprofloxacin** be used, in those patients who have elevated **CRP** or those who are positive for Chlamydia antibodies.

In a (randomized) study, 88 heart patients were treated with **Azithromycin 500 mg per day** for 2 days after that the dose was reduced to **250 mg** per day for **28 days**. After 6 months, those patients receiving Azithromycin had lower incidence of both angiographically confirmed restenosis and recurrent angina than those on placebo, (Circulation 1998; 97:1669-70).

In another large study which looked at infections with Helicobacter pylori and Chlamydia pneumoniae, in associated with coronary heart disease. This study was named the **S**outh **T**hames trial of **A**ntibiotics in **M**yocardial **I**nfarction and unstable **A**ngina (STAMINA). There were three groups in this study, and two groups on multiple antibiotic combinations. Within twelve weeks of starting antibiotic treatment C-reactive protein levels were reduced, with 36% reduction in death and Myocardial Infarction was noted. This reduction in inflammation persisted during the first year of follow up in the antibiotic treated group. Neither C-pneumoniae nor H-pylori antibody status was related to response in treatment. Antibiotic treatment significantly reduced adverse cardiac events in patients with acute coronary syndromes, but the effect was independent of H-pylori or C-pneumoniae seropositivity. The antibiotic combination used were **amoxicillin** (500 mg twice daily), **metronidazole** (400 mg twice daily), and **omeprazole** (20 mg twice daily). Second group used **Azithromycin** (500 mg once daily), **metronidazole** (400 mg twice daily), and **omeprazole** (20 mg twice daily). (Circulation. 2002 Sep 3;106(10):1219-23. Stone AF)

The STAMINA study shows two important observations, the H-pylori & C-pneumoniae antibodies were associated with inflammation, within the blood vessels which responded to antibiotics with reduced Cardiac events in antibiotic treated patients. The antibody levels against bacteria did not change which makes one wonder if long term antibiotic treatment is needed. Intravenous immunoglobulin (IVIg) therapy leads to a 40% reduction in the extent of plaque formation. It is likely that IVIg acts in part through anti-idiotypic antibodies. The role played by IVIg confirms the issue that with any antibiotic treatment we need to combine an anti-

inflammatory treatment.
Many other studies looking at causes of inflammatory heart disease have also found a relationship between elevated homocysteine levels and heart disease.
Conclusion: A causative role of ***C- pneumoniae*** infection in cardiovascular disease has been observed. The high frequency of infection found in human atherosclerotic tissue in comparison to normal tissue, the induction and progression of atherosclerotic like inflammation and the early results from antichlamydial intervention studies in humans are consistent with a causative role of ***C- pneumoniae*** in the disease process.

Testing for autoimmune atherosclerosis:

- **Check the CRP (if it is high then use an antibiotic).**
- **Antibodies to *C.-pneumoniae* & H-pylori**
- **Check homocysteine** levels (I do not check these levels but just treat with vitamins).

Treatment to target the source of inflammation in cholesterol:

- If the CRP is elevated then they need to be given **Azithromycin** (500 mg once daily), **metronidazole** (400 mg twice daily), and **omeprazole** (20 mg twice daily) for two weeks.
- If homocysteine is elevated then treat with vitamin B12, B6 and Folic acid.
- Fish oil up to 1 gram daily with an Asprin should be taken by all patients unless there are contraindications like stomach ulcers or bleeding disorders which can get worse by using Aspirin. CRP levels have been brought down by Fish Oil.

Chapter 8 Ophthalmic Autoimmune Diseases:

The eye is often compared to a camera. Light comes in through the cornea, pupil, and lens at the front of the eye just as the lens of the camera lets in light to the film. The light is then focused on the inside wall of the eye called the retina (as on the film in a camera). This picture is then sent to the brain along the optic nerve which connects the eye to the brain. When the eye turns red it is the result of inflammation. Even a bacterial or viral infection is accompanied by inflammation. Ocular inflammation may affect all eye layers, conjunctiva, sclera, and uvea. If we think of the eye as a multi layered ball, then the outer layer is the sclera a protective layer, the innermost is the retina the thin light gathering layer (eyes video screen), and the middle layer is the Uvea. The Uvea is made up of the iris (the aperture), the Ciliary body and the choroid. When any part of the uvea becomes inflamed then it is called Uveitis.

Autoimmune eye diseases:

- **Iritis**, Is the inflammation of the iris also called **anterior** uveitis. This condition is often associated with autoimmune disorders such as arthritis.
- **Uveitis** is inflammation of the **middle portion of the eye** and may affect the muscle that focuses the lens. This also may develop suddenly and last several months.
- **Retinitis** affects the **back of the eye**. Is rapidly progressive, making it difficult to treat.
- **Choroiditis**, or inflammation of the layer beneath the retina,

Iritis, retinitis, choroiditis and uveitis can all be caused by autoimmune diseases. The autoimmune process can be **triggered by injury to the eye.** Many systemic diseases cause diffuse inflammation by an autoimmune mechanism. These include tuberculosis, spirochaetal diseases such as Lyme disease and syphilis, sarcoidosis, Behcet syndrome, juvenile idiopathic arthritis, and HIV infection .Their role in autoimmune disease should always be suspected. Confirming the diseases by appropriate test will help direct the correct combination of antibiotic and anti inflammatory treatment.

The uveal tract represents the vascular organ of the eye. In addition to providing most of the blood supply to the intraocular structures, it acts as a conduit for immune cells, particularly lymphocytes, to enter the eye. Consequently, the uveal tract is represented in many intraocular inflammatory processes. Uveitis is probably a misnomer unless antigens within the uvea are the direct targets of the inflammatory process. A better term of the condition is "intraocular inflammation" (IOI).

In autoimmune diseases with intraocular inflammation (IOI), uveitis may be the first clinical manifestation and may represent the most severe sign. The conventional treatment of IOI includes prednisone and immunosuppressive agents, omega-3 oils, curcumin which are efficient in around half of the patients; however, their effectiveness is also limited by their side effects. The effects of intravenous immunoglobulin (IVIg) on ocular inflammation have been reported in a number of autoimmune diseases. They show favorable results in ocular cicatricial pemphigoid, ocular pemphigus, Wegener disease, Behcet's disease, inflammatory myositis. IVIg and assess their potential steroid-sparing effect. Whenever Iritis is noticed by a physician it should be a clue to that the patient may be developing autoimmune disease in the future.

Causes of autoimmune Iritis ankylosing spondylitis, reactive arthritis (including Reiter's syndrome), psoriatic arthritis, inflammatory bowel disease, **Behcets disease**, **sarcoidosis,** juvenile chronic arthritis, Vogt-Koyanagi-Harada syndrome (an inflammatory syndrome including uveitis with dermatologic and neurologic manifestations).
Testing: Blood tests for total white cells, vitamin B-12 levels, homocysteine level, folic acid level, pyridoxine level and cultures of eye fluids are done. E.S.R. is elevated. ANA, anti–Ro (SS–AA) antibody to check for Sjogrens and antithyroid antibodies to look for thyroid disorders.

Current treatment guidelines

- In an inflammatory disease of the eye there will always be an associated infection. I recommend Minocin as it has anti-inflammatory properties for two weeks. It is best to use a prednisone ointment or eye drops with the antibiotic. Doxycycline 100mg given orally twice daily can be used effectively.

- Immunosuppressive drugs recommend, Steroid eye drops or ointment may be needed. Other drugs are Azathioprine, Methotrexate, Mycophenolate Mofetil, Cyclosporine, Tacrolimus, Cyclophosphamide, and Chlorambucil.
- IVIG is very effective in ocular Pemphigoid / Pemphigus and if the treatment is not started early this condition can lead to blindness. The recommended I.V.I.g dose is 2g/kg every two weeks in divided doses
- Omega-3 oils at 2000-3000mg daily, curcumin twice daily, honey rubbed lightly on inflamed eye, use of Garlic, ginger in food and green tea are alternative supplements.

Double Vision in autoimmune diseases: If a patient develops double vision they need to be evaluated for autoimmune diseases such as, Thyroiditis, Myasthenia Gravis, Eaton Lambert Syndrome, Multiple Sclerosis, Guillain-Barre, Chronic Inflammatory Demyelinating Polyradiculoneuropathy, Lymes and Myositis. Please see treatment guidelines under the specific condition. Infections such as Botulism or Botox injections can also cause double vision. Giant cell Myocarditis patients present with double vision and Myositis as the first symptom. CRP and E.S.R. should be done on all patients; any one with CRP over 80 should be started on Intravenous steroids one gram a day.

Sympathetic Ophthalmia (SO): This is an autoimmune disease in which a penetrating injury to one eye produces inflammation in the fellow, non-injured eye. Sympathetic ophthalmia was known to Hippocrates over 2000 years ago. This rare reaction can follow a cataract removal procedure, ocular surgery and especially vitreo-retinal laser surgery. The uvea is involved in early stages later the Ciliary body gets involved. The release through bloodstream, of uveal pigment is thought to cause antibody production from the immune system, which in turn attack the normal eye and initiate uveitis in the fellow eye.

Symptoms: Early features of uveitis are floating spots and weakness of accommodation. The retina is rarely affected but papilloedema and glaucoma may result. Approximately two-thirds of SO cases occur within two weeks to two months following injury, with 90% occurring within the first year. Usually patients notice blurry vision and pain in both eyes without other symptoms outside the eyes. Eye examination shows red, swollen eyes.
Tests: No tests except, diagnosis is based on an injury which happened within a year.

Treatment: Early administration of systemic steroids, omega-3 oils, curcumin may be helpful. If the injured eye remains inflamed and there is little prospect of it recovering vision, then sympathetic ophthalmia an intravitreal injection of 4 mg of triamcinolone acetonide reduce the likelihood of sympathetic ophthalmia. Action is usually required within two weeks of injury. In Sympathetic opthalmitis a combination treatment with steroids and antibiotics has been used successfully, Penicillin and Azathioprine has been used. Long term remission can be achieved by

coricosporin started at 250 mg BID for two week and then cut down to 125 mg daily as maintenance for 2-3 months.

Optic Neuritis or Retrobulbar Optic Neuritis – sudden loss of vision: The optic nerve is an extension of the brain that connects the retina of the eye to the brain. The retina contains photoreceptors, cells that are activated by light and that connect to other retinal cells called ganglion cells. The ganglion cell, in turn, sends information through projections called axons into the brain. By this route, the optic nerve sends visual impulses to the brain. Optic neuritis is the most common optic nerve disease to affect young people. The average age at the first attack is 30 years, but teenagers and people at any age may develop this disease. The intense inflammation in the optic nerve can be seen by the MRI scan and even by looking in the eye. **Symptoms:** In optic neuritis, heat will make the symptoms worse, as a heated nerve will conduct electricity slowly, this process is termed **Uthoff's** phenomenon. On examination there can be swelling of the optic nerve seen when looked inside the eye, the optic disc looks chaulky white and with time will look pale. The pupil, located in the center of the iris, is the part of the eye which gets larger and smaller according to the amount of light. The optic nerve plays a role in this reaction to light; in the normal eye the pupil quickly becomes small after a bright light is brought in front of it. If one eye has retinal or optic nerve disorders, then if we shine light on the normal eye that pupil constricts, and then shine the light on the bad eye, instead of constricting the pupil dilates immediately in that eye, called a relative afferent pupillary defect.

Test: ESR is elevated, vitamin B-12, B-6 and Thiamine levels to look for deficiency. MRI scan of the head to look for tumors, strokes and inflammation in the optic nerve. Mycoplasma and Lymes antibodies in blood may be present. Homocysteine level or just give vitamins, below.

Treatment:

- Steroids 1-gram loading dose intravenous for three days followed by 100 mg a day prednisone for three days tapered over a month.
- If homocysteine is elevated give vitamin B-12 replacement with folic acid and pyridoxine. (can give these vitamins if homocysteine test is not available)
- If the MRI shows multiple lesions like Multiple Sclerosis then please look in the MS chapter for guidelines on treatment.

Orbital Myositis & Tolosa-Hunt syndrome or orbital pseudotumor syndrome: Inflammation and swelling of the muscles around the eye is termed orbital Myositis (Tolosa-Hunt syndrome or orbital pseudotumor). It can be seen in many conditions some examples are, thyroid orbital Myositis, Wegener's granulomatosis and sarcoidosis. This condition should be considered in patients who have unusual symptoms such as protrusion of the eyeball, painful eye movements, or pain that does not resolve within three hours. Myositis in thyroid myopathy is usually painless in onset, is similar in both eyes, slowly progressive, and associated with systemic manifestations of Graves disease (weight loss, enlargement of thyroid). Rarely **patients may present with double vision and Myositis, who within weeks can die if not treated with steroids as they have G.C.M** (Giant Cell Myocarditis)

Symptoms: Pain and swelling around the eye are the most common clinical features .In all cases, protrusion of the eyeball, swelling of the eyelid, painful eye movements, reduced or blurred vision are seen. Redness in the eye is seen.

Symptoms of thyroid myositis: limitation of the movement opposite to the affected muscle, and deterioration of color vision, visual field, and visual acuity may also occur in thyroid eye disease. These patients also have weight loss despite increased appetite, nervousness, and palpitations. They can also appear fatigued or drowsy.

Tests: E.S.R. is elevated, CRP is elevated and MRI Scan of the orbit should be done which can show swelling of the muscles. A culture of inflamed site for fungal or bacterial infections is usually obtained. Vitamin B-12 levels, Thiamine levels and B-6 levels with homocysteine levels can be measured.

Additional tests for Thyroid Myositis: laboratory testing for thyroid hormones T3 (triiodothyronine), T4 (tetra-iodothyronine) and TSH (thyroid stimulating hormone) are done.

Treatment of Orbital Myositis:

- **If CRP is in the 80-100** range hospitalizes the patient and give intravenous steroids at Gram a day for 5 days. **If CRP is below 80 then use oral Prednisone** is started for a few days at 50 mg daily and tapered down after the swelling becomes less. Methotrexate is used as a steroid sparing agent with antibiotics like Doxycycline 100mg twice daily.
- Those patients whose clinical or radiological features are associated with inflammation of the muscles will benefit from early systemic steroid therapy. Methotrexate given at a dose 20 mg per week (range 15-25 mg per week) in conjunction with folate supplements to help control inflammation. Patients need regular ophthalmic examinations, as well as serum liver enzyme levels and blood cell counts to monitor side effects of Methotrexate.

Treatment for thyroid Myositis:

- Propylthiouracil (Tapazole) are used to block the synthesis of thyroid hormone, propranolol (Inderal) is also used to slow down the increased metabolism.
- Systemic steroids, immunosuppressive agents like Azathioprine, cyclosporine or cyclophosphamide in combination with orbital irradiation are used in advanced Myositis.
- For both type of orbital Myositis, I have used **Vibramycine** and nano-electrical stimulators, to help get rid of chronic swelling around the eyelids.

Chapter 9) Skin & Hair Autoimmune Diseases

Autoimmune Urticaria: Urticaria is usually considered idiopathic in reality the chronic form is autoimmune. The chronic reoccurring Urticaria is like remitting relapsing autoimmune disease. It can be treated with anti-inflammatory medications. Chronic urticaria has been described in patients with Helicobacter pylori infection. Due to this there is a higher prevalence

of B-12 deficiency in Urticaria. Positive anti-H-Pylori antibody is found in most patients with Urticaria and the condition resolves with antibiotic treatment in sixty percent of the patients. Search for H-pylori should be included in the diagnostic management of chronic urticaria. There is an association between thyroid auto-immunity and chronic urticaria. Some Thyroiditis patients have positive antithyroid antibodies, which if treated helps correct the urticaria.
Symptoms: Urticaria, commonly known as hives, consists of areas of raised erythema and edema of the superficial dermis. There is swelling, itching, pain and rash of the skin.

Test: Vitamin B12 levels low. Check for thyroid antibodies. ESR is elevated. EBV & Herpes simplex antibody test.

Treatment of Urticaria:

- For H.pylori eradication began treatment with amoxicillin, clarithromycin and omeprazole for 14 days. About fifty percent of the patients will recover with above treatments. Those that do not respond need to be placed on levofloxacin (500 mg b.i.d.), amoxicillin (1 g b.i.d.), and omeprazole (20 mg b.i.d.) prescribed for 10 days. A urea breath test can be done to confirm if the treatment was effective. For Low B12 levels take a sublingual B12 formula or intramuscular injections weekly.
- If thyroid antibodies are positive treat with levothyroxine.
- Resistant patients may need Dapsone 50 mg daily to alleviate the condition.
- Urticaria patients, who have high antibody titers, to either herpes simplex virus or Epstein-Barr virus, will respond to Acyclovir 100mg given every six hours. In those with chronic urticaria who do not recover they need treatment with I.V.I.g protocol
- **Patients need to go on a MSG free & Celiac diet if urticaria does not clear up.**
- Electronic pulsar can be used to reduce urticaria.

Alopecia areata: Hair helps transmit sensory information they grow out of follicles, there are 5 million follicles on the body. One million of those are on the head. Loss of hair is called alopecia it is considered an autoimmune disease, the immune system mistakenly attacks the hair follicles, the tiny structures from which hairs grow. In most cases, hair falls out in small, round patches about the size of a coin. In many cases, the disease causes a few bare patches. In others hair loss is more extensive. Rarely, there is total loss of hair on the head (alopecia areata totalis). Family members may have a history of autoimmune diseases, such as diabetes, rheumatoid arthritis, thyroid disease, systemic lupus erythematosus, or pernicious anemia. Higher occurrence of thyroid disease, atopic eczema, nasal allergies, and asthma may be present in some patients.

Symptoms: Patches of hair falling out.

Test: Check for Iron deficiency in all patients especially during pregnancy. Check for thyroid deficiency (check antithyroid antibodies) and Vitamin B-12 (Cynocobalamine deficiency). Check for antigliadin antibodies. Check for H-Pylori antibodies.

Treatment:

- **MINOCIN:** Minocin 100 mg daily should be given to all new cases of alopecia. There is complete resolution of symptoms and hair regrowth is good, continue for two to three months. Take the medicine at night with water and no food.
- **Iron Supplements:** In those patients who have anemia or iron deficiency.
- With baseline serum vitamin B12 **levels below 350 ng/l**, need supplements of Cynocobalamine**.** (Sublingual formula daily or injections monthly)
- Give Zinc supplements to children with hair loss.
- **Omega -3** at a dose of 3000mg a day will grow hair in alopecia.
- **Corticosteroids:** Prednisone, 8 mg/kg body weight) intravenously on 3 consecutive days at 4-week intervals for at least 3 courses. Called the pulsed treatment.
- Proscar **finasteride** is effective in male pattern hair loss.
- **Melatonin** 0.1 % solution applied daily to scalp improves alopecia
- Postmenopausal women need Minoxidil solution to be applied to the scalp.
- **PUVA:** Photochemotherapy combining oral or topical methoxsalen and UV-A irradiation of the scalp improves alopecia.
- If low B12 levels are found then treatment with the antibiotic combination described under Urticaria for H.Pylori eradication should be done.
- Magnetic Pulser and Electronic pulsar will also grow hair with repeated application

A woman, with atopic dermatitis and alopecia areata universalis, was treated with subcutaneously administered interferon gamma, the viral infection cleared and four weeks later hair re-growth was observed. Complete remission of alopecia areata was documented. After four cycles of high-dose 500mg/kg intravenous immunoglobulin, a sustained remission of the atopic dermatitis was achieved.
In another case a young girl with immune deficiency was treated with IVIG and regrowth of eyelashes, eyebrows, body and scalp hair was observed in this patient. This has been reported several times and thus IVIg should be considered as a treatment for immune deficiency associated with alopecia.

Autoimmune Atopic Dermatitis or Eczema: Atopic dermatitis (AD) is a chronic, itching, inflammatory skin disease which is associated with asthma or hay fever and a familial occurrence of these conditions. The disease comes in attacks which improve with time, and then there are more attacks. Genetic factors are important in the development of AD. There are a number of different eczemas - which cause the skin to become inflamed and itchy. This condition is also called 'atopic eczema' or 'infantile eczema'. It affects people with dry and rough skin and may be caused by a variety of allergens. It often starts in childhood and tends to run in families. It often progresses to asthma and allergic rhinitis later in life.

Patients with atopic dermatitis often have elevated serum IgE levels and sensitization against a variety of environmental allergens, but there is also evidence that attacks of the disease occurs in

the absence of exposure to environmental allergens. There has been a significant association between the appearance of mite (Dermatophagoides pteronyssinus, D. farinae)-specific IgE and IgM antibodies reported in atopic dermatitis.
Some causes of atopic dermatitis can include:

- Food allergies (Which are more likely to affect children)
- Cow's milk and hen's egg are the foods most likely to make infantile eczema worse.
- The house dust mite -. Allergy to cats and dogs.
- Bacteria such as staphylococci may cause sudden severe outbreaks of eczema.
- Fungi like Candida, Malassezia yeasts, House dust mites or food.
- H.pylori infection.

Tests: Eosinophils and IgE are elevated, anti-nuclear antibodies and Antiphospholipid antibodies may be present. Antigliadin antibodies may be present. Combined skin prick and patch testing significantly enhances identification of food allergy in children. Especially for foods and Fungi.
Treatment of Eczema: Eczema triggers need to be avoided by patients. Eczema can be treated with low dose steroid ointments. Anti-histamines like benadryl can be used to make the skin less itchy and these should also help at night by reducing itchiness. Those patients who have Candida improve with antifungal treatments; Fluconazole is more effective than amphotericin B and nystatin, for fungal treatment. Tacrolimus is a topical immunosuppressive ointment without systemic effects. It may be useful in children and adults with severe atopic dermatitis. In resistant cases interferon treatment can be used. We recommend **Omega-3 oils as an anti-inflammatory in all people**. If the condition does not improve IVIg will usually resolve the dermatitis.

Vitiligo: Vitiligo is an autoimmune disease in which pigment producing cells (melanocytes) are destroyed by the immune system. Loss of the pigment cells results in irregularly shaped white patches on the skin. Any area of the body can be affected. Common locations are face, neck, eyes, nostrils, nipples, and genitalia. Reduced pigment is also seen at sites of injury and around moles. The hair on the scalp, eyebrows, eyelashes and body is affected. Patients with Vitiligo often showed diminished blood levels of folic acid, diminished levels of vitamin B12 serum and low levels of ascorbic acid plasma. The incidence of autoimmune disorders in these patients and their family members is higher, diabetes mellitus, rheumatoid arthritis and SLE are frequently seen. Many people report that their Vitiligo first appeared following a traumatic or stressful event, such as an accident, job loss, death of a family member, severe sunburn, or serious illness. Vitiligo is reported after interferon treatment.

Symptoms: Irregular depigmented spots begin to appear on different parts of the body. Especially after an injury they will develop within the injured area.
Test: Levels of B-12, Folic acid, Thyroid antibodies, antigliadin antibodies (celiac disease)

Treatment:

- Patients will benefit from sublingual supplements of vitamin B12, folic acid and fresh fruits taken daily. Patients need to be advised about sun exposure allowed only in the morning and evening. **They should avoid the full afternoon sunshine.**

- Combination therapy with **topical vitamin D**-(**3**) ointments and linear polarized infrared, UVA, solar irradiation, can be used as an alternative therapy for Vitiligo. Those who cannot have access to sunlight can use UVB lamps in winter time.
- Short term steroid creams can be used to help areas of skin if they are itching.
- Topical calcipotriol treatment was applied twice daily as 50 microg/gm cream or ointment is helpful for those patients who fail the sunlight exposure treatments.
- Narrow band UVB is succeeding psoralen and UVA irradiation as the main treatment of Vitiligo vulgaris. UVB combined with vitamin B12 and folic acid has been successful.
- The xenon-chloride excimer laser represents a new treatment modality for the management of stable vitiligo.
- Homepathic Hydrocodyl drops 30-60x 3-5 drops daily are used for Vitiligo.
- If thyroid antibodies are positive then treatment with levothyroxine. If antigliadin antibodies are positive then treat celiac disease, please see the diet section.

Pemphigus vulgaris (PV): PV is an autoimmune disease characterized by blisters and ulcers on the skin and mucous membranes, most commonly inside the mouth. The cells of the epidermis (upper layer of the skin) called keratinocytes, are cemented together at sticky spots called desmosomes. In pemphigus vulgaris immunoglobulin autoantibodies bind to a protein called desmoglein, which is found near the bottom of the epidermis. Resulting in keratinocytes separating from each other, and are replaced by fluid filled blister. Most patients present with lesions on mouth and genitals, later blisters on the skin may develop. The most common mucosal area affected is the inside of the mouth but others include eyes, throat, labia, vagina, cervix, penis, urethra and anus. **DHEA** a hormone, levels have been reported low in PV.

Pemphigus Foliaceus PF: In PF, Crusted sores or fragile blisters usually first appear on the face and scalp and later involve the chest and back.

Diagnosis: Nikolsky's sign is positive in Pemphigus. “This is present when pressure is put on the skin with the thumb; the epidermis appears to slide over the underlying dermis”. This test is positive in pemphigus group of blistering dermatomes, a positive Nikolsky's sign can be seen in toxic epidermal necrolysis (TEN) and staphylococcus scalded skin syndrome.

Tests: Biopsy Diagnosis generally requires a skin biopsy, which shows typical features of rounded-up separated keratinocytes within the blisters just above the bottom layer of the epidermis. In most cases, circulating pemphigus antibodies (Anti-desmoglein-1 antibodies) can be detected by a blood test. E.S.R. is also elevated in pemphigus patients. DHEA levels are low.

- **Treatment of Pemphigus:** Several studies show a high rate of response to Minocycline treatment in Pemphigus especially oral pemphigus. A dose of 50 to 200 mg daily has been reported. Minocin works in all types of Pemphigus (for pemphigus vulgaris, pemphigus foliaceous, or bullous Pemphigoid). Please see **antibiotic section** for details.
- A low dose of prednisone needs to be given for a short time to control inflammation at 30 mg a day and can be tapered in two to three weeks to a lower dose and stopped.

- **Pyridostigmine** also know as mestinon is generally used for Myasthenia. However it has been found useful in all forms of Pemphigus. With the use of mestinon at a dose of 60mg three times a day, one can reduce the amount of steroid dose. **Dapsone** has also been found to be useful in the treatment of Pemphigus, especially in children it is used as a combination treatment with prednisone.
- It has been shown in multiple studies that IVIg is a treatment of choice. Please read the **IVIg section** for dose for 9 months. See the **CIDP section** for more immune treatments.

Bullous Pemphigoid (BP) is a chronic blistering autoimmune disorder of the skin. Which can ranges from mildly itchy welts to blisters and infection, and may affect a small area or be widespread. Some patients with BP have autoimmune diseases such diabetes and rheumatoid arthritis. Exposure to drugs like furosemide, penicillin's, mechanical and physical trauma, burns from radiation, sun or heat, will increase the risk of getting Pemphigoid. Bullous means a blister (a thin sac filled with clear fluid). The skin in BP is itchy, large red welts and hives appear during the formation of blisters. Widespread blisters appear in areas that flex or move (flexural areas). Some patients in BP develop blisters in the mouth, throat and esophagus.

Cicatricial Pemphigoid is a disease of the elderly. Lesions arise on mucous membrane in the nose, mouth, eyes, esophagus, larynx, urethra and anus. Recurrent lesions will produce scarring, gums are commonly involved and can cause gingivitis.

Symptoms: Small patches of itchy skin are followed by blisters developing a week later. The blisters are firm, the fluid is clear, but may be blood-stained. Any area of skin can be affected but arms, legs, armpits, and groin are the most common sites. The body is covered in blisters but rarely the blisters are in one area often in legs. The inside of the mouth is rarely affected.

Diagnosis: The diagnosis must be confirmed by skin biopsy. A special skin biopsy test (a direct immunoflorecsence biopsy) may also be needed. Blood tests can show Pemphigoid antibodies.

Treatment is focused on relief of symptoms and prevention of infection.

- Vibramycine and Minocycline are very useful for mild to moderate disease. They do not work on bacteria, but act directly on the immune system. They can be used in combination with potent topical steroid creams for more rapid relief. Several studies have shown a high rate of response to Minocycline treatment in Pemphigoid. A dose of 100-200 mg daily has been used. Side effect of hyperpigmentation of skin lesions which disappear after Minocin is stopped. Minocin works in all types of Pemphigoid.
- (Prednisone 1 mg/kg/day) plus Azathioprine (2 mg/kg/day) the bullae rapidly disappear. The dose must be adjusted frequently, and side effects must be monitored. A fairly high dose is needed initially, and once the blisters have stopped appearing, it is slowly reduced over many months or years. As steroids have some undesirable side effects, try to reduce the dose as low as possible. If this is done too quickly, the blisters reappear.

- In resistant cases Dapsone is given in combination with steroids.
- IVIg is recommended for treatment at a dose off 400mg/kg on alternate days for 5 days and repeated every four weeks for 9 months. Please see the IVIg section for details.
- Curcumin, Omega-3, Celiac diet, honey are helpful please see details in the **diet section.**

Lichen planus (LP): Lichen planus is a common autoimmune skin disease that comes in episodes. The onset may be gradual or quick. It is proposed that LP results from molecular mimicry to helicobacter pylori (Hp). It was reported in several studies that Hp is associated with atrophic gastritis and LP. In a study circulating basement membrane zone (BMZ) antibodies were present in erosive (LP); it was shown that epidermal-binding BMZ antibodies were seen in 61% of the patients of LP. This disease involves multiple sites in the body and has relapses and remissions. It has been associated with a number of other infections, Candida, hepatitis-C. A study of 303 patients in Italy showed Anti-HCV antibodies were common in LP patients.

Symptoms: Lichen planus appears as shiny, flat-topped bumps that often have an angular shape. These bumps have a reddish-purplish color with a shiny cast due to a very fine scale. The disease can occur anywhere on the skin, but often favors the inside of the wrists and ankles, the lower legs, back, and neck. The mouth, genital region, hair and nails are affected in some patients. Thick patches may occur, especially on the shins. Blisters may rarely occur. Bumps may appear in areas of trauma on some patients. Lichen planus of the mouth most commonly affects the inside of the cheeks, gums and tongue. Oral lichen planus is more difficult to treat and typically lasts longer than skin lichen planus. Oral lichen planus typically appears as patches of fine white lines and dots. This is associated with poor oral hygiene
Tests: Antibodies against H-Pylori are usually positive, oral Candida needs to be screened, antibodies against HCV need to be checked.

Treatment:

- Anti H-Pylori treatment with metronidazole should be tried for a week. In a study a 95% response was seen in patients treated with oral metronidazole, 500 mg twice daily, for 20 to 60 days and were followed up for a period of 5 to 36 months.
- Topical steroids such as betamethasone propionate ointments are generally applied for 4 week course. A thin smear rubbed in once a day and stopped when the lesions have flattened. Brown marks are often left at the sites, which take several months to fade. Steroid injections into affected areas may be useful for localized disease. In widespread disease prednisone 40 mg daily for two weeks and then tapered and stopped this will often clear up the lichen planus completely. Other treatments include long term antibiotics, oral antifungal agent, phototherapy, methotrexate and hydroxychloroquine. Tacrolimus ointment can be used.

Rosacea: Rosacea is a common autoimmune allergic condition characterized by symptoms of facial flushing and a spectrum of clinical signs, including erythema, telangiectasia, coarseness of skin, edema, papules, pustules, ocular lesions and an inflammatory papulopustular eruption resembling acne. Rosacea affects mostly adults, usually people with fair skin, between the ages of 30 and 60. About 16 million Americans have this skin condition. Although it's more common in women, men may develop the disorder. Left untreated, rosacea tends to be progressive, which means it gets worse over time. Rosacea is remitting and relapsing, it flares up for a period of weeks to months and then signs & symptoms lessen for a while before rosacea flares up again.

Rosacea fulminans is a sub type of rosacea, occurs exclusively in women well past adolescence. It's confined to the face, covering most of the surface with many fluctuant nodules and papules. Seborrhea prior to onset is typical. The patients respond well to **isotretinoin** in combination with topical and systemic corticosteroids. The response is superior more rapid than in patients treated with oral antibiotics. Rosacea fulminans is an indication for topical or systemic corticosteroids. **Rhinophyma** develops when severe rosacea is left untreated over a long period of time. The papules gradually increase in size. When these nodules converge on the nose, they give the nose a swollen, red appearance.

High prevalence of Helicobacter pylori (Hp) infection seen in patients with rosacea, with evidence of dermatological improvement in patients treated with antibiotics for this infection. In a study done on Rosacea patients after eradication of Hp, 51 out of 53 treated rosacea patients became Hp negative. The symptoms of rosacea disappeared in 51 patients, markedly declined in one and remained unchanged in one patient. Conclusion from this study is that Hp eradication helps a majority of patients with Rosacea
Young women who are taking a multivitamin a day may develop Rosacea. If they stop the vitamin in time the rosacea will go away. **Rosacea is associated with daily high dose intake of vitamin B-12 and B-6.**

Symptoms: Rosacea starts with facial flushing which like any other autoimmune condition comes in attacks. If the condition is not treated it takes other forms and telangiectasia, coarseness of skin, edema, papules, pustules, all may form.

Test: Antgliadin antibody, antithyroid antibodies, H-pylori antibodies (B12-B6 levels)

Treatment:

- One week anti-Hp therapy with omeprazole (20 mg bd.), clarithromycin (500 mg bd.) and metronidazole (500 mg bd.) (See the Gastric & duodenal ulcer section for details)
- Systemic treatment includes metronidazole, doxycycline, **Minocycline**, and clarithromycin. If the patient does not respond to the topical antibiotic then oral antibiotics are recommended. (Please see the antibiotic section for details)
- Topical Metronidazole cream and gel are used for papulopustular rosacea.
- Ocular involvement is common in patients with cutaneous rosacea and can be treated with orally administered or topical antibacterial.
- Once rhinophyma starts to the only treatment is by surgical or laser.

- Patients need to follow a strict diet, wearing hats in the sun and scarves in the cold to control the disease triggers. Regularly applying topical medication should help most patients. Avoid too much exercise, avoid alcohol, and avoid too much makeup, hot baths, steroids, spicy foods, stress anger and embarrassment. Avoid B-12, B6 vitamins.

Livedoid vasculopathy (LV): Is a chronic vascular disorder seen in middle aged women characterized by persistent painful ulceration of the feet. Peripheral spider veins (telangiectasia) and increased pigmentation (hyperpigmentation) white atrophic scars on the dorsum of the feet. LV starts in the legs or feet and can spread to the abdomen and hands accompanied by a neuropathy. These ulcerations are recurrent and chronic with spontaneous remissions and relapses which may be seasonal during the winter and summer months. The disease has been observed in patients with factor-V Leiden mutation, antiphospholipid antibody syndrome, hyperhomocysteinemia, protein-C deficiency and increased platelet activation (risk of blood clots in all these disorders). **Case report:** A 49-year-old woman with livedoid vasculopathy. The patient presented with an elevated homocysteine level caused by renal insufficiency, vitamin-B6 deficiency and reduced vitamin-B12 concentration. **Vitamin treatment reversed her condition**.

Symptoms: Pain with hyperpigmented lesions producing a livedoid pattern, ulcerations on both ankles and white atrophic scars on the dorsum of the feet. (Numbness in feet)
Tests: Biopsy demonstrates an increased blood vessels formation and vessel occlusion with erythrocytes. The small number of leukocytes and the lack of nuclear fragments around the small vessels are the most important signs. Low vitamin B-6 level, low folic acid level, low vitamin B-12 level and **high homocysteine levels**. CRP is elevated.

- **Treatment:** Therapies that benefit include aspirin, coumadin, dipyridamole (5), low molecular weight heparin (6), pentoxifylline (7), enoxaparin (3), nifedipine (8), and tissue plasminogen activator (9). In addition, tobacco cessation should be advised.
- **Sublingual replacement of B-12, folic acid and vitamin B-6.** (can reverse the disease)

Linear IgA bullous dermatosis of childhood

Linear IgA bullous dermatosis mainly affects preschool-aged children.

Diagnosis: Histological and immunofluorescence studies

- **Treatment:** Dapsone is considered the first-line therapy with prompt response from most patients. However, it may be contraindicated in certain conditions such as glucose-6-phosphate dehydrogenase deficiency.
- **Flucloxacillin** treatment for four months can induce complete remission in some patients and can be considered the first line of treatment for this disease.

Acne: Acne is a common disorder and is easily diagnosed. The surface of the skin has lots of small sebaceous glands just below the surface. These glands make an oily substance called sebum that keeps the skin smooth and supple. Tiny pores (holes in the skin) allow the sebum to come to the skin surface. Hairs also grow through these pores. Acne is caused by the over

activity of the sebaceous glands that secrete oily substances onto the skin. Testosterone in people prone to acne triggers the sebaceous glands to produce an excess of sebum. At the same time, the dead skin cells lining the openings of the hair follicles (the tubes that hold the hair) are not shed properly and clog up the follicles.

Treatment: For treatment please follow all the guidelines in the diet chapter. With this also increase the Omega-3 fatty acid intake. Start, **Vibramycine 100mg daily** for six weeks and then take this on alternate days for two months. Use Benzoyl peroxide or azelaic acid (Skinoren) or clay to wash your skin daily for six months. Use a magnetic stimulator to reduce inflammation. Follow diet guidelines and eliminate sugars.

Eczema: This again is a very common condition, it can occour on the cheeks of new borns, in hands, around ears and produce chronic skin lesions. The treatment is very similar to Acne and you have to follow dietary guidelines in the diet chapter. Start a course of an antibiotic erythromycin in children and Vibramycine in adults. Apply honey and olive oil mixture on the lesions. Increase the consumption of omega-3 fatty acids on a daily basis.

Meleasma / Cholasma, also known as *meleasma*, appears as a blotchy, brownish hyperpigmentation developing in the sun exposed areas of the face; pigmentation develops slowly and fades with time. Cholasma usually affects women but occasionally is seen in young men who use after-shave lotions, scented soaps, and other toiletries. It is also caused by excessive sun exposure, after pregnancy and anti-seizure medication.

Treatment: Topically treatments include application of 4% hydroquinone solution daily. Use Vibramycine 100mg daily for two weeks, then 100mg three times a week (Mon, Wed, and Fri). Omega-3 oil use 1000mg daily. Avoid sunshine; avoid application of perfumes and cosmetics to face.

Chapter 10) Rheumatic Autoimmune Disorders:

Rheumatoid arthritis (RA): Rheumatoid arthritis is triggered by Mycoplasma. RA is two to three times more common in women than in men and generally strikes between the ages of 20 and 50. Rheumatoid arthritis can also affect children. The diagnosis is based upon clinical examination and elevated ESR or CRP along with x-rays showing early damage in the joints. Investigators have shown that Mycoplasma which is a small bug without a cell wall causes arthritis in humans. In 1949 at the International Congress on Rheumatic Diseases reported the relationship between Mycoplasma and joint disease. National Institutes of Health **(NIH) issued a research grants in 1950, to Thomas Brown, M.D., who reported an immunologic reaction of antigen and antibody (with Mycoplasma as the suspected antigen) as the cause of rheumatoid disease**. Further support of Mycoplasma as a causative agent and antigen was proven in 1964, when a high incidence of Mycoplasma antibodies in the blood of rheumatoid arthritis patients and lupus patients was found. **Also recognized was a 4:1 higher incidence** of Mycoplasma antibodies in females suggesting a correlation with the **higher incidences of**

rheumatoid arthritis in females. **In1989, NIH requested grant applications for the controlled clinical trials of tetracycline therapy for rheumatoid arthritis**. The preliminary results of the clinical trials, known as **MIRA or Minocycline in Rheumatoid Arthritis**, were promising and the **NIH requested grant applications for studies of Mycoplasma as causes for rheumatoid diseases in 1993** and for a study for intravenous antibiotics for rheumatoid arthritis in 1994. The result of the MIRA clinical trial stated, that Patients who suffer from mild to moderate can benefit from Minocycline. A review of ten randomized controlled trials involving 535 patients were reviewed, reviewers reported Minocycline was associated with a clinically improvement in disease activity in RA with no absolute increased risk of side effects.

Symptoms of RA:

- Pain and swelling in joints, especially in the smaller joints of your hands and feet
- Generalized aching or stiffness in joints after sleep or after periods of rest
- Reduced motion of the affected joints, Deformity of your joints over time
- Weakness in muscles attached to the affected joints
- Fatigue, which can be severe during a flare-up , Low-grade fever
- General sense of not feeling well (malaise)

In RA, the joints in the wrists, hands, feet and knees are most often affected. Later in the disease, shoulders, elbows, hips, jaw and neck can be involved. It generally affects both sides of your body at the same time. Small lumps, called rheumatoid nodules, may form under the skin at pressure points and can occur at elbows, hands, feet and Achilles tendons.

Test: Check CRP and ESR both are elevated. Check for Mycoplasma. (X-ray of joint)

Treatment: What precaution to use: Limiting sugar and grains is a critical element of the treatment program. Patients who are unable to decrease their sugar intake are less likely to improve with the antibiotic protocol. All patients need to go on a pure vegetable, fruit, rice, milk, beef, chicken and fish diet. No alcohol, no beer, and no sugar, only honey is allowed in this diet.

Antibiotic Therapy: What antibiotic to give for reactive arthritis:

- **Minocin or Doxycycline** 100 mg. is taken on alternate days should be given three tablets a week. It is important to take medication on alternate days, as long term use of the drug can cause toxicity. Tetracycline type drugs can cause a permanent yellow brown discoloration of the teeth. This can occur in last half of pregnancy and in children up to eight years old. One should not routinely use tetracycline in children. If patients have severe disease, one can consider increasing the dose to as high as 200 mg three times a week. Minocin can cause nausea & vertigo, taking the dose at night helps to decrease vertigo. If one encounters a resistant form of rheumatic illness, intravenous

administration should be considered. Most people take the doses 100mg at **night every Monday, Wednesday and Friday.**

- **Clindamycin:** It is important to use the intravenous (IV) form of treatment if the disease is severe. Scleroderma is a particularly severe form of rheumatic illness that should receive IV treatment. Patients with long standing disease are started with daily intravenous clindamycin for five days. The first two days, 300 mg. of clindamycin are given in 250 cc 0.9% saline infused over an hour. (D5W solution is avoided due to yeast overgrowth seen in patients). The third and fourth day if the patient tolerates 600 mg. is given, if the patient can tolerate the fifth and subsequent days 900 mg is used. After the initial daily intravenous series, IVs may be administered once weekly or once every other week or as the physician determines for the patient. The IVs are continued until all lab figures return to normal, which may take longer than a year, sometimes several years for patients with severe or long standing disease. Lab results should then be monitored for several months longer, to be sure that the patient remains stable, before discontinuing the IV. Clostridium-difficile-pseudomembranous-enterocolitis can result by administration of clindamycin. Uncontrollable diarrhea results with antibiotics, to avoid this use acidophilus or yogurt which promotes the growth of the healthy gut flora. Clindamycin Orally, the single dose is 1200 mg once a week. For intramuscular injections, 300 -600 mg. taken once a week can be used. For sensitive patients, a local anesthetic may be applied to the injection site. Changing the needle tip, after drawing the medication into the syringe and before injecting, will avoid the problem of tissue irritation at the injection site, because it is the trace amount of medication on the tip of the needle that causes the tissue irritation.
- **Prednisone:** Patients with severe disease can use prednisone 5 mg daily. If a flare-up results due to the antibiotics then take a 5mg prednisone daily. They can use an additional tablet at night if they are in really severe flare. This is the first medicine one should try to stop as soon as their symptoms permit. Usually one lowers the dose of prednisone by about 1 mg per week. If a relapse of the symptoms occurs, than further reduction of the prednisone is not indicated. Blood levels of cortisol peak between 3 and 9am. It would, therefore, be safest to administer the prednisone in the morning. The most significant side effect of steroids is osteoporosis. Other side effects that usually occur at higher doses include adrenal insufficiency, cataract formation, Cushing's syndrome, diabetes, ulcers, herpes simplex and tuberculosis reactivation, insomnia, hypertension, myopathy, mood disorders and renal stones.
- One also needs to be concerned about the increased risk of peptic ulcer disease when using steroids & conventional non-steroidal anti-inflammatory. Persons receiving both of these medicines may have a 15 times greater risk of developing an ulcer. Use Magnesium supplements and drink milk or take yogurt between meals to help reduce the chances of stomach ulcers.
- Use **omega-3 fatty** acids 2-3 grams a day, use **curcumin** twice a day. Use whole eggs 2-3 a week
- **Remission:** The disease seems to be controlled if the morning stiffness, joint pain, joint swelling becomes less. It can also be checked by the lowering of the WBC and sedimentation rate.

Dr. Brown successfully treated over 10,000 patients with this protocol. He found that significant benefits from the treatment. In some patients the above protocol may not work they should follow the treatment guidelines for CIDP. Generally steroids, Remicade, non steroidal will help control symptoms.

Ankylosing Spondylitis (AS): This arthritis affects the spine, hips, shoulders, and knees affecting people in late adolescence or early adulthood. The hallmark of AS is the involvement sacroiliac (SI) joints (junction of spine and pelvis). The tendons & ligaments around the bones and joints in the spine become inflamed, resulting in pain and stiffness. Eighty percent of the patients are positive for HLA B-27. The disease course is highly variable, while some patients have episodes of transient back pain only, others have more chronic severe back pain that leads to differing degrees of spinal stiffness over time. In almost all cases the disease is characterized by acute painful episodes and remissions (periods where the problem settles). Respiratory, gastrointestinal or urinary infections are common in three months leading to the first symptoms. Heavy physical activity, stress, pregnancy, injury & surgery have been reported as triggers.

Symptoms:

- Chronic back pain for many months.
- Back pain during the night. (less distractions raise the pain level at night)
- Back stiffness lasting for extended periods in the morning or after periods of rest.
- Pain and tenderness in the ribs, shoulder blades, hips, thighs, shins, heels and spine.
- Recurring eye inflammation, redness, blurred vision, and sensitivity to bright light
- Improvement with exercise and motion
- Spinal stiffness in the mornings

Test: X-Ray of the spine shows a bamboo spine due to deformed vertebral bodies into an abnormal square shape. CRP & E.S.R. are elevated.

Please see the treatment guidelines under the rheumatoid Arthritis section (p 114)

Osteoarthritis (OA): Osteoarthritis behaves like an autoimmune disease, OA used to be called a degenerative joint disease and the most common form of arthritis. About $50 billion a year is spent on medical costs. Many studies have shown inflammation involved in OA, called a reactive arthritis. Osteoarthritis involves the breakdown of joint cartilage affecting every joint in the body, including the little finger joints, large hips, knees, lower back and feet. Initially OA may strike only one joint, later multiple joints become arthritic. These OA patients respond to anti inflammatory treatments including steroids, CRP is elevated in all patients with active arthritis. In reality OA an autoimmune disease. Antibodies against joint cartilage proteins were first reported in 2000 in OA, an IgG-type anti-TPI autoantibodies (triosephosphate isomerase antibody) are detected in the synovial fluid samples from the patients with OA, produced by the antigen-driven mechanism, this has a potential to be used as a diagnostic marker for OA. The presence of an antibody is enough proof to consider OA as an autoimmune arthritis. **Salmonella, Yersenia infections** are frequently associated with osteoarthritis; I consider OA as autoimmune arthritis which is caused by molecular mimicry thus treatment should be similar to other autoimmune arthritis.

Symptoms:

- Pain in any joint during or after use, or after a period of inactivity

- Discomfort in any joint before or during a change in the weather
- Swelling and stiffness in a joint, particularly after using it
- Bony lumps on the middle or end joints of your fingers or the base of your thumb
- Loss of joint flexibility or development of stiffness.

Tests: CRP level, X-ray joints which shows loss of joint space. The diagnosis is made on clinical examination of swollen joints.

Treatment: Following 16 months of treatment with Doxycycline in a recent study, indicated that the loss of joint space in the affected knee was **40% less** among participants taking Doxycycline. Tetracyclines have recently been shown to have "**chondroprotective**" effects in inflammatory arthritis. **Please see treatment guidelines under rheumatoid arthritis section page 114.**

Psoriasis is a chronic, inflammatory skin disease. Involving knees, elbows, scalp, trunk, and nails. The inflamed skin cells are thought to cause the silvery white scales that are characteristic of plaque-type psoriasis. There are several types of psoriasis.
Symptoms: The red, thickened and rough patches of psoriasis may occur anywhere, but are commonly found on the scalp, elbows, knees, palms and soles. Other symptoms include:

- Silvery white scales
- Pitted or dented fingernails and/or toenails
- Red lesion in the folds of the buttock abdomen, face and arms
- Joint pain suggesting arthritis
- Numbness in feet (neuropathy)

Types of psoriasis

- **Guttate psoriasis:** Is usually triggered by a bacterial infection such as strep throat. Usually repeated episodes of skin lesions like sores are seen on trunk, arms, legs and scalp, especially with ongoing sub-clinical streptococcal throat infections.
- **Plaque psoriasis:** Plaque psoriasis is the most common presentation of psoriasis and affects the typical areas of the elbows, knees, umbilicus and lower back.
- **Pustular psoriasis.** A rare form of psoriasis occurs in patches over hands, fingertips or feet. Pus filled blisters appear after the skin becomes red and tender. Blisters may reappear several times accompanied by, chills, itching, weight loss, fever and fatigue, accompanied by sub-clinical streptococcal infections.
- **Inverse psoriasis.** The areas in the armpits, groin, under the breasts and buttocks, patches of red, inflamed skin are seen. Common in overweight people and is exacerbated by friction and sweating.
- **Erythrodermic psoriasis.** May be triggered by sunburns, by steroids and medications, peeling red rash develops over the whole body that may itch or burn.
- **Psoriatic arthritis.** Psoriatic arthritis causes pitted, discolored nails and the swollen, painful joints and conjunctivitis. Symptoms range from mild to severe. Stiffness and joint damage is seen.

Diagnosis: There are no specific tests for psoriasis. Rarely a skin biopsy will be done to confirm the diagnosis. ESR and CRP are elevated or normal.

Treatment:

- In Guttate the psoriasis is associated with tonsils infection. If repeated attacks of tonsillitis occur consider removing the tonsils. **Streptococcal throat infections can cause exacerbation of chronic plaque or** guttate **psoriasis. Psoriasis patients should report sore throat to their physician and that early treatment of streptococcal throat infections will benefit from penicillin.** Benzathine penicillin 1.2 million units, was given I.M. every two weeks. After 24 weeks Benzathine penicillin is reduced to 1.2 million units once a month used up to two years.
- **Vitamin D:** It is used in the treatment of moderate psoriasis. This cream, ointment, or solution is applied to the skin 2 times a day or use cod liver oil daily.
- Coal Tar: Coal tar is applied topically and is available as shampoo, bath oil, ointment, cream, gel, lotion, ointment, paste, and other types of preparations. The tar decreases itching and slows the production of excess skin cells.
- Corticosteroids. These creams or ointments are usually applied twice a day, but the dose depends on the severity of the psoriasis.
- Tree Bark Extract. Apply the cream, ointment, or paste sparingly to the patches on the skin. On the scalp, rub into affected areas. Avoid the forehead, eyes, and any skin that does not have patches. Do not apply excessive quantities.
- For arthritis associated with Psorasis, Start patient on Vibramycine 100mg twice a day, for two weeks. Also see the rheumatoid section for treatment.

Reactive Arthritis and Reiter's Syndrome: Reiter's syndrome is a clinical triad of **urethritis**, **conjunctivitis**, and **arthritis**. Reactive arthritis usually begins one to four weeks after a urinary or gastrointestinal tract infection. Causative organisms include **Chlamydia**, **Ureaplasma**, Shigella, Salmonella, Yersinia, and Campylobacter species. The arthritis tends to involve a **single joint**, preferentially affecting the joints of the **lower extremities**. It is of sudden onset, within a few days, many painful and swollen joints develop in an asymmetric distribution. Weight loss and fever has been seen in people with reactive arthritis. Persons with HLA-B27 are at increased risk for developing Reiter's syndrome after sexual contact or exposure to infections.

Symptoms:

- Acute diarrhea is a presenting manifestation with Shigella, Yersinia, or Salmonella infection. Diarrhea precedes the appearance of joint symptoms by up to one month.
- Conjunctivitis (red-eye) is present in up to 50 percent of patients
- Urethritis is non-infectious type; the urethritis may be mild or severe.
- Oral ulcers are common and may be painless, and a painless lesion of the glans penis, is present in males patients with reactive arthritis.
- Skin lesions on palms of the hands or the soles of the feet.

Test: HLA-B27 gene is present, ESR is elevated, and Chlamydia antibodies may be present.

Treatment

- Begins with NSAIDs. Sulfasalazine has been shown to be effective in patients with chronic reactive arthritis. Intra-articular corticosteroid injections can be effective in controlling disease in patient joints.
- Because of the bacterial etiology in reactive arthritis, there has been a possible role of antibiotic therapy in patients with the disease. Treatment options for uncomplicated urogenital infections include a single 1-g dose of Azithromycin orally, or doxycycline at a dosage of 100 mg orally twice per day for seven to 14 days. (can repeat dose)
- For conjunctivitis use an either doxycycline 100 mf daily for 2 weeks or Erythromycin ophthalmic ointment can be used.
- Magnetic Pulsar, electronic pulsar, Turmeric are all very effective in single joint involvement.

Scleroderma & C.R.E.S.T: Scleroderma is an autoimmune disease that can cause thickening, hardening, or tightening of the skin, blood vessels and internal organs. Scleroderma is chronic, which means it can last a long time. This is one disease in which the patients never gain weight, due to the effect it has on tightening their skin they all look skinny. They also have very hard hands, with skin around the fingers tight. They have difficulty swallowing as the esophagus is tight, so is the stomach wall tight and they cannot tolerate large meals. There are two types of scleroderma localized and systemic.

A)-Systemic Scleroderma (SS) also called systemic sclerosis, the immune system causes inflammation in the small blood vessels and the collagen-producing cells located in the skin and throughout the body. SS causes the small blood vessels in the fingers to be inflamed; this causes injuries on the hands and fingers to heal slowly. In severe cases, ulcers form on the hands and fingers. People with Systemic Scleroderma are usually cold-sensitive. The inflamed small blood vessels and the reduced blood supply cause cold temperature sensitivity. Systemic Scleroderma patients also have problems with their heart, lungs and gastrointestinal tract. These problems occur as tissue builds up in the skin and organs due to inflammation.

B)-Localized Scleroderma Localized Scleroderma is called **Morphea** affects the collagen-producing cells in just some areas of the body, and usually does not affect the internal organs and blood vessels. Localized Scleroderma can be seen as patches of thick skin or as a line of thick skin. The line may extend down a leg or arm.

C)-A sub type of scleroderma is called **CREST** which has a distinct set of characteristics that give the syndrome its acronymic name. These characteristics include:

- **C**alcinosis**.** Tiny calcium deposits form under your skin, on elbows, knees and fingers, can occur almost anywhere, in the body.
- **R**aynaud's phenomenon**.** Due to inflammation in the blood vessels the hands become cold.
- **E**sophageal dysfunction**.** Due to tightness of the stomach and swallowing tube (esophagus) the swallowing and retention of fluids in the stomach is difficult.

- **S**clerodactyly**.** Thick hard skin starts to calcify. This bone like hard areas can be seen on X-ray and visually.
- **T**elangiectasia**.** Small blood vessels start to form on lips and fingers look like small spiders.

Treatment:

- **Minocin or** Doxycycline has been reported to reverse the clinical findings in this disease and stop all further progression. A dose of 100 mg at night should be taken without food and lots of water. Treatment should continue over several months, three month minimum. **For the complete antibiotic protocol see the rheumatoid arthritis section.**
- Nifedipine, in dosages ranging from 30 to 60 mg daily, reduces the severity of Reynaud phenomenon and cold intolerance. Nifedipine is well tolerated, and the most common adverse effects are headaches, flushing, and edema of the feet and ankles. Pentoxifylline (400 mg, 3 times daily), alone or in combination with nifedipine, reduces blood viscosity by increasing red blood cell deformability and can be used to improve capillary function.
- Nanopulser electronic unit will reverse skin lesions within days.

Autoimmune Vasculitis: Vasculitis is an inflammation within the blood vessel walls. In all case this inflammation is autoimmune. Inflammation within the wall of the blood vessels will cause thickness of the vessel; inflammation in the lumen will cause thrombosis or occlusion of the vessel. These patients have symptoms which remit and relapse in cycles. Sub types of the inflammation are the following syndromes:

Giant Cell Arteritis, GCA (temporal arteritis) or **AION**: The optic nerve is an extension of the brain that connects the retina of the eye to the brain. The retina contains photoreceptors, cells that are activated by light and that connect to other retinal cells called ganglion cells. These, in turn, send information through projections called axons into the brain. By this route, the optic nerve gets visual impulses to the brain. Ischemic optic neuropathy, or "stroke of the optic nerve" also causes loss of vision in one eye can be autoimmune in most cases. **Anterior ischemic optic neuropathy (AION)**, may be caused due to acute loss of blood flow and ischemia to the front (anterior) part of the optic nerve (also called optic nerve head), which is supplied mainly by blood vessels called posterior ciliary arteries. The stroke is usually caused by inflammation in the blood vessels due to vasculitis triggered by the immune system. GCA is the most common form of vasculitis in the elderly usually seen in older women who present with a history of difficulty in chewing, headaches, scalp lesions and have large dilated temporal arteries. The patients will not touch the scalp as it hurts and they stop combing their hair. They will point to the area of the pain without touching it. The diagnosis is secured by an elevated **E.S.R**. This condition is a medical emergency if not treated the patient can go blind. Remember these are long term conditions and patients have to be treated for years. The most important complication of giant cell arteritis is visual loss in one or both eyes due to AION or retinal artery occlusion. Usually, visual loss is irreversible even with therapy.

Symptoms: Several instances of amaurosis fugax (transient blindness) may precede the blindness by up to six months Patients may have a new-onset headache, Pain on chewing may be unilateral, but it is more often bilateral (jaw claudicating), shoulder or hip pain (proximal myalgia), weight loss, and fever may lead to the diagnosis. Loss of vision in the affected eye with pupil reacting poorly to light reflex is diagnostic of an optic nerve lesion, in retinal or optic nerve disorders, if we shine light on the normal eye that pupil constricts, and then shine the light on the bad eye, instead of constricting the pupil dilates immediately in the bad eye. That is what is called a relative afferent pupillary defect. Some patients notice mini episodes of visual loss called amaurosis fugax while they are chewing food.
Laboratory Tests: Erythrocyte sedimentation rate is elevated, CRP is high, and anti-cardiolipin antibodies may be positive in arteritis, but none of this proves the diagnosis. Temporal artery biopsy is the gold standard for diagnosis of giant cell arteritis. Due to skip lesions, a negative result does not exclude the diagnosis. Homocysteine levels can be checked to look for elevation.
Treatment: Corticosteroid (prednisone) is the drug of choice to treat giant cell arteritis. Therapy is required for a long time, monitored by parameters of inflammation (ESR, CRP). A viral cause has been suspected but not confirmed in giant cell arteritis. An increased prevalence of antibodies against parainfluenza virus type-1 was reported in patient's giant-cell arteritis. Long term treatment is recommended with monthly monitoring of E.S.R. Using asprin one a day is recommended. Vibramycine 100 mg daily twice daily, for 8 weeks should be tried. (See chapter 28). Omega-3 oils are also effective at doses of 3000mg daily to reduce inflammation.

Takayasu arteritis was first described by a **Japanese Dermatologist**; it is a chronic inflammatory condition that affects the largest blood vessel in the body (the aorta) and its branches. The "typical" patient with Takayasu arteritis is a woman under the age of 40 who complains of headaches. Takayasu arteritis is occasionally called "pulseless disease", because of the difficulty in detecting peripheral pulses that sometimes occurs as a result of the narrowing of the blood vessel. On examination patients will usually have loss of pulses in arms and bruits in the neck. Large blood vessels are inflamed and sedimentation rate or CRP is elevated. These patients usually go to the neurologist seeking attention for headaches. The disease has been known to get worse after pregnancy and undiagnosed patients will develop stiffness and difficulty walking. Rarely severe stenosis in the subclavian artery will result in blood pressure difference between two arms, more then 15mm/Hg difference. Stenosis of subclavian will also cause mini strokes causing spinning type feelings. Mini strokes called TIA (transient ischemic attacks) may cause shining spots in the vision which may last upto hours. Takayasu patients may develop an iritis before the diagnosis of Takayasu.

Symptoms: Most young women present with complaints of headaches and sometimes they start to see shining lines in their eyes without a headache. Some will have complaints of arm pain, weakness and tiredness. Patients complain of generalized fatigue. Some may hear a noise in their

ear, which is caused by their pulse. Usually no pulses can be felt in the arms and on listening for bruits many are present in the neck and thighs. Blood pressure cannot be obtained in the arms.

Test: CRP and Sed rate both are elevated. Carotid ultrasound will show a swelling in the wall of the carotid artery (easily missed). MRI angiogram can show inflammation in arteries.

Treatment of Takayasu:

- A study done in Japan on twelve patients used **Minocycline 100mg twice** a **day for three months**. All the patients responded to treatment and nine went into complete remission of the disease. Another author reported improvement with **Clarithromycin** in Takayasu disease. Important medication to give is an Asprin to prevent mini strokes daily, and Fish oil twice a day to reduce inflammation. I do not recommend surgery if there is severe stenosis I/V steroids or IVIg can be used to reduce inflammation.
- **Disease responds well to prednisone and methotrexate**. Prednisone is started at 30 mg a day and the E.S.R. is monitored, dose is adjusted based upon the E.S.R. It is best to maintain the sed rate below 15mm/hr. (Please see the CIDP treatment section for a list of all the drugs which can be sued in autoimmune conditions).
- This randomized, placebo-controlled trial aimed to investigate the efficacy of a single course of IVIg (total dose 2 g/kg) in previously-treated systemic vasculitis with persistent disease activity in whom there was an intention to escalate therapy. Following the trail CRP levels were reduced after IVIg treatment and the effect lasted about three months.
- Another trail done at St George Hospital with IVIg this time in Wegener's granulomatosis resulted in all six patients improving. IVIg was well tolerated and all six patients had early reductions in disease activity. (Relapses will be seen after stopping IVIg treatment).
- Omega-3 oils, in dose of 3 gram daily with an Asprin or Turmeric should be used by all patients unless there are contraindications like stomach ulcers or bleeding disorders which can get worse by using Aspirin. Omega-3 oils need to be continued for long term and can be used to prevent relapses in Vasculitis.

Behcet's Disease (BD): This disease was first described by a Turkish dermatologist in 1930. Behcet's disease is most common along the "Old Silk Route", which spans the region from Japan, China in the Far East to the Mediterranean Sea, including countries such as Turkey Afghanistan, Pakistan and Iran. In Japan BD is the commonest cause of Blindness.
Behcet's disease involves blood vessels of all sizes and types, **and involving veins as well as arteries**. Because of the diversity of blood vessels it affects, manifestations of Behcet's may occur at many sites throughout the body. Recently (BD) has been associated with and Helicobacter pylori (HP), in a study of 13 patients with BD, the number and size of oral and genital ulcers diminished significantly and various clinical manifestations such as ulcers regressed after the eradication of HP.

Symptoms of Behcet's disease include recurrent ulcers in the mouth (resembling canker sores) and on the genitals, with eye inflammation. The disorder may also cause various types of skin

lesions, arthritis, bowel inflammation and encephalitis (inflammation of the Brain, which can cause confusion and loss of consciousness or seizures).

Test: **E.S.R. is elevated,** check for H-Pylori antibodies.

Diagnosis: A criteria put forth by an international group to help diagnose BD includes,

- Recurrent oral ulceration (at least three occasions in a year). In addition, a patient must also meet two of the following four criteria for Behcet's disease:
- Recurrent genital ulcerations,
- Eye inflammation (uveitis or retinal vasculitis),
- Skin lesions (erythema nodosum, lesions, acne),
- Positive "pathergy test". The pathergy test is a simple test in which the forearm is pricked with a small, sterile needle. Occurrence of a small red bump or pustule at the site of needle insertion constitutes a positive test. Although a positive pathergy test is helpful in the diagnosis of Behcet's, only a minority of Behcet's patients demonstrate the pathergy phenomenon

Treatment: We recommend using omeprazole (20 mg bd.), clarithromycin (500 mg bd.) and metronidazole (500 mg bd.) For two weeks. (In all patients, can repeat)

- For disease that is confined to (mouth, genitals, and skin), Azithromycin was effective in decreasing folliculitic lesions and reducing the healing time of oral ulcers. In BD topical steroids and non–immunosuppressive medications such as colchicines may be effective. Some patients require chronic, low doses of prednisone to reduce inflammation.
- In the event of serious end–organ involvement such as eye or central nervous system disease, both high doses of prednisone and some other form of immunosuppressive treatment with Azathioprine, cyclosporine, cyclophosphamide or chlorambucil.
- Neurological events such as Transverse Myelitis (Inflammation of spinal cord): use steroids, cyclophosphamide, or interferon-alpha. For detailed treatment look under CIDP.
- Omega-3 Oils are effective for controlling inflammation at a dose of 3000mg daily.

Churg-Strauss Syndrome (CSS): is an inflammation of blood vessels (vasculitis). This disease was first described in 1951 by Dr. Churg and Dr. Strauss A rare type of vasculitis which is often preceded by a history of **asthma**, and the disease begins with **sneezing and nasal congestion** (**allergic rhinitis**), often with **nasal polyps** and **sinusitis**. <u>If steroids doses are reduced quickly in asthmatics it can result in the development of CSS.</u>

Symptoms are asthma-like respiration. There is fever, involvement of skin, kidney and lung with eosinophilia. Later it may cause a neuropathy with numbness and pain.

The Criteria for diagnosis must have any four of the following findings.

- Asthma;
- Eosinophilia; (Blood cells which cause allergy)
- Mononeuropathy: (**facial palsy**, **hand weakness** or **drop foot**)
- Temporary infiltrates on chest X-rays;
- Paranasal sinus abnormalities. (Infection or inflammation in sinuses)

Test: ESR also called (erythrocyte sedimentation rate) is usually elevated. **IgE** is elevated. Skin and Food allergies need to be tested. Test for antigliadin antibody and H-pylori antibodies.

Treatment: Two week course of Doxycycline 200mg daily should be given and if it helps then 100mg alternate day treatment should be continued for another three weeks. CSS responds to prednisone. Initially, 40 mg/day prednisone is used. After 1-2 weeks this high dose of prednisone is gradually tapered down. Other immunosuppressive drugs, such as Azathioprine, cellcept, methotrexate, or cyclophosphamide may be used.
In cases which are resistant to treatment will greatly benefit from IVIg. It works well if there is multi organ involvement. Please see the IVIg section for dosing information.
Omalizumab is a recombinant humanized monoclonal antibody directed against immunoglobulin E (anti-IgE) to inhibit the immune system's response to allergen exposure, Omalizumab may become a useful tool for the treatment of CSS.

WEGENER'S is uncommon necrotizing vasculitis, with tumor like inflamed lesions called granuloma; these lesions are seen in the entire respiratory tract, and accompanied with kidney dysfunction called (glomerulonephritis). The lesions closely resemble those in polyarteritis nodosa. **Gum tissue grows thick with distinctive red and granular appearance of the gums** (**strawberry gingival**) due to inflammation. Rarely inflammation of the lacrimal gland is the first presenting symptom.

Symptoms are weakness, tiredness, weight loss, sinusitis, joint pains (polyarthralgia), ulcerations of the nasal septum, signs of renal disease, and fever. The disease occurs in young adults. Either sex may be affected. Death occurs in a matter of months, most often from kidney damage. Patients can present at age 80 with sinusitis unresponsive to antibiotic treatment.

Test: E.S.R. is elevated CRP and is elevated and slightly elevated c-ANCA (cytoplasmic-antineutrophil cytoplasmic antibody). Patients with the limited form of Wegener's granulomatosis are occasionally seronegative and respond well to therapy.

Treatment of Wegners: The first drug to try is Cotrimoxazole (**Septra or Bactrim**) Sulfamethoxazole and trimethoprim combination is used to treat infections, such as bronchitis, middle ear infection, urinary tract infection, and traveler's diarrhea. It is also used for the prevention and treatment of *Pneumocystis carinii* pneumonia (PCP) which contain. Cotrimoxazole seems to reduce the number of relapses in patients with this chronic disease at a dose of one tablet twice a day. **This can lead to complete clinical remission.** Dramatic improvement is seen with oral cyclophosphamide and prednisolone. Those who are unresponsive to above treatment may respond to cyclosporine. (More in the renal section)

Sjogren's syndrome is an autoimmune disorder in which immune cells attack and destroy the glands that produce tears and saliva. Sjogren's syndrome is associated with rheumatic disorders such as rheumatoid arthritis, may affect other organs of the body including the kidneys, blood vessels, lungs, liver, pancreas, and brain. In some cases this also causes an autoimmune neuropathy which should be considered as C.I.D.P. (treatment described in the neurology

chapter). Sjogren's syndrome affects 1-4 million people in the United States. Most people are more than 40 years old at the time of diagnosis. Women are 9 times more likely to have Sjogren's syndrome than men.

Symptoms: The hallmark symptoms of the disorder are dry mouth and dry eyes. In addition, Sjogren's syndrome may cause skin, nose, and vaginal dryness. There may be numbness in the feet or hands and arthritis with fatigue.

- Dry mouth, dry eyes, Dental cavities
- Fatigue and Fever
- Enlarged parotids which is a salivary gland, located behind the jaw and in front of your ears , Difficulty swallowing or chewing
- Change in sense of taste , Hoarseness
- Oral yeast infections, such as candidiasis
- Irritation and mild bleeding in your nose
- Skin rashes or dry skin , Vaginal dryness
- Dry cough that doesn't produce sputum
- Joint pain, swelling and stiffness

Test: H-Pylori antibodies present, ESR & CRP elevated. ANA antibodies are usually positive. Antibodies specific to Sjogrens syndrome (SS): anti-SS-A and SS-B; is (usually positive)

Treatment: The best treatment is to use vitamin B-12 on a daily basis. We recommend using omeprazole (20 mg bd.), clarithromycin (500 mg bd.) and metronidazole (500 mg bd.) For two weeks. For the treatment of arthritis in Sjogren's please see the guidelines described under rheumatoid arthritis section. Artificial tears are used to keep the easy wet. If a neuropathy is associated with Sjogrens the treatment is by following guidelines in the CIDP section.

Dermatomyositis & Polymyositis: Dermatomyositis is an autoimmune disorder that consists of inflammatory myopathy and skin manifestations. Polymyositis is an autoimmune inflammatory myopathy without any skin involvement. The average age at diagnosis is 40, and is seen twice as commonly in women as compared to men. In childhood these disorders occurs between 5 -12 years of age. The younger patients show a better prognosis.
Patients with dermatomyostis present with many systemic symptoms. The most common are proximal muscle weakness, difficulty speaking (dysphonia) or difficulty eating (dysphagia). Associated with shortness of breath, visual changes, abdominal pain and internal malignancy (small cell cancer can be present in dermatomyositis).

In Myositis the autoimmune attack targets the muscles; there is loss of muscle fibers in the hips and shoulders. People have difficulty getting out of the chair and difficulty holding their arms above the head. Women notice they cannot comb their hair. Children, who previously could

jump up from the floor, will use their hands to get up from the floor and use their hands by keeping them on the knees to push them up in a standing posture called (Gowers Sign).

Dermatomyositis skin signs:

- **Gottron's papules**, raised reddish skin lesions over the fingers, elbow or knee
- **Gottron's sign**, little spots or blemishes reddish, over fingers , elbow, knees
- **Mechanic's hand**, fissured, scaly hands with peeling skin.
- **Periungual telangiectasia** Small tiny blue or red blood vessels show up around the skin of the finger surrounding the nail
- **Shawl sign** reddish spots slightly raised distributed in a "shawl" pattern over the shoulders, arms and upper back.
- **Proximal Weakness,** difficulty raising arms and difficulty getting up from a chair.

Polymyositis patients just present with weakness and do not have any skin findings.

Diagnosis

- Neck flexor weakness (tested by placing the hand on the forehead and weakness can be seen as the person cannot move the head forward) along with weakness in elevating arms above shoulders or difficulty in getting out of a chair, it's called proximal weakness. Abnormal laboratory tests include elevated E.S.R., ANA can be positive CPK and LDH are usually elevated. Dermatomyositis patients need chest X-ray to rule out malignancy along with stool guaiac (blood test in stools at least three samples to check for malignancy). Polymyositis patients do not need any tests for malignancy.
- The muscle enzymes are usually elevated (CPK, LDH). I recommend a muscle biopsy; I have found this to be reported normal in spite of the patient having clinical Myopathy.
- Muscle Biopsy is usually diagnostic. It shows inflammation lots of white blood cells accompanied by muscle fibers showing atrophy in some areas. This is a classic finding in any autoimmune diseases. You will see some normal cells, some inflammation and some atrophic cells. (Biopsy should be done before the EMG test).
- EMG/NCV shows a myopathy pattern. Myopathic short duration, low-amplitude polyphasic units on voluntary activation appearance of small amplitudes polyphasic waves, there is rapid recruitment of motor units and complete interference pattern of reduced amplitude on weak effort. Increased spontaneous activity with fibrillations, complex repetitive discharges, and positive sharp waves;

Treatment of Myositis (Polymyositis –Dermatomyositis):

- Both conditions response to prednisone at a dose of 2mg/kg and this confirms the inflammatory myopathy. Case reports have shown that alcohol, and statins may cause the above syndromes. Other drug induced causes are penicillamine, nonsteroidal anti-inflammatory agents (nifluric acid and phenylbutazone), hydroxyurea (Hydrea), pravastatin (Pravachol), clofibrate (Atromid-S) and ipecac. Removal of the offending drugs will reverse the myopathy.

- Many studies have shown a benefit of low dose **Minocin 100 mg** taken on alternate days three times a week. Minocin needs to be taken for several months before a benefit is seen. Complete remission of all symptoms is obtained in most patients with Minocin. **Please see full protocol under Rheumatoid arthritis** section page 114.
- Magnesium supplements at 400mg two or three times a day help with the inflammation. If this is not available see the diet section or use MagPhop homeopathic supplement at 30-60 x potency 3-5 drops daily. Omega-3 are very useful for long term.
- Short term use of steroids is helpful in majority of the patients. For the protocol on immune modulator treatment look under CIDP treatment guidelines. Steroids are not recommended for long term therapy as they will cause proximal muscle weakness in the long run. I.V.I.G. helps please see the IVIg section for infusion guidelines
- If the patient does not improve with anti-inflammatory treatment then they need to be on a Gluten free diet. Which is they only eat Fruits, vegetables, Milk products, Fish, chicken and Beef. No Wheat, Rye or Barley and oats. Creatinine supplements are helpful if the patients have muscle atrophy.

Systemic Lupus Erythematosus is a chronic (long-lasting) autoimmune disease which affects joints, muscles and nearly every part of the body. **SLE is the single biggest killer of women all over the world**. Sharing a bedroom during childhood was associated with a higher risk of developing lupus in a study. A history of diarrhea type illness, rubella or mumps during the first year of life was also significantly associated with developing SLE later in life. New attacks of SLE are associated with exposure to, Hepatitis-C virus (HCV), Herpes-Zoster, Epstein-Barr virus and cytomegalovirus (CMV).

Drug-induced lupus shares characteristics with autoimmune lupus erythematosus (SLE). Some of the drugs which can trigger SLE are Minocycline, statins, anti-TNF-alpha agents, sulfadiazine, hydralazine, chlorpromazine, isoniazid, methyldopa, penicillamine, quinidine, beta blockers and anti antiepilepsy. The syndrome is characterized by arthralgia, myalgia, pleurisy, rash and fever in association with antinuclear antibodies in the serum. The recognition of drug-induced lupus is important because it reverses within a few weeks of stopping the inducing drug.

. **Symptoms:**

- Discoid Skin rash (scaly, disk-shaped sores on the face, neck or chest)
- Butterfly shaped rash over the cheeks and across the nose
- Sensitivity to sunlight, at times so severe they cannot tolerate the sun.
- Arthritis (pain, stiffness in joints) Fever, Anemia , Fatigue , Muscle aches
- Serositis (inflammation around the heart, lungs, & abdomen, causing pain and shortness of breath)
- Sensitivity to cold (Raynauds phenomenon) associated with CMV infection.
- Nausea ,Vomiting and diarrhea , Lack of appetite, Weight loss
- Kidney failure (protein leak) , Hypertension
- Seizures, strokes, confusion, Ulcers in the mouth.
- Immune deficiency (risk of infection)

Tests:

- A sedimentation rate (ESR) or C-reactive protein (CRP) are elevated.
- A urine analysis to detect kidney problems shows elevated protein.
- Chest X-rays to detect lung damage, EKG to detect heart problems.
- ANA antibody may be positive.(even the lowest titer is considered positive)
- Anti Hepatitis-C antibody may be present.
- IgG level & IgG subclass levels may be low showing immune deficiency.

Treatment Options:

- **Clarithromycin**, a Macrolides antibiotic, **used for 10 weeks** has led to clinical improvement in patients with SLE.
- If Hepatitis-C antibody is found then a combination therapy with, pegylated interferon and ribavirin is given or electronic pulsar is used. Prednisone and immunosuppressive drugs are primary treatment of SLE, for the complete management of immunosuppressive drugs please checks treatment guidelines under the **CIDP section**. IVIg is very effective treatment for SLE. If a deficiency of IgG or IgG subclass are seen then treat the immune deficiency with IVIg.
- Immunosuppressant in SLE can be accompanied by emergence of viral infections. There are many viruses associated with SLE; antiviral antibodies can be tested against all of them. Available antiviral treatments are. Chemo prophylactic regimens for cytomegalovirus (CMV), Epstein-Barr virus, herpes simplex are **oral acyclovir**, **intravenous and oral ganciclovir, famciclovir, valganciclovir and valacyclovir.** People with primary varicella-zoster virus (VZV) can receive VZV immune globulin after contact with either varicella or zoster. With treatment the prognosis is good and long term survival reported. Antibodies against all the viral infections are contained in IVIg including varicella zoster. If Varicella Zoster immune globulin is not available IVIG can be used in its place. Please see the IVIg section for IVIg dose guidelines. Electronic pulsar will work equally well without the above antiviral.

Antiphospholipid Syndrome (APS): Antiphospholipid syndrome, also known as Hughes syndrome, is an autoimmune disorder characterized by elevated levels of multiple antibodies (Y shaped proteins) that are associated with blood clots in veins and arteries. This condition is well known for causing an easily treatable infertility syndrome. **It is also associated with multiple complications of pregnancy including poor fetal growth.** In young people it is considered a common cause of heart attacks and strokes. **Celiac disease can cause APS syndrome.** Lupus anticoagulant (LAC) and anticardiolipin antibody (aPL) are antibodies associated with APS Syndrome. **In one study 85 % of APS patients had chronic active gastritis**. After helicobacter pylori eradication, disappearance of antiphospholipid antibodies syndrome has been reported. **Another study reported showed eradication of helicobacter pylori led to disappearance of ACA, LAC antibodies in 84 children.**

APS can present as:

- **Vascular thrombosis** (blood clot involving artery or vein)

- **Embolism** (blood clot that travels and occludes a distant blood vessel)
- **Infertility** (or as recurrent pregnancy loss).
- **Thrombocytopenia** (a low platelet count),
- **Pulmonary hypertension** (high blood pressure in the arteries that supply the lungs)
- **Sensorineural hearing loss** This is sometimes also called "nerve deafness"
- **Brief stroke-like episodes** transient weakness, numbness or loss of vision
- **Heart valve problems**, sometimes requiring valve surgery or valve replacement
- **Skin rash** Persistent or transient blotchy, lacy bluish rash (called livedo reticularis)
- **Skin ulcers**, commonly on the legs or feet due to occlusion of small blood vessels.
- **"Catastrophic" APS** – a life-threatening condition in which clots form in small blood vessels involving heart, lungs, brain, kidneys and causing them to dysfunction.
- **Seizures, Epilepsy & mini Strokes**.

Conditions associated with APS include:

- **Systemic Vascular Thrombosis:** The deep veins of the legs are the sites of blood clots, these clots break loose and form smaller clots, which can travel and involve virtually any vein or artery. Any patient presenting with thrombosis should be suspected for APS.
- **Pregnancy Loss and Other Complications:** APS is associated with infertility and recurrent miscarriages. Most studies have estimated 20-percent of pregnant women have aPL antibodies; most of these women do not have any signs or symptoms. Some women have recurrent (two or more) pregnancy losses. Pregnancies occurring in women with APS are at increased risk of miscarriage, fetal prematurity, and preeclampsia (high blood pressure during pregnancy). Pregnant women with APS are prone to develop deep vein thrombosis in the period following childbirth until the uterus returns to normal size.
- **Skin Disorders:** Livedo reticularis (mottled discoloration of the skin), ulcers on the skin, usually on the legs, and sometimes skin necrosis (black areas of skin after tissue dies).
- **Seizures, Stroke, TIA and neuropathy:** Strokes, (blood clotting a vessel of the brain). Multiple strokes can sometimes lead to a condition called **multi-infarct dementia.** Transient ischemic Attacks (TIA) are mini strokes from which the patient recovers fully within 24 hours. Seizures, chorea (uncontrolled dancing hand or arm movements), migraines, Guillain-Barre syndrome, neuropathy, transverse myelitis (a disorder caused by inflammation across the spinal cord), and multiple sclerosis have been seen in APS.
- **Heart Valve Disease:** Heart valve disease called **Libman-Sacks endocarditis** is sometimes seen in patients with aPL antibodies. In this condition, growths on the heart valve can break off and travel through the blood stream, causing embolic events.
- **Other Autoimmune Disorders:** APS is associated with other autoimmune disorders, including myasthenia gravis, Graves' disease, autoimmune hemolytic anemia.

Diagnosis: APS is suspected if a person experiences one or more episodes of thrombosis or pregnancy loss. Laboratory diagnosis of APS shows positive antiphospholipid antibodies (aPL) and the lupus anticoagulant (LA). Sed rate & CRP are elevated.

Treatment for APS

- If a person has **aPL** antibodies and a thrombotic event, a short-term course of **heparin** (an anticoagulant, which is a type of medication used to prevent blood clots from forming or getting bigger) is followed by long-term sometimes life-long treatment with **aspirin** 80 mg tablet taken daily.
- **Antibiotics: I recommend using typical 2 wk anti-H-Pylori therapy including omeprazole (20 mg bd.), clarithromycin (500 mg bd.) and metronidazole (500 mg bd.) (bd= twice daily)** (Please see the **gastric chapter** for more combinations).
- In women with moderate to high levels of aPL antibodies and a history of pregnancy loss who wish to get pregnant again. Aspirin alone can work in 70% of these patients. Once the patient gets pregnant they are also started on heparin 1000 units subcutaneously daily.
- Non responders to the above treatment. Make sure these patients have been evaluated for celiac disease; please see the celiac disease section for diagnosis and treatment. See the **IVIg section** for dose guidelines to control recurrent abortion during pregnancy.
- Steroid and cyclophosphamide pulses are used in all cases with neurological, cardiac and abdominal diseases. Check the **CIDP treatment** section for other drugs that can be used.

Fibromyalgia: Fibromyalgia syndrome (FMS) is a condition characterized by, soft tissue pain, non restful sleep, fatigue and areas of tenderness known as tender points. A study on FMS recently reported antibodies to serotonin receptors. Gangliosides and phospholipids antibodies are also found in about 70% of the patients with FMS. Other autoimmune diseases are usually associated with FMS. Frequent remissions and relapses are seen in FMS, the disease targets mainly women. People with Fibromyalgia have alterations in sleep pattern and changes in neuroendocrine transmitters such as serotonin, substance P, growth hormone and cortisol, along with dysregulation of the autonomic nervous system.
Symptoms of Fibromyalgia are usually triggered by injury which leads to poor sleep. The brainwave recordings of Fibromyalgia patients in sleep, show disturbance of the non-REM (non-**r**apid **e**ye **m**ovement) sleep phase, due to intrusions of alpha waves with infrequent progression to deeper stages of sleep. The alpha waves are only present when a person is awake and eyes are closed. As soon as the eyes open alpha disappears. These findings correlate with patient reports of awakening repeatedly and having unrefreshed sleep. Release of growth hormone occurs primarily during stages 3 and 4 of sleep. Patients with fibromyalgia have low insulin growth factor (IGF) levels, an indication of low growth hormone secretion. During the night our bodies produce melatonin which helps the body relax. Higher levels of melatonin cause inflammation, this type of sleep related inflammation is seen in many autoimmune including Fibromyalgia. FMS and rheumatic arthritis patients, wake up with stiffness and pain, **caused by increased melatonin production during sleep.** The pineal gland produces melatonin at night and produces histamine during the sunlight hours to help keep us active. In comparison the mouse pineal is exactly opposite and produces histamine during the night to help the mouse stay active in darkness**. Humans by creation are not suited for work during the dark hours.**

Mycoplasma and Lymes infections are frequent in Fibromyalgia patients and are an important cause of FMS. Recent reports show a higher rate of fibromyalgia in breast implant recipients.

Fibromyalgia symptoms: Stress is a common symptom & will usually trigger neck pain, sleep becomes disturbed early. Numbness, pain or stiffness can start on left or right side of the body. These symptoms will usually spread on that whole side. Attacks of diarrhea and constipation may start in some people. Pain shifts from one area to another, can be present all over the body. Pain and stiffness are worse in the morning, as the day goes on, stiffness and pain become less. Patients have tender points in their neck, shoulders, elbows, chest, hips, knees and ankles. Touching the tender points causes pain. Patients complain of "knots" in the neck and back, they hear grinding sounds on movement and assume their bones are cracking. The sound is actually caused by tight muscle fibers, as they are stretched. Poor sleep is common, and the person wakes up tired. They complain that they have the feeling of being run over by a truck. Fibromyalgia and Chronic Fatigue are overlapping conditions so please review both disorders. Painful and inflamed muscle fibers will appear swollen after activity.

Diagnosis: Fibromyalgia is easily diagnosed by history alone. The only examination needed is of tender points which are present over neck, shoulders, elbows, hips, knees and ankles. Tender point examination is done by placing your finger on the painful area and pushing it so that enough pressure is put so that the nail bed changes color from white to pink. This pressure on affected patients will cause pain. The patients will move slightly due to this pain when they are being examined. No blood tests are needed or x-rays are required for the diagnosis. A diagnostic criterion has been made by the American academy of Rheumatology but they have specified it should only be used for research purposes. Most of my patients will not fit these criteria,

Treatment:

- I recommend a two week trial of **doxycycline 200 mg daily** in all patients with Fibromyalgia. If this trail is of benefit then it can be repeated in responders, with a dose of 100mg on alternate nights. This is advised due to large number of patients being tested positive with Chlamydia pneumonia. Please see the **chapter 28** for details.
- **Azithromycin** 500mg on every Saturday and Sunday is recommended for 6-8 weeks.
- Supplement of **magnesium** will help with the pain and the improving sleep, dose 400 mg twice a day or just eat the leafy green vegetables rich in magnesium. The Brains biological clock and magnesium status are linked. Central magnesium regulation controls the suprachiasmatic nuclei and of pineal gland, which makes melatonin.
- **Mag Phosp** a homeopathic supplement 30-60x 3-5 drops a day helps pain.(mix in water)
- **DHEA:** Supplement is for those patients who have low cortisol, should be taken early in the morning before getting out of bed. Women need to watch out for the associated short temper they will get. DHEA tightens up the skin & makes the muscles stronger.
- **Vitamin B-**12, 1000 mcg sublingual & intramuscular supplements are effective in reducing pain, improving brain functions, energy levels and stamina.
- **Exercise**. Aerobic and strength-training activities and **stretching have been associated with a cure in FMS**. Stretching three to four times a day with brisk walking also helps. **Simple stretching has led to complete reversal of this disease.**
- **Acupuncture**. Acupuncture is an extremely useful analgesic treatment for FMS.
- **Hypnosis.** hypnosis improved functioning and reduced pain more than physical therapy
- Hyperbaric oxygen (HBO) therapy is effective in fibromyalgia.

- Drinking **warm** full 100% milk at night increase tryptophan and serotonin at night for a better sleep. Warming of the milk activates tryptophan in the milk. Tryptophan supplements in the body are converted to serotonin. This takes care of the depression. Tryptophan is available as a supplement; people can try this in place of milk.
- **Omega -3, 2000mg daily** is associated with improvements in sleep quality and fatigue.
- Please see the muscle stiffness chapter at the end of this book.
- Colostrum will also help in fibromyalgia as it provides IgG and helps relax muscles.
- Trigger point injections are helpful when injected subcutaneously into the painful area.

Chronic Fatigue Syndrome / Gulf war syndrome (GWS)**:** Chronic Fatigue syndrome (CFS), FMS (fibromyalgia) and Gulf war syndrome are inter-related. I find all three syndromes are just different expressions of the same problem. In chronic fatigue the main symptom is tiredness, which does not go away with normal sleep. I have discussed how elevated melatonin keeps these patients awake discussed in the FMS chapter above. In all humans a good night sleep should make them fresh again, this does not happen in CFS/FMS/GWS. Patients with CFS have frequent infections, they can be viral or bacterial, most common reported pathogen is Mycoplasma. Chronic fatigue syndrome can result from diverse causes which include exposure to toxins, pesticides, infections and every patient needs a tailor made workup. There are several immunological abnormalities reported in CFS, along with hormonal disturbances specially reduced production of cortisol. In a recent insecticide exposure 26 women developed fibromyalgia and chronic fatigue which caused long term disability. The pain component in these disorders is due to FMS.

Symptoms: Fatigue, tiredness no energy which is present even after a good night rest.

- Short-term memory loss or concentration problems
- Sore throat, frequent infections, night sweats, fever
- Multi-joint pain without joint swelling or redness
- Bowel disorders , constipation, diarrhea
- Headaches, Brain fog, Muscle pain
- Non-refreshing sleep, dry eyes, Increased thirst
- Post-exertional malaise lasting more than 24 hour, shortness of breath
- Lymph nodes palpable

Tests:

- Hormonal test. Check TSH, T3, T4, antithyroid antibodies, morning cortisol levels.
- Infections: antibodies against Cyto Megalo Virus, Epstein Barr virus, Human Herpes Virus 6, Chlymadia, H.-Pylori, Borrelia, Candida and Amoebae, Mycoplasma
- Immunological: IgG levels and IgG subclass levels.
- General Tests: CBC, CRP, B12 , B6 , Magnesium levels

Treatment:

- If any Hormonal or vitamin deficiency is found the specific deficiency needs to be treated. If B-12 deficiency is found automatically give h-pylori prophylaxis treatment as

shown in the gastric section. **Give B-12 intamuscular or sublingual daily even if no deficiency is found.**

- If the IgG levels or IgG-subclass levels are low then treatment with IVIg should be given. If IVIg is not available use colostrum supplement look at the end of this book in the colostrum section.
- If Borrelia or Chlymadia antibodies are present then give **200 mg Doxycycline** daily for two weeks. (**We recommend this antibiotic for all patients**) Dietary guidelines in the diet section should be followed. Please see **chapter 24** for antibiotic protocol.
- Some of the Gulf War veterans have been exposed to depleted uranium which result in Lymphoma or leukemia this would require treatment in a cancer center. Electronic pulsar treatment is effective in 70% of the patients. Consuming olive oil and cottage cheese in the morning, eating fruits using **dichloroacetate** (DCA) will help the cancer.
- Magnesium and Omega-3 supplements are beneficial for all patients.

Mixed Connective Tissue Disease (MCTD) & UCTD (undefined connective tissue disease):
These diseases are called 'overlap-syndromes'. Patients with MCTD have symptoms of lupus, scleroderma, myositis and rheumatoid arthritis, appearing together with antibodies against one specific antigen, namely RNP (**r**ibonuclear **p**rotein **a**ntibody). It is thought to be a distinct disease entity and called MCTD. Polyvinylchloride (PVC) exposure is associated with MCTD. Sjogrens syndrome is very common in MCTD. The prognosis is favorable if the disease is adequately treated. There is a tendency for MCTD to evolve into SLE or systemic sclerosis. In the last stages of MCTD development of pulmonary hypertension, scleroderma or renal crisis can result in death.
At times the patient's symptoms may not be well defined. That is why the term UCTD (**undefined connective tissue disease**) is used. Commonly Raynauds phenomenon, joint pains, arthritis and muscle pains symptoms are usually present. The evolution is very diverse, some patients remain in early phase and never progress while others evolve quickly into a real form of lupus or another type of connective tissue disease.

Symptoms of MCTD:

- **Arthritis**: multiple joints can have arthritis.
- **Esophagus** (difficulty in swallowing)
- **Heart inflammation** of hearts outer covering layer called pericardium causes (pericarditis) may be acute. The heart muscle itself gets inflamed resulting in (Myocarditis), which may cause heart failure or arrhythmia.
- **Lungs**: (shortness of breath)
- **Myositis** (inflammation of muscles causing shoulder, arm and hip weakness)
- **Neurological**, aseptic meningitis (severe headache without an infection), seizures, encephalopathy, transverse Myelitis, ataxia, aseptic meningitis, blindness, trigeminal sensory neuropathy, polyneuropathy and entrapment neuropathy seizure and gait disturbance , reversible dementia, psychological issues, facial nerves paralysis is seen.
- **Sjogrens syndrome**: Mucous membranes of skin (mouth, vagina) and the eyes may be dry due to the Sjogrens Syndrome.
- **Trigeminal Neuralgia:** Attacks of pain in the face or jaw are usually the first symptoms of MCTD syndrome.

- **Raynaud's phenomenon**: (hands feet and nose are painful on exposure to cold).
- **Rena**l involvement is rare
- **Swollen fingers** (due to mild arthritis)
- **Sclerodactyly** (thin fingers with hard tight skin and limited mobility).

Diagnosis of MCTD: The diagnosis is based on complaints, symptoms and organ involvement and on the presence of **anti-RNP antibodies.** This is the only connective tissue disease for which one specific type of antibody is necessary to make a diagnosis.

Treatment of MCTD:

- Treatments with a **Doxycycline** for 6 weeks are very useful. Most of my cases reverse in two weeks and have not relapsed.
- **Clarithromycin**, a Macrolides antibiotic, used for 10 weeks has led to clinical improvement in patients with UCTD.

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Chapter 11 Psychiatric Autoimmune Disease

Autism: Autism consists of behavioral symptoms with dysfunction in social interaction and communication in affected children. It is typically associated with restrictive, repetitive behavior and manifests within the first 3 years of life. Autism has multiple causes (etiologies) with both genetic and environmental, dietary contributions, which may explain the spectrum of behaviors seen in this disorder. One proposed etiology for autism is viral infection which can cause an autoimmune reaction. The mechanism, by which viral infection may lead to autism, be it through molecular mimicry of the central nervous system (CNS), through infection elsewhere in the body acting as a trigger for disease in the CNS. There have also been several studies reporting either gluten (in grain) or casein (in milk), or both casein and gluten can trigger the immune dysfunction. Autoantibodies (IgG) to **n**euron-**a**xon **f**ilament **p**rotein (NAFP) and **g**lial **f**ibrillary **a**cidic **p**rotein (GFAP) are significantly increased in autistic patients. Studies showing elevated brain specific antibodies in autism support an autoimmune mechanism. Virus specific antibodies associated with measles virus have also been demonstrated in autistic subjects

There was a relationship between vaccination and Autism. Environmental exposure to mercury is believed to harm human health by modulation of immune homeostasis. A mercury link with the immune system had been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines. However those vaccines containing Thimerosal have been phased out in U.S.A. Still there are reports that some children have higher mercury levels in their hair analysis. Mercury occurs naturally in the environment. According to FDA toxicologist, approximately 2,700 to 6,000 tons of mercury is released annually into the atmosphere naturally by degassing from the Earth's crust and oceans. Another 2,000 to 3,000 tons are released annually into the atmosphere by human activities, primarily from burning household and industrial wastes, and especially from fossil fuels such as coal. A significant

percentage of children with autism develop anti-SK (streptokinase), anti-gliadin and casein peptides and anti-ethyl mercury antibodies

Multiple reports show an association between CMV and Autism. One autistic child who also had (ALPS) was treated with **steroids** and made a good recovery. A report on two case of autism which developed at age 3 after a infection were treated with **ACTH** both patients improved, and one of them who got ACTH soon after the infection **had complete resolution of his symptoms.**

Some of the abnormalities seen in autism may be caused by chemicals like MSG, causing hyperstimulation of the glutamate receptors. Glutamate is the most abundant excitatory neurotransmitter in the nervous system. In excess, glutamate triggers a process called excitotoxicity, causing neuronal damage and eventual cell death. Microinjection of glutamate into neurons produces spontaneous seizure like activity. Many reports have shown increases of glutamate in blood and platelets of autistic subjects. Autopsy studies in subjects with autism have shown specific abnormalities in the glutamate receptors and glutamate transporters in the cerebellum. These abnormalities may be directly involved in the pathogenesis of Autism. Glutamate maintains its toxicity in animals even when administered orally. Males appear to be more sensitive than females to excitotoxins triggers. Excess excitotoxins cause an imbalance in the flow of calcium, which leads to activation of a complex inflammatory cascade, release of inflammatory mediators and ultimately causes the death of neurons.

Symptoms of autism: The symptoms will present in each child differently. For instance, a child may have some trouble learning to read or exhibit extremely poor social interaction.

- Problems developing nonverbal communication skills, such as eye-to-eye gazing, facial expressions, and body posture.
- Failure to establish friendships with children the same age.
- Lack of interest in sharing enjoyment, interests, or achievements with other.
- Lack of feelings. People with autism may have difficulty understanding another person's feelings, such as pain or sorrow.

Test: Testing for food allergies needs to be done and if any allergies are found then they should be addressed. Testing for IgG and IgG subclass levels should be done. If low levels, of (IgG or IgG subclass) are found, then the child is considered suffering from an immune deficiency and treatment with IVIg may be required. All the patients with autism should get a Gastro-intestinal evaluation to look for inflammation and antigliadin antibodies should be checked to evaluate for. **E.E.G.** can be done to evaluate for epilepsy. **M.R.I.** scan of the head is done to evaluate any brain damage.

Treatment recommendation**: Autistic children need to be placed on a special diet.**

- The diet needs to be free of excitotoxins triggers from the diet. This simply involves reading labels and closely monitoring food and supplement intake to avoid excitotoxins. Excitotoxins are neurotransmitters such as glutamate or aspartame that can excite the

nerves to death when their levels are not regulated properly. Foods or supplements that contain excitotoxins include MSG (monosodium glutamate), glutamic acid, glutamine, NutraSweet, aspartame, aspartame, and cysteine. Mercury and aluminum can also serve to trigger glutamate release. **MSG is found in most of the food prepared by major fast-food chains, in ice creams and restaurant foods**

- A diet free of Milk (casein free) to rule out milk allergy, and free of wheat, rye, barley, millet, oat (gluten free) to rule out Celiac disease. This diet should contain all the vegetables, corn, fruits, honey, rice, eggs, chicken, beef, fish and water. There is no ketchup in this diet if you want ketchup then get the gluten free. Try your child on this (casein free & milk free) diet for a month and if you see improvement, then you can try to introduce, milk products, slowly. If the child, cannot tolerate the milk products switch back to the Vegan diet (vegetarian diet). Conversely you need to try the gluten products and see if the child tolerates them. If the child can tolerate the gluten products then you will only need the milk free diet.
- If evidence of an H-pylori infection is found, then it needs to be treated. Gastritis responds to the use of colostrum and even by drinking IVIG in a cup orally.(Please see colostrum and IVIg section at the end of this book)
- If exposure to mercury is suspected then **try to remove Mercury by chelating**, Chinese parsley (**Cilantro**) cilantro has been used.(Has been used by dentist successfully to remove mercury in the body from dental amalgam adult dose is 100mg daily)
- If the child has a history of exposure to an infection and symptoms developed after infections, then Adrenocorticotropic hormone **ACTH** to reduce inflammation.
- A supplement that some parents feel is beneficial for an autistic child is Vitamin B6, taken with magnesium (which makes the vitamin effective). The result of research studies is mixed; some children respond positively, some not at all or very little.
- Behavior therapy and Omega -3 supplements are recommended in all cases. Cod Liver Oil is one of the best supplements at 1000mg daily. Reduce CLO in summer months or replace with Fish oil. Omega -3 are a ACTH replacement.
- If IgG or IgG-subclass levels are low consider IVIg treatment. Low levels mean the person has immune deficiency. Those who cannot get IVIg can try colostrum.
- For **epilepsy** treatment please see the **epilepsy section**.

P.A.N.D.A.S. & O.C.D. (N.I.H. guidelines) Obsessive compulsive disorder and other behavior disorder in children can be an autoimmune reaction triggered by streptococcal infections and have been called, **P**ediatric **A**utoimmune **N**europsychiatry **D**isorders **A**ssociated with **S**treptococcal infections. The following guidelines have been issued for PANDAS diagnosis.

Diagnosis of PANDAS is a clinical diagnosis, which means that there are no lab tests. Instead clinicians use 5 diagnostic criteria for the diagnosis of PANDAS

- Presence of Obsessive-compulsive disorder and /or a tic disorder
- Childhood onset of symptoms (age 3 years to puberty)
- Symptoms which are Waxing & Waning
- Association with group A Beta-hemolytic streptococcal infection (a positive throat culture for strep. or history of Scarlet Fever.)
- Association with neurological abnormalities (motor hyperactivity, or adventitious movements, such as chore form movements).

Like any other autoimmune disorder the symptoms are waxing & waning. Children with PANDAS seem to have dramatic ups and downs in their OCD and/or tic severity. Tics or OCD which are almost always present at a relatively consistent level do not represent an episodic course. Many kids with OCD or tics have good days and bad days, or even good weeks and bad weeks. However, patients with PANDAS have a very sudden onset or worsening of their symptoms, followed by a slow, gradual improvement. If they get another streptococcal infection, their symptoms suddenly worsen again. The increased symptom severity usually persists for several weeks, but can last for several months or longer. Children with PANDAS often experience one or more of the following symptoms in conjunction with their OCD and/or tics:

- ADHD symptoms (hyperactivity, inattention, fidgety)
- Separation anxiety (Child is, clingy and has difficulty separating from the caregivers. The child will not go to a different room from the parents.)
- Mood changes (irritability, sadness, emotional liability)
- Sleep disturbance, Joint pains
- Night- time bed wetting and/or day- time urinary frequency
- Fine/gross movement changes (e.g. changes in handwriting)

Test: for PANDAS: ASO (anti-streptococcal antibody) titer, which rises 3-6 weeks after a strep. Infection will be elevated in children with PANDAS. It is important to note that some grade-school aged children have chronically "elevated" titers. These may actually be in the normal range for that child, as there is a lot of patient variability in titer values. Because of this variability, doctors will often draw a titer when the child is sick, or shortly thereafter, and then draw another titer several weeks later to see if the titer is **"rising"** – if so, this is strong evidence that the illness was due to strep. (Of course, a less expensive way to make this determination is to take a throat culture for Strep at the time that the child is ill.)

Treatment of PANDAS:

- Penicillin antibiotics treat the sore throat or pharyngitis caused by the streptococcus. In PANDAS, the antibodies produced by the body in response to the streptococcus are the cause of the problem, not the bacteria themselves. **Penicillin and Azithromycin** Biaxin prophylaxis were found to be effective in decreasing streptococcal infections and

neuropsychiatric symptom among children with PANDAS who were treated for a year. The dose should be reduced and patients can be given even 50 mg weekly of Biaxin for long term prophylaxis.

- **Plasma exchange and IVIG** were both effective for the treatment of severe, streptococcus triggered OCD and tics, and that there were persistent benefits of the interventions results of a controlled trial of plasma exchange (also known as plasmapheresis) and immunoglobulin (IVIG) for the treatment of children in the PANDAS subgroup was published in The Lancet, Vol. 354, October 2, 1999.

Neuropsychiatric autoimmune syndromes & Autoimmune Depression:

Depression is one of the more common symptoms of autoimmune diseases, and commonly missed diagnoses by the general practitioner today. While an otherwise healthy patient can suddenly present with symptoms of primary depression, confusion, hallucinations, suicide attempts is difficult to understand. Though this is happening in quite a few medical patients, but most of them are not being diagnosed as having an underlying autoimmune problem. I propose that sudden psychiatric outbursts, suicides are the result of autoimmune disease. **A quick diagnosis combined with anti-inflammatory treatment can avoid hospitalizations and improve the person's quality of life**. Instead of usual psychiatric medications, immune modulators are better suited for these patients. Autoimmune disorders in general and SLE and primary Sjogrens in specific are potential causes of psychiatric manifestations.

Here is a case study of a young man who was admitted in the hospital for agitation. During the hospital stay he had auditory hallucinations and felt persecuted. He received antidepressant and the condition remitted in a few days. He was discharged, a few months later he was readmitted for agitation. He became calm quickly and was discharged home. A few months later, he was found in a coma, and admitted to the hospital. The spinal tap revealed blood cells. C.T scan of the head showed fresh blood within the spinal fluid. The diagnosis of cerebral bleeding due to vasculitis was made. After regaining consciousness, the patient complained of reduced vision. This was believed secondary to inflammation in the nerve going to the eye, and the patient's vision improved with prednisone. He was sent home after he was able to walk. He was admitted again with suicidal ideas, his mood improved progressively with antidepressant treatment. Later this patient started having memory problems and disorientation. Signs of confusion rapidly disappeared without treatment. His mood felt better after starting fluoxetine (Prozac) 40 mg/day. After being hospitalized for four occasions in one year, the diagnosis of Systemic Lupus Erythematosus with secondary Sjogren's syndrome was made. He received cyclophosphamide 2-gram intravenously, monthly six times. His vision improved, ocular dryness resolved, mood was stable and he did not suffer from hallucinations or delusion. (This is a true story reported in the medical literature). There are many patients like this one who still get treated by routine antidepressants. They keep returning to neurological and psychiatric facilities, some commit suicide and few if ever get diagnosed as having an autoimmune disease.
American College of Rheumatology has developed nomenclature and case definitions for neuropsychiatric lupus syndromes. The time has come to extend these guidelines to nearly all autoimmune disorders which can present with depression. This depression has a tendency to

cycle and is accompanied by remissions and relapses. Undiagnosed patients can suddenly committee suicide. The autoimmune depression is commonly seen in women after childbirth.

Tests: MRI scan for new brain lesions, EEG to check for epilepsy, Sedimentation rate and CRP are usually elevated. Antibodies like anticardiolipin and ANA are present. Complement levels are lower. B-12 levels, Thiamine levels and B-6 levels need to be checked as autoimmune gastric disease may cause deficiency of these vitamins.

Symptoms: Patients present with headaches, hallucinations, mood disorders, confusion, anxiety, strokes, visual disorders, memory disorders, seizures, weakness and numbness.

Treatment: Early treatment can stop the disease in its tracks. Antibiotic like **Rapamycin**, 2mg/day orally has helped many patients who were previously untreatable.
Prescription of corticosteroids or immunosuppressive drugs and specific antidepressant drugs, making sure to avoid lupus-inducing drugs in SLE and drugs with anticholinergic side effects which can make the eyes and mouth dry in Sjogrens syndrome. For the whole list of medications effective in autoimmune disorders please see the CIDP treatment section.

Post-traumatic stress disorder (PTSD): I am presenting my findings to show PTSD is an autoimmune disorder. PTSD is associated with other autoimmune diseases and tends to occur more frequently in women. PTSD is a debilitating condition that can develop following terrifying events. People with PTSD have persistent frightening thoughts and memories of their ordeal and feel emotionally numb, especially towards people they were once close to. PTSD was first brought to public attention by Vietnam War veterans, but it can result from any number of traumatic incidents. These include violent attacks such as mugging, rape, or torture; being kidnapped or held captive; child abuse; serious accidents such as car or train wrecks; and natural disasters such as floods or earthquakes. The event that triggers PTSD may be something that threatened the person's life or the life of someone close to him or her. PTSD also develops in innocent by-standards and rescue workers, such as massive death and destruction after a building is bombed or a plane crashes. It has been seen in patients undergoing complex surgery.
Studies have shown elevated levels of CRP an inflammatory market in people with PTSD. In other studies Interlukin-6 (IL-6). Which is released by inflammatory cells and is a mediator of bone resorption was found to be elevated in the saliva of people suffering from PTSD. Anaerobic bacteria are more frequently seen in patients with PTSD.

There is evidence that a part of the brain called amygdala-hippocampal region is involved in PTSD. The removal of this region and the resulting disconnection between right and left amygdala-hippocampal areas results in chronic PTSD symptoms. Smaller hippocampal volume has been reported in PTSD patients and this does not return to normal size in long term studies. People with PTSD have sudden blackouts, attacks of rage during which they have assaulted other people without any recollection of events later on. These attacks are most likely epileptic seizures. Thought studies done in PTSD patients to check for epilepsy they have been inconclusive, however many case reports have reported epilepsy in PTSD patients. Some have related epilepsy due to increased use of alcohol. Some studies done used peripheral electrodes to

monitor seizures. Peripheral electrodes will not demonstrate deep hippocampal seizures. **The loss of hippocampal cells seen in PTSD is probably due to inflammation and epilepsy.**

Treatment PTSD: In pre-surgical heart patients a dose of steroids was given before surgery and no symptoms of PTSD were seen in the patients getting steroids. I think the use of steroids would benefit the people suffering from PTSD. As PTSD is associated with a high mortality and development of other autoimmune diseases, these patients need anti-inflammatory treatment. Blackouts reported by patients should be investigated in epilepsy centers and appropriately treated. Please see the **epilepsy section** for management of seizures under inflammatory conditions. PTSD needs to be managed like an autoimmune disorder. Omega-3 oil supplements (fish oil, Flaxseed oil, olive oil) are of benefit taken from 2-3 grams a day. Curcumin taken twice a day helps, prednisone at onset helps lower symptoms. Course of broad spectrum antibiotics like Vibramycine and good oral hygiene help (see chapter 23, 24). CES units are helpful (C-27).

Schizophrenia: This is an autoimmune triggered thought disorder and very similar to P.A.N.D.A.S. Schizophrenia can be triggered by streptococcal infection, Toxoplasma gondii, Chlamydia (C.psittaci, C. pneumoniae and Chlamydia trachomati), Mycoplasma, cytomegalovirus, and human herpesvirus type-6.

- **Symptoms:** Schizophrenia patients usually complain of **hearing voices in their heads**. These voices may tell them to do things even consider suicide. One patient complained that "they" had implanted a camera in his eyes. From this camera, "they" could see what he was doing. We all hear voices in our head but very few actually start believing in them. Usually these patients complain that someone is following them. They will often look outside the windows; usually say that either the police or some security agency is chasing them. They often look at the doors, to see if they are locked. Paranoid ideas are common; they are in constant fear of being observed. These patients may also be able to see space ships from outer space. They will communicate with people or things not seen by others. Patients usually bring with them advanced architectural drawings and scientific plans which they have been working on for years. Some patients behave like they have become rich investors and will have detailed knowledge to impress bankers, who may even consider awarding them a loan. Some complain of being followed.

  Tests for Schizophrenia:
- Serum and CSF antibodies to Toxoplasmosis gondii, Chlamydia (C.psittaci, C. pneumoniae and Chlamydia trachomati), Mycoplasma, cytomegalovirus, and human herpesvirus-6.
- ASO titers are usually elevated.

Traetment Plan: The patient can be treated based upon the test results. If there is a history of exposure to cats and Toxplasmosis is confirmed by antibodies then treat with **pyrimethamine**. If

the patient has elevated ASO titers then treat with benzathine penicillin. For Mycoplasma and Chlamydia use **Vibramycine and Azithromycin**. IVIg will be universally effective in most patients. Electronic Pulsar treatments help most patients without any accompanying medication.

Chapter 13 Autoimmune Gastrointestinal Disorders

Autoimmune inflammatory gastritis (AIG) atrophic gastritis or chronic gastritis:

The stomach acts as the storage area for meals and can hold up to 1.5 liters of food and fluid. Special cells (**parietal cells**) secrete hydrochloric acid that helps break down food in the stomach. Other cells release protein-digesting enzymes (**pepsinogens**) which become active in the acid environment and starts digesting protein. A substance called (**intrinsic factor**) which is necessary for the body to absorb vitamin B12 from the diet is also released here. Contractions of the stomach are important for grinding and mixing ingested food with the gastric secretions.

Autoimmune inflammatory gastritis (AIG) is a disease leading to shrinkage of the stomach (**gastric atrophy**), lowering of acidity (**hypochlorydria**), and eventually causing vitamin-B12 deficiency which results in pernicious anemia. Helicobacter pylori (H-p) infection is the cause of chronic gastritis which if left untreated progresses to atrophic gastritis. H-p gastritis is usually life long disease. Atrophic gastritis causes B-12 deficiency. **In patients presenting with B12 deficiency an evaluation needs to be done for autoimmune atrophic gastritis.** H-p infection is among the most common bacterial infections in humans and it is associated with, chronic gastritis, duodenal & gastric ulcers, mucosal atrophy, gastric carcinoma and gastric lymphoma

Symptoms of AIG:

- Upper abdominal pain, burning, indigestion either worse or better when you eat
- Nausea and Vomiting, Loss of appetite, Weight loss
- A feeling of fullness in your upper abdomen long after eating
- Weakness, faintness, tired feeling, no energy, **black or dark stools**

Diagnosis OF AIG:

- **Upper gastrointestinal endoscopy.** An endoscope with a thin tube containing a tiny camera, through your mouth (or occasionally nose) and down into your stomach to look at the stomach lining and check for inflammation and may remove a tiny biopsy of tissue which show lymphocytic infiltrates in the gastric mucosa biopsy
- **Blood test.** Red blood cell count to see whether you have anemia, which means that you do not have enough red blood cells. Anemia can be caused by bleeding from the stomach.
- **Stool test.** This test checks for the presence of blood in your stool, a sign of bleeding. Stool test may also be used to detect the presence of *H. pylori* in the digestive tract.
- **Serum anti-parietal cell autoantibodies** are detectable the level is higher in early stages level is lower in late atrophic stages and then risk of stomach cancer is relatively higher.
- **B12 Vitamin** may be low in the blood. Serum pepsinogen-I and h-pylori antibodies seen.

Treatment of autoimmune Gastritis: H. pylori infection is associated with a number of important diseases including chronic active gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, gastric polyps, and gastric cancer.
Please see the antibiotic treatment guidelines in the Gastric ulcer section below.

Gastric & Duodenal ulcer (Autoimmune): The small intestine is divided into three functional regions: the duodenum, jejunum, and ileum. The stomach empties its contents into the duodenum, which is the first part of the small intestine. Here the contents are mixed with pancreatic enzymes (juices) and bile and most of the carbohydrates are absorbed in the duodenum. The cells lining the duodenum contains specialized groups of cells that produce chemicals which help digestion, provide immune defenses, and hormones that help to control coordination of digestive process of the intestine. These cells can be damaged by inflammation triggered by Helicobacter pylori (Hp), this causes Hp gastritis including duodenal ulcers, gastric ulcer, autoimmune gastritis, gastric carcinoma and gastric lymphoma. The role of Hp in duodenal ulcerogenesis is not associated with acid hypersecretion. Ulcers in the duodenum are autoimmune as there is low yield of Hp in duodenal biopsy. This Hp induced autoimmune injury in an important mechanism in duodenal ulcerogenesis; it results in the release of inflammatory cells produced as a result of molecular mimicry into the gastric and intestinal lumen. It affects the duodenum with delayed gastric emptying which is a vicious cycle. The slower the emptying of food the higher is the exposure to inflammation leading to greater gastritis. Aspirin like drugs can make an ulcer worse make sure the affected person should stop taking these medications.

Symptoms:

- **Pain** in the upper abdomen just below the sternum (breastbone) is the common symptom. It usually comes and goes (remitting relapsing). Abdominal pain can occur before meals, or when the person is hungry. It may be eased if you eat food, or take antacid medicines. The pain may wake the person from sleep.
- **Fullness** after a meal is felt by many people. Sometimes food makes the pain worse.
- **Bleeding** from the ulcer. This can range from a 'trickle' to a life-threatening bleed.

Test: Upper gastrointestinal endoscopy and H pylori antibodies are present.

Treatment: Treatment regimens include a two week **bismuth** based “pepto bismol therapy for two weeks.

1. Metronidazole (500 mg twice a day) and clarithromycin (500 mg twice a day) and a proton pump inhibitor (such as omeprazole 20 mg twice a day) for 14 days.
2. Amoxicillin (1 gram twice a day) and clarithromycin (500 mg twice a day) and a proton pump inhibitor (such as omeprazole 20 mg twice a day) for 14 days.
3. Amoxicillin (1 gram twice a day) and Metronidazole (500 mg twice a day) and a proton pump inhibitor (such as omeprazole 20 mg twice a day) for 14 days.
4. Bismuth subsalicylate (2 tablets 4 times a day) and tetracycline (500 mg 4 times a day) and either Metronidazole (250 mg 4 times a day) or clarithromycin (500 mg 3 times a day) for 14 days.

After the person has completed one of the above regimens, they need to be continued on a proton pump inhibitor (Omeprazole), Cimetidine, Ranitidine, or sucralfate for an additional 4-6 weeks. This will help allow the ulcer to heal completely. This course of therapy should destroy the bacterium in more than 90% of people. There are increasing reports of H. pylori being resistant to metronidazole. Therefore, in areas where there is a lot of resistance to this antibiotic, the other treatment options are being used first. If the person is treated for H. pylori and the ulcer does not come back, no further evaluation or treatment is needed. If the ulcer does come back, then they need testing to see if the H. pylori have truly been destroyed. Please see the diet section on how to avoid H.pylori infections. Honey, curcumin, Omega-3 oils are also helpful.
A quicker way to get rid of the gastritis is magnetic stimulation with a pulsar.

Celiac disease: Celiac disease (CD) is an autoimmune gastrointestinal disorder. A condition manifesting in genetically predisposed patients after exposure to wheat gluten. CD is characterized by inflammation, leading to injury to the cells lining the small intestine. The inflammation occurs due to molecular mimicry to gliadin, a protein found in such gluten-containing foods as **wheat**, rye, millet, oats and barley. Once gluten containing food is ingested by genetically susceptible patients, immune attack against the cells called Villi is triggered resulting in destruction of Villi. The mucosal damage and subsequent malabsorption of nutrients leads to symptoms of weakness, infertility, neuropathy with anorexia, bloating, constipation, and diarrhea. It is estimate that more than 2 million people in the United States have celiac disease statistically, celiac disease is on the rise in the United States.

Gluten is a, protein found in wheat, rye, oats, millet and barley. CD may be associated with neurological disorders, and the prevalence of epilepsy is higher in patients with CD. The antigliadin antibodies frequently found in CD patients are (antigliadin-A and antigliadin G antibodies respectively). Celiac disease is very damaging to the small intestine and can create many other problems, such as electrolyte imbalances, cardiac arrhythmias, villus atrophy, and short stature because of the diminished ability to properly absorb nutrients

Symptoms and Observations in Celiac disease: Some people with CD may have no symptoms.

- White matter lesions in the brain, which can cause epilepsy, cerebellar ataxia (difficulty in maintaining balance)
- **Cerebral occipital calcifications and epilepsy**
- Selective IgA deficiency, (Immunoglobulin A deficiency)
- Constipation or diarrhea, **pale foul-smelling**, fatty stool, abdominal bloating
- **Weight loss or weight gain**, Fatigue tired all the time.
- Unexplained anemia -(**a low count of red blood cells causing fatigue**)
- Bone or joint pain, muscle cramps, Osteoporosis, osteopenia – weak bones
- Cardiomyopathy- enlarged heart
- Behavioral changes- short temper (Psychiatric)
- Swollen lymph nodes around the intestines and Lymphoma
- Tingling numbness in the legs (from nerve damage) Neuropathy
- Iron deficiency anemia's due to reduced absorption of iron
- Missed menstrual periods (often because of excessive weight loss)

- **Infertility**, recurrent miscarriage
- **Short Stature** cannot gain weight in infants and children. Loss of weight.
- Pale sores inside the mouth, called pathos ulcers
- Tooth discoloration or loss of enamel
- Itchy skin rash called dermatitis herpetiformis
- Hepatitis (inflammation of the Liver)
- **Eyelid drooping**, and (Holmes-Adie syndrome) absent ankle jerks & eyelid drooping

Reactions to ingestion of gluten can be immediate, or delayed for weeks or even months. Some observations that demand attention in CD are,

- **Short stature** refers to being under-the-average height. Short stature results when childhood celiac disease prevents nutrient absorption during the years when nutrition is critical to a child's normal growth and development. Children who are diagnosed and treated before their growth stops may have a catch-up period
- **Lymphoma and adenocarcinoma** are cancers that can develop in the intestine.
- **Osteoporosis** is a condition in which the bones become weak, brittle, and prone to breaking. Poor calcium absorption contributes to osteoporosis.
- **Miscarriage and congenital malformation** of the baby, such as neural tube defects, are risks for pregnant women with untreated celiac disease due to malabsorption of nutrients.
- **Higher incidence in Down syndrome.** (In a study of 55 patients with Downs, 21 were found to have antigliadin IgG and IgA antibodies. Some also showed low albumin.)
- **Lactose Intolerance.** Develops in Celiac Disease.

Celiac disease can be confused with irritable bowel syndrome, iron-deficiency anemia caused by menstrual blood loss, Crohn's disease, diverticulitis, intestinal infections, and chronic fatigue syndrome. Since celiac disease is hereditary, family members, particularly first-degree relatives-meaning parents, siblings, or children of people who have been diagnosed-may wish to be tested for the disease. About 5 to 10 percent of an affected person's first-degree relatives will also have the disease. In 5 -10% of people with type-1 diabetes have biopsy-confirmed celiac disease and 5 to 10 percent of people with Down syndrome will be diagnosed with celiac disease.

Tests: The serum antgliadin antibodies can be tested. Additionally a biopsy of the small intestine can be done to evaluate for Villi atrophy. More than 90% of patients with celiac disease have the human leukocyte antigen (HLA DR3), (HLA DQ2), and (HLA DQ8).

Treatment of Celiac disease:

- Diet without Gluten (No Wheat, Rye, Barley, Millet, oats) "Plain without additives" **Meat, fish, rice, fruits, milk, cheese, yogurt, eggs and vegetables** do not contain gluten, so people with celiac disease can eat as much of these foods as they like.
- Cookies, Pasta, cakes, crackers, canned food especially soups, ketchup, mustard and soy sauce contain Gluten check the labels.

- Minority of patients who fail to respond to a gluten-free diet may require intervention with immunomodulating drugs, omega-3 oils, sublingual B-12 supplements, colostrum.
- Many studies show that infections may cause Crohn's disease and ulcerative colitis which can co exist with CD there are reports that antibiotics, a course of **Cipro 500-mg twice a day for ten days and metronidazole 250-mg four times a day** on alternate weeks for a month is helpful, check liver tests monthly. Tell patients to stop the metronidazole if they feel any strange nerve sensations.
- In resistant cases prednisone at 15 mg daily can be used and tapered after two weeks to help reduce inflammation.
- Several case reports have shown infliximab being used to induce a remission in refractory patient's with CD. Azathioprine has been used to induce remission in patients unresponsive to dietary treatment and sometimes steroids have been used.

Crohn's disease: Is a chronic, recurrent inflammatory disease of the intestinal tract, affecting the ileum (ileitis, regional enteritis), which is the last portion of the small bowel also involves the colon (Crohn's colitis). The condition begins as small, microscopic areas of inflammation which grows gradually. The lining of the bowel can then become ulcerated and the bowel wall thickened due to inflammation. Eventually, the bowel may become narrowed or obstructed. The bacteria that grow in the lower gut may, act to promote inflammation by molecular mimicry. The condition occurs in both sexes and among all age groups, although it most frequently begins in young people. Jewish people are at increased risk of developing Crohn's, while African Americans are at low risk, which indicates a genetic link in this disease.

Symptoms: When the **ileum** (final section of the small intestine, near the appendix) is involved, recurrent pain may be experienced in the right lower abdomen. This pain mimics acute appendicitis. Diarrhea (sometimes bloody) may occur, along with fever and weight loss. **Crohn's disease often affects the anal area where there may be a draining sinus tract called a fistula**. The disease usually runs the usual remitting relapsing course. Patients may develop Arthritis, eye and skin problems, in rarely chronic liver conditions and cancers may develop.

Tests: X-rays of the small intestine and colon (upper GI series and barium enema) are usually required. A visual examination (sigmoidoscopy) of the lining of the rectum and lower bowel is necessary. A exam of the colon (colonoscopy) is the best way of diagnosing the problem.

Treatment: Fasting on alternate days should be tried. Celiac diet should be tried on all patients, see the Celiac disease section. Increasing fluids in the diet help eliminate the toxins.

- **Antibiotics** Frequently a bacterial infection is present in Crohn's disease, antibiotics are often used to treat this problem. Commonly used are ciprofloxacin (Cipro 500 mg twice a day for two weeks) and metronidazole (Flagyl) 250 mg four times a day on alternate weeks for two weeks. The course can be repeated as needed. See the antibiotic section.
- **Cortisone or Steroids** Prednisone low dose is used to control flare ups, a dose of 40 mg is used at first and slowly tapered to 5 mg a day. A three week course is recommended.

- **Anti-inflammation drugs** Sulfasalazine (Azulfidine), a group of drugs called the 5-aminosalicylates. These drugs are useful in maintaining a remission, once the disease is brought under control. They are most effective when the disease is present in the colon. These are available in oral and enema preparations.

For a complete list of drugs including IVIg which is very effective in treating inflammation please see the list of drugs under the CIDP treatment guidelines. **Imuran or Azathioprine is avoided in Crohn's patients** as it is associated with an increased incidence of Pancreatitis.

Ulcerative Colitis: Ulcerative colitis is called **i**nflammatory **b**owel **d**isease (IBD), the general name for diseases that cause inflammation in the small intestine and colon. It can be difficult to diagnose because its symptoms are similar to other intestinal disorders and to another type of IBD called Crohn's disease. Crohn's disease differs because it causes inflammation deeper within the intestinal wall and can occur in other parts of the digestive system including the small intestine, mouth, esophagus, and stomach. Ulcerative colitis can occur in people of any age; it affects men and women equally and appears to run in families, with reports of up to 20 percent of people with ulcerative colitis having a family member or relative with ulcerative colitis or Crohn's disease. A higher incidence of ulcerative colitis is seen in Whites and people of Jewish descent. It is associated with bacteria called **Fusobacterium varium**.

Symptoms of ulcerative colitis: The most common symptoms of ulcerative colitis are abdominal pain and **bloody diarrhea**. Patients also may experience anemia, fatigue, weight loss, loss of appetite, rectal bleeding, skin lesions and joint pain

Tests in ulcerative colitis:

- Blood tests are done to check for anemia, which could indicate bleeding in the colon or rectum. The CRP & Sed rate may be elevated showing signs of inflammation.
- A stool sample can also reveal white blood cells, whose presence indicates ulcerative colitis or inflammatory disease. In addition, a stool sample allows the doctor to detect bleeding or infection in the colon or rectum caused by bacteria, a virus, or parasites.
- Colonoscopy or sigmoidoscopy are the best methods for making a diagnosis of ulcerative colitis and ruling-out other conditions like, Crohn's disease, diverticulitis, or cancer.

Treatment of UC: Amoxicillin, Vibramycine or Flagyl daily for 2 weeks should be given to eliminate Fusobacterium varium. Rest of medical management is described under the Crohns section; honey is an excellent supplement which will heal lesions in crohn's. Magnetic pulsation will terminate an attack quickly of colitis in all autoimmune diseases.

Autoimmune acalculous cholecystitis ACC (acalculous = no stone): The gallbladder is a small pear-shaped organ connected to the liver. The function of the gallbladder is to store bile which is made by the liver. Bile is a digestive liquid which emulsifies fats and neutralizes acids in partly digested food. The release occurs only with fatty foods.
Inflammation can occurs in any organ and the gall bladder is not spared. Unlike stones causing obstruction and pain in inflammatory gall bladder disease, there is vasculitis. Inflamed blood vessels cut of the blood flow to this organ. On Ultrasound the gall bladder is enlarged, it may

contain sludge. Usually the patients have SLE or Sjogrens. Microscopic examination of the gallbladder shows necrotizing angiitis of small arteries. Usually involves children, young women and rarely older men. The young women can have repeated attacks with multiple medical tests being negative; the diagnosis can be delayed for 8-10 months. If this condition can be diagnosed early, treatment with steroids can avoid surgery. It is estimated that cholecystitis occurs in 20 million people in the United States, and 500,000 people will undergo cholecystectomy annually.

Symptoms of ACC: Right upper abdominal pain. The pain is precipitated by fatty meals.

Tests of ACC: E.S.R. & CRP and WBC are elevated in response to inflammation. Abdominal ultrasound and CT scan showed enlargement of the gallbladder and sludge without within the gallbladder without any stones. Antiphospholipid antibodies are positive.

Treatment of ACC: Early treatment with **steroids** can help avoid surgery. If Antiphospholipid antibodies are seen, subcutaneous or intravenous heparin and asprin should be given, as severe multi organ failure can occur, due to blood clot formation and embolism. If steroids are not used and pain persists, then vasculitis will cause necrosis, within the gall bladder, which will require a emergency cholecystectomy.

Autoimmune hepatitis: The liver, located in the upper right side of the abdomen, acts as a filter to remove toxins (harmful substances) and waste products from the body, stores vitamins, minerals, and iron. It breaks down digested protein to amino-acids, eliminates chemicals from the body. All the blood coming from the stomach and intestines passes through the liver. The liver helps the body digest food and breaks down fats, by producing a substance called bile, which is stored in the gallbladder. Other functions, of the liver, include, processing hemoglobin and producing blood-clotting factors. A healthy liver filters blood, at a rate of about 1.5 quarts per minute.Autoimmune hepatitis is a disease in which the body's immune system is deceived to attack liver cells. This causes the liver to become inflamed (hepatitis). It occurs at any age and is more common among women than men between ages 12-40. About half of those have other autoimmune disorders, such as type-1 diabetes, kidney disease, thyroid disease, Sjogren's syndrome, autoimmune anemia, and ulcerative colitis.Autoimmune hepatitis includes hepatitis-C (HCV), Epstein Bar Virus (EBV) and Celiac disease associated hepatitis.

Symptoms: Fatigue is a common symptom of autoimmune hepatitis. Other symptoms include

- Jaundice, enlarged liver, fatigue,
- Itching, skin rashes, (abnormal blood vessels) on the skin
- Abdominal discomfort & joint pain
- Nausea vomiting loss of appetite
- Dark urine pale or gray colored stools

Diagnosis: These patients do not have hepatitis-A or B, they have hepatitis-C antibodies (anti-HCV positive). For at least six months these patients should have no sign of any other disease, causing liver failure, due to copper overload (**Wilson disease**), **alpha-1**-antitrypsin deficiency or liver failure due to iron overload called (**haemochromatosis**). Above diseases can be ruled out by obtaining copper levels in urine and iron levels in blood.

- **Blood tests**. A routine blood test for liver enzymes can help reveal a pattern typical of hepatitis, in autoimmune hepatitis; the immune system makes antinuclear antibodies (ANA), antibodies against smooth muscle cells (SMA), or liver and kidney microsomes (anti-LKM antibodies). The presence of these antibodies helps confirm the diagnosis of autoimmune hepatitis. Blood tests also help distinguish autoimmune hepatitis from viral hepatitis (such as hepatitis B or C) or a metabolic disease (such as Wilson's disease). Antibodies to check for celiac disease should be part of this evaluation. CRP and E.S.R. will be elevated.

- **Liver biopsy**. A tiny sample of the liver tissue, examined under a microscope, helps diagnose autoimmune hepatitis and tells how serious it is. Biopsy will show inflammation.

Treatment of hepatitis:

- Autoimmune hepatitis is treated with daily doses **Prednisone 20 to 40** mg per day and the dose can be lowered if the lab tests show improvement. The goal is to find the lowest possible dose that will control your disease. Early treatment stops the disease from getting worse, but may actually reverse some of the damage.
- **Azathioprine** (Imuran) is also used to treat autoimmune hepatitis. Like prednisone, Azathioprine suppresses the immune system, but in a different way. It helps lower the dose of prednisone needed, thereby reducing its side effects. Azathioprine and prednisone can be used together once your disease is under control.
- Most people will need to take prednisone, with or without Azathioprine, for years. Some people take it for life. Corticosteroids may slow down the disease, but everyone is different. In about one out of every three people, treatment can eventually be stopped. The disease can go into remission, with a lessening of severity of symptoms. Some people with a remission will see the relapses or disease return, they just need longer immunosuppression. Supplement of garlic in hepatitis is recommended.
- In HCV positive disease interferon is used. If the antgliadin antibody is positive then please see the section for Celiac disease for dietary guidelines.
- Magnetic pulsation of the Liver will resolve attacks of Hepatitis quickly,

Primary biliary cirrhosis (PBC) is a disease characterized by inflammatory destruction of the small bile ducts within the liver. PBC eventually leads to cirrhosis of the liver. It is an autoimmune disorder affecting mainly women.

Symptoms are pruritus (itching) and jaundice (yellow skin).

Test most commonly abnormal is elevated serum alkaline phosphatase.

Treatment is by Colchicine which helps inhibiting liver fibrosis and improves laboratory values. Vitamins, calcium and Ursodiol (Actigall or Urso), a bile acid help improve the patients condition. Liver Transplant is an option. Avoid alcohol in all forms.

Autoimmune Pancreatitis: AIP was first described by Yoshida in 1995. The pancreas is a small gland (weighing less than 8oz) located close to the stomach. Pancreas is an unusual gland; it has both endocrine and exocrine functions. Its endocrine function produces three hormones, **insulin** and **glucagon**, which control processing of carbohydrate metabolism. The third hormone, called **vasoactive intestinal polypeptide** (VIP) which controls intestinal movements, too much of the VIP causes a watery diarrhea and dehydration. The pancreas exocrine function produces digestive enzymes (trypsin, chymotrypsin, lipase, and amylase). These enzymes are passed into the duodenum through a channel called the pancreatic duct. In the duodenum, the enzymes begin the process of breaking down a variety of food components, proteins, fats, and starches.

Autoimmune pancreatitis (AIP) is a recently recognized benign condition with a presentation similar to pancreatic neoplasia but responds to corticosteroid therapy. **This is a relatively new autoimmune disease and a very important one. Millions of dollars are spent on the treatment of this disorder and the patients still fair poorly.** Patients present with pancreatic masses clinically and radiographically simulating pancreatic carcinoma, and bile duct strictures.

Recent report shows an association of Helicobacter pylori (H) infection, with AIP. In almost half the cases, autoimmune pancreatitis coexists with other autoimmune diseases such as Sjogrens syndrome, extra hepatic cholangitis, primary biliary cirrhosis, autoimmune hepatitis, gastric peptic ulceration, Thyroiditis and orbital pseudo tumors. Celiac disease can also cause an autoimmune pancreatitis which respond to dietary changes and steroids. The serum IgG4 determination provides a useful means of distinguishing autoimmune pancreatitis from other disorders of the pancreas or biliary tract. IgG-4 elevation will not be seen in all the cases of AP. There maybe some involvement of the liver and gallbladder due to mild inflammation in some cases. Lymphoplasmacytic sclerosing pancreatitis is also a autoimmune disorder.

Symptoms: Patients usually present with a 3-4 month history of **recurrent abdominal pain**, **jaundice** and **abdominal swelling**. There is Celiac and peripancreatic lymphadenopathy

Tests: Patients have an elevated serum levels or abnormalities in following

- Hypergammaglobulinemia, **(High levels of IgG)**
- High serum **IgG subclass 4 levels (IgG4)**
- Pancreatic enlargements on C.T scan of the abdomen and pseudocysts.
- Pancreatic duct strictures on Endoscopic retrograde pancreatography (ERP)
- C-reactive protein (CRP) is elevated, Sedimentation rate elevated
- Antibodies against human carbonic anhydrase, are frequently present
- ANA usually positive (can be negative)

Treatment, Pancreatitis should **be treated with 50 mg of prednisone daily.** This should be tapered after a week to 40 mg daily and then tapered by 10 mg every month. Omega-3 supplements can be used.

- Once the patient is treated with corticosteroids the elevated serum IgG4 level falls. Within two months of being on prednisone the patients is usually back to normal.
- H-pylori prophylaxis with antibiotics as mentioned under gastric ulcer treatments section.
- After prednisone is stopped start a anti-inflammatory treatments like aspirin.
- For non-responders consider IVIg and prednisone or plasmapheresis
- In properly treated cases, surgery and surgical complications can be avoided.
- Omega-3 supplements help, curcumin helps for long term prophylaxis.

Whipple's disease is a infectious disease that typically infects the bowel. It causes **malabsorption** primarily but may **affect any part of the body** including the **heart, lungs, brain, joints, and eyes.** It interferes with the body's ability to absorb certain nutrients. Whipple's disease causes weight loss, incomplete breakdown of carbohydrates or fats, and malfunctions of the immune system. When recognized and treated, Whipple's disease can usually be cured. Untreated, the disease may be fatal. Whipple's disease is caused by bacteria named ***Tropheryma whippelii*.** Patients have diarrhea, consists of multiple watery stools per day

Symptoms include diarrhea, intestinal bleeding, abdominal pain, loss of appetite, **weight loss**, fatigue, and weakness. **Arthritis** and **fever** often occur several years before intestinal symptoms develop. arthritis involve mainly the peripheral joints such as knees, elbows, fingers, ankles, and shoulders Skin hyperpigmentation with neurological symptoms of, increased sleep or loss of sleep, seizures, hemiparesis, dementia, ataxia, polyuria, loss of vision and swelling in the eye. Anemia is present in 90% of the patients. Lymph nodes are palpable and Lymphoma may be present. Ca

Diagnosis is based on symptoms and the results of a biopsy of tissue from the small intestine or other organs that are affected. PCR test is usually positive.

Treatment start with Doxycycline 100mg for two weeks then use trimethoprim-sulfamethoxazole (Septra) daily for a week then alternate day treatments for two years. Non responders are to be treated with ceftriaxone, chloroamphenicol.

Chapter 13 Autoimmune Hemolytic & Lymphoproliferative Diseases

Auto-immune Lymphoproliferative Syndrome. ALPS or **A**utoimmune **L**ympho**P**roliferative Syndrome. The word *lymphoproliferative* describes the unusually large numbers of white blood cells (called lymphocytes) stored in the lymph nodes and spleens of people with ALPS. Very low red blood cell counts (hemolytic anemia) are seen. Other common findings are below.

- Very low platelet counts (thrombocytopenia or ITP) that cause bruises, nose bleeds, and pose a risk for hemorrhage (excessive bleeding). Little blue or reddish spots called petechiae may also show up on the skin.
- Very low white blood cell counts (neutropenia), risk for bacterial infection.
- Less often, other autoimmune problems can occur in any organ

The immune system of people with ALPS is efficient in fighting germs. The problem in ALPS begins after an infection is over. In ALPS, apoptosis (programmed cell death) does not take place. Due to an excessive immune response, the white cells (lymphocytes) numbers are not reduced by the body, as it should after an infection is over. As a result, excess T and B cells gather in the lymph glands, liver and spleen. In ALPS, the B cells make a mistake. Instead of making antibodies against germs, the B cells make antibodies against platelets, red blood cells, or other cells. These antibodies become stuck to the platelets and red blood cells, which then get stuck in the spleen. The spleen has to work extra hard to filter out the sticky cells and the spleen gets big.

Symptoms: Weakness, fatigue, tiredness, pale color, excessive bruising, bleeding from the gums, multiple infections. Abdominal enlargement is present due to big spleen. Lymph nodes are enlarged all over the body.
Tests: CBC shows reduced red blood cells and increased lymphocytes, Platelets are reduced, Hemoglobin is reduced, Abdominal MRI will show a enlarged spleen, bone marrow biopsy and immunoglobulins test.
Diagnosis: Is based upon abnormal tests above and enlarged spleen, lymph nodes.

Treatment: Steroids are the first line of treatment for autoimmune episodes, like hemolytic anemia and *ITP*. One common steroid is **prednisone**. It is often given for a short time, but sometimes it is needed for longer periods. When prednisone is not enough to treat the episode, other drugs, such as Imuran and cyclosporin, may also be prescribed. *Blood Transfusions* are useful to replace red blood cells when anemia is severe.

- *Vaccines* are important to help prevent infections. The fewer infections you have, the less often you will need to "call in your troops." Which activates the disease.
- *IVIG and Rituxan are future treatments for ALPS.*
- *Omega-3 supplements help reduce inflammation.*

Autoimmune Hemophilia: Hemophilia has been called the Royal disease, it was seen in the European royal families, it is an inherited, bleeding and coagulation disorder. Children with hemophilia, lack the ability to stop bleeding, due to, low levels or absence of specific proteins, called "factors," in their blood. Clotting Factors, helps prevent excessive bleeding. There are many factors in the blood, which are involved in the function of forming clots to stop bleeding. A child with hemophilia is missing, or has a low supply of, one of the factors needed in order for the blood to clot. Two factors that affect blood clotting are factor VIII and factor IX. In about one-third of the children with hemophilia, there is no family history of the disorder. Yet some adults acquire this in later life. In late onset hemophilia the cause is mostly autoimmune and they have autoantibodies. Neutralizing alloantibodies (inhibitors) to factor VIII or factor IX develop in approximately 25% of patients with haemophilia-A and 3% of patients with haemophilia-B treated with factor concentrate. **Patients with high titre inhibitors do not respond to high doses of factor replacement and demonstrate resistance to treatment**.

Symptoms: Excessive bleeding due to poor clotting of blood.
Test: Neutralizing alloantibodies (inhibitors) to factor VIII or factor IX are present.

Treatment Alloantibodies against factors are rare but can cause life threatening bleeding, requiring costly, factor replacement and prolonged immunosuppression. These patient's have rapid resolution of the autoantibody, after treatment with **Rituximab** and low dose prednisone. Patients receive, 375 mg m(-2) of intravenous rituximab weekly for 4 weeks, followed by monthly infusiona, (up to 5 months) until inhibitor disappearance and establishment of normal Factor VIII pharmacokinetics (recovery and half-life). If long term treatment is required then cyclophosphamide is used.
Treatment of acquired Hemophilia. After two plasmaphereis sessions, no subsequent bleeding episodes are seen. Inhibitor levels decrease to undetectable levels within a median of 3 days, factor substitution can be stopped within a median of 12 days. Long-term follow-up (7 months-7 years) showed an overall response rate of 90% for complete remission.

The autoimmune hemolytic anemias (AIHA) are characterized by the premature destruction (hemolysis) of red blood cells, at a rate faster than they can be replaced. Acquired hemolytic anemias, are autoimmune diseases, which occur when the body's natural defenses against invading organisms destroy its own healthy tissues. Normally, the red blood cells (erythrocytes) have a life span of approximately 120 days before being removed by the spleen. In hemolytic anemias the erythrocyte destruction is much faster. Autoimmune hemolytic anemia occurs in different forms**, including warm antibody hemolytic anemia and cold antibody hemolytic anemia**. The appropriate therapy of autoimmune hemolytic anemia (AIHA) is dependent on the correct diagnosis and type of hemolytic disorder. Although, the majority of cases are warm AIHA, there are several distinct types of cold AIHA and a number of drug-induced etiologies of AIHA, which must be investigated, to determine if stopping a drug will induce a remission.
In **warm antibody** hemolytic anemia, the self-generated antibodies (autoantibodies) attach themselves and cause the destruction of the red blood cells, at **temperatures above normal** body temperature. In contrast, in the cases of cold antibody hemolytic anemia, the self-generated antibodies (autoantibodies) attach themselves and cause the destruction of the red blood cells at **temperatures below normal** body temperature.

Symptoms of AIHA:

- Pale skin appearance
- Yellowing appearance of the skin, eyes, and mouth
- Dark color of the urine
- Fever, weakness, dizziness, confusion.
- Intolerance to physical activity.
- Enlargement of the spleen and liver.
- Increased heart rate (tachycardia), and heart murmur.

Test: Autoimmune hemolytic anemia as the cause is confirmed when blood tests detect increased amounts of certain antibodies, attached to red blood cells (direct antiglobulin or Coombs test) Enzyme essays for antibodies against hepatitis-C, parvovirus B19 and Epstein-Barr virus.

Treatment of AIHA:

- In warm AIHA, corticosteroids intravenous pulses are standard treatment, followed by consideration of splenectomy in difficult cases. If steroids and splenectomy are insufficient, other forms of immunosuppressive Azathioprine is started. In cold AIHA, **keeping the patient warm** in often sufficient, but therapy directed at an underlying lympholiferative disorder may be helpful.
- Inadequate responses to therapy indicated by Hemolysis, and worsening anemia require transfusion therapy. When transfusion is urgently required and compatible blood cannot be located, incompatible blood may be provided as a life-saving measure.
- In the cold antibody type also known as paroxysmal cold hemoglobinuria, a disorder in which exposure to cold temperatures triggers massive hemolysis, is characterized by a unique biphasic cold autoantibody called the Donath-Landsteiner antibody. The treatment begins by keeping the patient warm, then plasmapheresis, prednisone, immunosuppressive drugs can be used.

Iron-deficiency anemia: **Iron** deficiency **is** the most frequently occurring anemia throughout the world. Gastrointestinal bleeding is the most common cause of iron deficiency in adult men and is second only to menstrual blood loss as a cause in women. Iron-deficiency anemia is not a autoimmune disease itself but a manifestation of an underlying autoimmune disease. Iron deficiency is a known complication of achlorhydria (reduced production of gastric acid) and may precede the development of pernicious anemia. (Vitamin B-12 deficiency anemia)

.**Symptoms and signs**: Persons suffering from iron deficiency anemia have pale skin color and experience shortness of breath, dizziness and frontal headache. Person cannot sleep well at night, due to continuous movements of legs (Restless leg syndrome).

- Tests: For iron status is the serum ferritin. C-reactive protein (CRP) should always accompany the analysis of serum ferritin. Routine blood tests to measure the size of the blood cells called CBC are done. Which show small size of red blood cells.
- Antigliadin –antibodies to check for celiac disease are obtained. H-pylori antibodies are checked and sed rate which is elevated.

Treatment: Treatment needs to target replacing the iron stores is usually done with oral iron therapy. The main indications for parenteral iron therapy are intolerance to oral iron, intestinal malabsorption and poor compliance to an oral regimen. (The best treatment plan looks into what caused the poor absorption of iron, celiac disease, colitis or gastritis induced by H-pylori. Please look for proper treatment plan for each disease under the section of Gastritis.)

ITP an autoimmune disease (Immune thrombocytopenia)**:** Immune thrombocytopenic purpura (ITP) is an autoimmune bleeding disease. Immune refers to the immune system's involvement in this disorder. Antibodies, part of the body's immunologic defense against infection, attach to blood platelet, cells that help stop bleeding, and cause their destruction. Thrombocytopenia refers to decrease in blood platelet. Purpura refers to the purplish-looking areas of the skin and mucous membranes (such as the lining of the mouth) where bleeding has occurred as a result of decreased platelet.
Idiopathic thrombocytopenic purpura is among the disease showing a stronger link with H-pylori infection. Review of the literature shows that H-pylori eradication in patients with idiopathic thrombocytopenic purpura is effective in increasing platelet count in approximately half of the cases. Acute (temporary) thrombocytopenic purpura is commonly seen in young children. Symptoms often, follow a viral infection. About 90 percent of children recover within a year and ITP doesn't return. ITP is considered chronic when it has lasted more than 6 months.

Symptoms: The main symptom is bleeding, which can include bruising "ecchymosis" and tiny red dots on the skin or mucous membranes "petechiae". In some instances bleeding from the nose, gums, digestive or urinary tracts may also occur. Rarely, bleeding within the brain occurs.

Tests: Platelets are reduced; H-Pylori antibodies may be present. A bone marrow test to verify that there are adequate platelet-forming cells (megakaryocyte). This will help rule out cancer.

Treatment:

- Most patients are given a short course of prednisone which usually gives a good response. Long term treatment with prednisone should not be given as it can cause cataracts or other neuromuscular complications.
- Following H-Pylori antibiotic treatment, half of the patients will not require any future drug treatments for ITP. Please read duodenal ulcer section for The H-Pylori protocols.
- IVIg treatments should be given to resistant cases and read IVIg dose protocol is in the IVIg chapter. If H.pylori eradication is not done, IVIg treatment may not help. Many other drugs are used in the treatment please look under CIDP treatment section. Some people will do a splenectomy if everything else has failed. Steroids work but are best avoided, can be used for the short term, as they can cause cataracts in children.

Lymphoma in autoimmune diseases: Lymphomas results from increased numbers of lymphocyte (an immune cell). Abnormal production of proteins prevents the lymphocyte cells from dying when they should, the same protein causes rapid cell division that produces more lymphocytes. These malignant lymphocyte cells accumulate to form tumors that enlarge in the lymph nodes and spread throughout the lymphatic system, including spleen or bone marrow. Lymphoma can also appear outside the lymphatic system.

Common infective organism like, "**H-pylori, C-jejuni, B-burgdorferi, C-psittaci, and hepatitis-C virus (HCV)**, all have been associated with gastric lymphoma, immunoproliferative small intestinal disease, cutaneous lymphoma, ocular lymphoma, and spleen lymphoma.

Many organs are targeted by an immune process due to the lymphoproliferative disease: they include **skin** (paraneoplastic pemphigus, vasculitis, and urticaria), **nervous system** (neuropathy, multifocal motor neuropathy), **hematological** (immune anemia, acquired bleeding disorders), **rheumatologic** (arthritis, systemic vasculitis, and myositis) and renal (cryoglobulinemia, glomerulopathies). A higher prevalence of autoantibodies, such as antinuclear antibodies, Antiphospholipid antibodies are seen in autoimmune lymphomas. Autoimmune diseases and lymphoma type malignancies are closely related. Lymphomas occur more frequently in the course of autoimmune diseases. An increased incidence of malignant lymphoma transformation has been described in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's syndrome (SS), and autoimmune thyroid disease. Patients with lymphoma may generate autoantibodies against various auto antigens. Anti-ssDNA antibodies were detected in the sera of 25% of patients with lymphomas, which become the cause of other autoimmune disease like Sjogrens, SLE and RA.

Symptoms in Lymphoma:

- Bone pain, arthritis
- Spinal cord involvement
- Anemia is seen with low levels of red blood cells, Low platelet levels, bone marrow
- Hypogammaglobulinemia caused by a decrease in immunoglobulin production
- Enlarged lymph nodes are rubbery and discrete and later become matted.
- Waldeyer's ring (lymph-nodes around the tonsils) Lymph nodes in chest (Mediastinal) and abdomen (retroperitoneal) lymphadenopathy may cause pressure symptoms on various organs. (**A**) Congestion and edema of the face and neck can result from pressure on the superior vena cava (superior vena cava or superior mediastinal syndrome), and (**B**) ureteral compression from pelvic lymph nodes may interfere with urinary flow and cause secondary renal failure.
- The acute illness of adult T-cell leukemia-lymphoma is characterized by a fulminating clinical course with skin infiltrates, lymphadenopathy, hepatosplenomegaly, and leukemia. The leukemic cells are malignant and hypercalcemia often seen.

Tests in Lymphoma:

- **Antibodies for** H-pylori, C-jejuni, B-burgdorferi, C-psittaci, and hepatitis-C virus (HCV) should be tested.
- Biopsy of bone marrow and lymph nodes
- MRI of the abdomen to look at tumors.

Treatment of Lymphoma:

- Ocular adnexal lymphoma can be treated by **doxycycline 300mg** daily for 3 weeks.

- A subset of H. pylori-positive gastric MALT lymphomas, **including infiltrative tumors, may respond to antibiotics**. The likelihood of early complete remission seems to be greatest for superficial and distal tumor, **amoxicillin 750** mg three times daily, and **clarithromycin, 500 mg** three times daily; combined with a proton pump inhibitor (lansoprazole or omeprazole) and bismuth subsalicylate. Eighty percent of gastric lymphoma maybe in continuous complete histologic remission after treatment..
- The monoclonal antibody anti-CD20 (rituximab), able to suppress the tumor cells and change the B-cell repertoire is the most promising treatment to cure immune disorders related to NHL. So far, rituximab has been successfully used in mixed cryoglobulinemia and cold agglutinins secondary to NHL.
- Nonresponders can be considered for ekectronic pulser, magnetic pulser therapy.

Cryoglobulinemia: Normally, immunoglobulins help the body fight infection. But when someone has cryoglobulinemia, these immunoglobulins clump together at low temperatures and cause organ damage and illness. Only three immunoglobulins (IgA, IgM and IgG) are involved in causing cryoglobulins. Cryoglobulinemia may be associated with liver disease, infections, rheumatic disease, multiple myeloma or lymphoma. Cryoglobulins are abnormal forms of protein molecules that precipitate at cold temperatures and redissolve at normal body temperature. When a person with cryoglobulinemia is exposed to cold, they may experience impaired circulation in the small blood vessels due to clumping of these proteins. This may lead to color changes in the skin, hives, ulcers and bleeding into the skin (purpura). Cryoglobulinemia can affect anyone, but the majority of people with cryoglobulinemia are in their 40s or 50s. Twice as many women as men have this disorder. **Cryoglobulinemia is not inherited.** Cryoglobulins disease is subdivided into **monoclonal** if only one type of antibody is involved example IgM or **polyclonal** if multiple immunoglobulins are involved (IgG, IgM, IgA). However the treatment is the same regardless of which chains are involved.
These disorders in a way are similar to Waldstrom's macroglobulinemia, monoclonal gammopathy of undetermined significance (MGUS) or its malignant form, multiple myeloma. All of which show abnormalities in immunoglobulins.

Cold agglutinins or cold autoantibodies are present in everyone at low titers. These natural cold autoantibodies occur at low titers of 1:60, normally and have no activity at higher temperatures. Pathologic cold agglutinins occur at higher titers and react at 29-30°C and sometimes at 37°C.

Symptoms of Cryoglobulinemia: Cold induced bleeding in the urine, or cold induced cough with bleeding, cold-induced skin rashes (urticaria), and arterial thrombosis with gangrene, bluish discoloration (cyanosis), retinal hemorrhage, cold hand (Raynaud's phenomenon), and arterial thrombosis are seen. Higher level of type-I cryoglobulins is associated with symptoms of hyperviscosity (poor circulation).

The Type-II and Type-III cryoglobulins are mixed (IgG, IgM, and IgA), they may be associated with arthritis, vasculitis, renal failure (glomerulonephritis), strokes or seizures. In patients with **m**ixed **e**ssential **c**ryoglobulinemia (**MEC**), a syndrome may occur that is associated with arthritis, palpable purpura, weakness, palpable lymp-nodes and hepatosplenomegaly. Glomerulonephritis (renal failure) is common in MEC. The MEC syndrome is often sequelae of infection with Hepatitis-B or Hepatitis-C virus, and may respond to interferon therapy.

Test : Person may have anemia, low platelets, low white cell counts, complement blood levels show, Low C4 levels. Serum antibodies usually present are:

- Hepatitis C virus (90%), Hepatitis B: Some patients.
- Myocplasma pneumonia antibodies.
- Cold agglutinin titer is elevated 1:2,048.
- Clonal B-cell infiltrates: Seen in Bone marrow or Liver biopsy.

Treatment:

- Warm blood transfusion is given, the patient is kept warm and immunosuppressive treatment with high dose steroids is effective. If the person has Mycoplasma infection , then Minocin/ Doxycycline 100 mg twice a day for two weeks should be used.
- In Hepatitis-C infection 6 or 8 million units (MU) of interferon alpha-2b every day for 2 weeks and then three times a week for 22 weeks plus 600 mg of **ribavirin** is helpful.
- Plasmapheresis and Rituximab are also useful in unresponsive patients

Acute intermittent porphyria (AIP) Porphyria has been suggested as an explanation for the origin of vampire and werewolf legends, based upon a number of similarities between this condition and the folklore. Similarity was based on people with porphyria having sun sensitivity. Porphyria cutanea tarda presents clinically as a pathological sensitivity of skin exposed to light causing scarring, skin and neurological symptoms. Porphyria is described here as it can be mistaken as a autoimmune disorder. It causes **epilepsy, neuropathy, reversible encephalopathy, abdominal pain crises, liver failure, skin lesions and neuropsychiatric disturbances**. In rare instances, however, AIP patients have presented with **acute cortical blindness.** Extreme photosensitivity is seen in porphyria. Medical history has suggested that the insanity exhibited by King George III was the result of porphyria. **British royal family (besides hemophilia), also carries a gene for porphyria.** Porphyria is a complex disorder and eight sub-types have been described. **Low plasma melatonin** levels in porphyric women suggest that a defect of the pineal hormone may be responsible for the recurrent aspect of porphyric attacks.

Symptoms: Cutaneous porphyrias Sunlight triggered blisters, itching, & swollen skin.
Symptoms in acute porphyrias:

- Pain in the chest, abdomen, limbs, or back;
- Blackouts or other spells of unresponsivness, family history of spells,
- Numbness, tingling, paralysis, or cramping; Visual Loss, Liver failure, abdominal pain.
- Vomiting; constipation; and personality changes or mental disorders.
- Ultraviolet light transforms porphyrins in the skin into toxins that cause skin fragility. The dorsal surfaces of the hands are the principal sites of bullae formation due to sun exposure & trauma. Shortly after bullae form, they rupture and become painful erosions that heal as atrophic scars. Hypertrichosis (particularly involving the face and forehead), hyperpigmentation, hypopigmentation, and excessive wrinkling also may occur.

Testing: Porphyria can be easily diagnosed by examining urine which turns dark on exposure to sunlight. Analysis of porphyrinogens in blood, urine and stool is elevated.

Treatment:

- Intravenous therapy with ham-arginate and antiepileptic therapy with gabapentine.
- **A high carbohydrate diet** is recommended in porphyria.
- **Chloroquine** (Aralen) Anti-inflammatory activity by and may have photoprotective effect. Use in porphyria requires small doses once a week. Larger doses may cause severe hepatic necrosis and death. Binds porphyrins and enhances excretion
- **Do Not Take These in Porphyria:** Barbiturates, Carbamazepine, Chloroquine, Ergotamines, Erythromycin, Estrogens, Ethanol, Ethosuximide, Fentanyl, Furosemide, Griseofulvin, Halothane, Hydralazine, Iron-compounds, Methyldopa, Nortriptyline, Phenytoin, Primidone, Pyrazinamide, Rifampin, Sulfonamides, Sulfonylureas, Theophylline, Tolbutamide, Valproic acid.

Chapter 14 Ear Autoimmune disorders: **Autoimmune inner ear disease, sudden hearing loss, vertigo or tinnitus & (Menieres)** Autoimmune inner ear disease or "AIED" consists of a syndrome of progressive hearing loss, noises in the ear or dizziness which is caused by antibodies, produced by our immune system, attacking the inner ear cells. The symptoms may remit and relapse and hearing loss can fluctuate between ears.

The ear is among the immune privileged areas, the body may not know about the inner ear antigens, and following injury they are released, then the body may mount an attack on these foreign antigens. Molecular mimicary triggered by a virus or bacteria also causes the immune system to generate antibodies causing accidental inner ear damage because the ear shares common antigens with a virus or bacteria.

Reduced hearing accompanied by ringing, hissing, roaring (tinnitus) which remits and relapses over months is commonly seen. Variants are bilateral attacks of hearing loss and tinnitus which resemble Menieres disease, and attacks of dizziness accompanied by abnormal blood tests for self-antibodies. Sudden onset of hearing loss is very common. Some patients with AIED may have balance symptoms.

Autoimmune sensorineural hearing loss (ASHL) originally was defined by the presence of progressive hearing loss (with or without vertigo) and a positive response to (prednisone) therapy. The hearing loss can be of sudden onset in one or both ears. Usually the remitting relapsing pattern is seen. Hearing loss can be rapidly progressive sensorineural type.
AIED is usually seen in people with following disorders, Systemic Lupus Erythematosus (SLE), Sjogren's syndrome (dry eye syndrome), ulcerative colitis, Wegener's granulomatosis (runny nose, cough and kidney involvement), Bechet's, rheumatoid arthritis, and scleroderma (tight skin over hands and face) can cause or be associated with AIED.

Symptoms of AIED are sudden hearing loss in one ear; sometimes it may involve both ears. The hearing loss can progress over weeks or months, symptoms can be waxing & waning Patients may feel fullness in the ear and experience spinning attacks. Patients also complain about something blocking the ear. Hearing may comeback. Symptoms can start after excessive use of gentamycine type of antibiotics.

Test: Antibodies to anti-68-kd antibodies, RPR to test for syphilis, antithyroid antibodies, antigliadin antibodies to test for celiac disease, Borrelia antibodies (IgG & IgM) for Lymes disease, CRP and E.S.R. are usually elevated. Ear testing will show sensorineural hearing loss.

Diagnosis of AIED is difficult and is often mistaken for otitis media, or sensorineural hearing loss. People with Menieres disease have AIED as the underlying cause.

Treatment:

- Doxycycline 100mg taken twice a day, for two weeks, will reverse most of the hearing disorders. Use fish oil 3000mg taken daily and cod liver oil at least twice a week.
- Prednisone 20- mg daily for 2 days then 10 mg a day, and then taper over two months. E.S.R. should be checked and treatment should continue if the E.S.R. remains elevated.
- Enoxaparin (Heparin) administered subcutaneously at a dose of 2,000 IU twice daily for 10 days will resolve AIED. Start Cod liver oil daily or alternate day as tolerated.
- The patients not responding to oral steroids can try intratymphanic, the simplest procedure (and the least expensive) reported so far. Simply have the patient administer dexamethasone themselves through a ventilation tube. A tube is placed in the posterior-inferior quadrant of the Ear Drum. Patients are instructed to lie on their side and place 5 drops in the affected ear once every other day. Decadron 1 mg/ml.
- Immunosuppressive drugs including methotrexate, cyclophosphamide, azathioprine, mycophenolic mofetil, and intravenous immunoglobulin (IVIg) can be used if there is no response from the steroid treatment.
- Nystatin a antifungal, has been found useful in a small study dosage is 500,000 units four times daily. As a powder, this is 1/8 teaspoon in an ounce or two of water; as a tablet, this is one tablet each dose; and as the suspension, this is one teaspoon per dose. It comes in many forms, including oral suspension (mixed in 50% sucrose to deaden its bitterness), oral tablets, powder, creams or ointments, and vaginal tablets.
- In the hyperbaric chamber, all patients breathed 100% oxygen at 2.8 bars, for 60 minutes twice a day, either until recovered or for a maximum of 30 sessions. This treatment is investigational no dramatic improvements have been seen, some patients complain about increased hearing loss related to high pressure on their ear drums from this treatment.

Vogt-Koyanagi-Harada syndrome: Vogt-Koyanagi-Harada (VKH) syndrome is a disease affecting several organs, eyes, ears, skin, hair and the nervous system. The etiology remains cell-mediated autoimmune disorder in patients genetically susceptible to antigenic components of melanocytes. VKH usually occurs in adult life, in which severe bilateral inflammation of the iris (**iridocyclitis**), ciliary body and choroid of the eye is **associated with relapsing meningitis**, deafness, alopecia, depigmentation of the skin and eye, symmetrical loss of pigment (**vitiligo**) and whitening of the ends of the hairs (**poliosis**). There is a tendency towards recovery of sight,

but it is not always complete. The syndrome usually occurs in young adults in **Japan and Italy**. Mental and growth retardation may occur in some rare familial cases. There is a association of hepatitis-C patients, especially people with **darkly pigmented skin who are being treated with interferon and ribavirin tend to develop VKH**.

Symptoms: Inflammation and redness of eyes, retinal detachments, cotton-wool spots in fundus, headaches, ringing in the ears, and ordinary sound will appear uncomfortable like ringing of the telephone, someone speaking. **Hair fall out and turn white over the eyelashes, eyelids and patches of hair in the front.**

- Bilateral chronic iridocyclitis (redness inflammation of the eye).
- Retinal-detachments, inflammation of the optic disc and iritis.
- Tinnitus (buzzing in ear), neck stiffness, memory problems.
- Alopecia, poliosis (patch of white hair), vitiligo (white patches).

Treatment: We think the treatment of the VKH syndrome should be early and aggressive.

- High doses of systemic corticosteroids and intravenous immunoglobulin, cycles.
- Patients on interferon and ribavirin therapy need to be closely monitored for ophthalmologic complications, by periodic check-up of the optic fundi, for a prolonged period, during interferon treatment as VKH can develop rapidly in these patients. Please also see the CIDP treatment protocol for details.
- Doxycycline 100 mg twice a day for two weeks should be combined with Fish oil taken twice a day for three weeks.

Chapter 15 Endocrine Autoimmune disorders.

Sheehan's syndrome; or **Empty Sella Syndrome;** and **relapsing remitting Lymphocytic Hypophysitis:** The **pituitary gland** lies within a bony cave called (**sella turcica**) at the base of the brain. Pituitary is small in size at less 8 mm it controls all the hormones in the body. The pituitary gland has a central role in body growth, metabolism, and reproduction functions. It is connected to the brain by a thin (pituitary stalk**)** which is a direct extension of the **hypothalamus** (part of the brain which controls sex, weight, sleep, anger, blood pressure and temperature). During pregnancy the pituitary gland enlarges and in rare case may develop inflammation. This inflammation during pregnancy has been called Sheehan's syndrome. If the swelling is severe it may cause blindness by compressing the visual tracts which are coming from the eye and heading toward the brain. Sheehan's syndrome usually presents as a visual disorder in women who are not able to **lactate** and developed **reduced menstrual bleeding** and later no menstrual periods (**amenorrhea**). This is a postpartum disorder due to inflammation within the pituitary gland. If the patient did not seek medical attention, then over the years they develop generalized edema, progressive s fatigue and weight gain. MRI scan done at this late stage of the autoimmune disease shows the usual atrophy of the pituitary gland, the radiological name for this is **empty sella syndrome**. Pituitary cell antibodies are usually positive in early stages. Recently patients have been reported to have relapsing remitting symptoms of amenorrhea, visual changes, presenting with features of a mass lesion and loss of pituitary function. In these cases C.S.F. studies have shown increases in white cells, biopsy shows lymphocytic hypophysitis

and the swelling responds to steroids. In the long run if steroids are tapered the syndrome reoccurs, without treatment patients eventually develop the **e**mpty **s**ella **s**yndrome (E.S.S.). Once ESS has developed the patient will need chronic thyroid replacement.

Case report **:** A 25-year-old woman had headaches for a year after giving birth, associated with loss of menstrual periods and increased production of milk. M.R.I of the head revealed a enlarged pituitary gland; blood tests showed slightly elevated prolactin. Prolactinoma was diagnosed and bromocriptine was started at a dose of 5 mg daily, followed by restoration of the menstrual cycle. Two years later she developed adrenal insufficiency. M.R.I showed a pituitary mass was unchanged, but hormonal investigation showed complete hypopituitarism and no hyperprolactinemia. Nuclear antibodies were negative. Inflammatory-Lymphocytic hypophysitis was suspected; in the absence of visual complication, prednisone was started at a daily dose of 60mg for 3 months. A **gradual recovery of all pituitary hormones was observed** and magnetic resonance imaging showed a reduction in the pituitary mass. Prednisone was progressively decreased within next six months. **Six months after the end of steroid treatment**, the patient relapsed and a biopsy of the pituitary confirmed the diagnosis of autoimmune hypophysitis.

Symptoms: Rare first manifestations can be mental symptoms; depression, unable to concentrate, agitation, seizures, visual hallucination and sometimes **have false beliefs**. Common symptoms are visual loss, double vision, headaches; reduced or increased production of milk **reduced or increased menstrual cycle**. Increased thirst associated with fatigue and weakness. Rarely, a swelling develops in the neck due to thyroid inflammation.

Blood tests: Low sodium (hyponatremia) can be seen due to central diabetes insipidus. Normal or low levels of TSH, **ACTH**, FSH, and LH with low levels of T4, cortisol, and estradiol suggest Sheehan's syndrome. Low levels of IGF-I suggest growth hormone deficiency. MRI imaging is the optimal imaging technique for this area, MRI will show inflammation and mass, this is not a cancer. Prolactin levels are elevated. Spinal tap will show lymphocytes. Pituitary biopsy shows lymphocytic hypophysitis. Positive ANA, antithyroid antibodies and pituitary cell antibodies, (antibodies can be absent in 30% of the cases). E.S.R. & CRP are usually elevated.

Treatment: steroid treatment should be started (125 mg methylprednisolone intravenously on days 1, 2, and 3, followed by 40 mg/d orally). As this is a chronic condition with relapses azathioprine should be started as an alternative long term treatment at a dose of 1 mg /kg. Patients need a close follow up for monitoring E.S.R., clinical symptoms and dose of immunosuppressants should be adjusted based upon clinical tests. Steroids dosage can be tapered over two to three months. I recommend a long term 1-2 year treatment with Imuran. A daily asprin should be given to all patients. Surgery can be avoided in nearly all patients.

Hashimoto's Thyroiditis **(also called autoimmune or chronic lymphocytic thyroiditis)**

Hashimotos disease is a problem with the thyroid gland located in the neck. The thyroid gland makes hormones called throxine that control how the body uses energy. In Hashimoto's disease, the immune system begins to attack the thyroid gland, causing it to become swollen and irritated. When this happens, the thyroid can't make hormones as it should. Although Hashimoto's disease can affect people of all ages, it's most common in women who are between 30 and 50 years of age. If someone in the family has had thyroid disease, you may have an increased risk for Hashimoto's disease. Hashimotos is associated with Yersinia infection.

Symptoms of **Hashimoto's Thyroiditis**

- Swelling of thyroid gland with fullness or tightness in the throat.
- Trouble swallowing food or liquids.
- Swelling or bump (called a goiter) in the front of your neck.
- Feeling of tiredness, forgetfulness,
- Depression, coarse dry skin, slow heartbeat,
- Weight gain, constipation and intolerance to cold.
- Many people with this disease have no symptoms at all.

Test: Blood test testing for T3, T4, TSH and antithyroid antibodies.

Treatment:

- Synthetic thyroxine (levothyroxine), Does not have triiodothyronine.
- Natural extracts containing thyroid hormone derived from the thyroid glands of pigs are available. These products contain both thyroxine and triiodothyronine. Extracts are available by prescription only
- Glandular concentrates sold in natural foods stores are dried concentrates of glands derived from animals. These products are not regulated by the Food and Drug Administration, and their potency isn't guaranteed.
- Thiamine replacement by sublingual or oral tablets help symptoms.
- Magnetic necklace have helped many patients and the use is recommended.
- Inflammation can also be reduced by using antibiotics Biaxin and **Vibramycine** finally the size of the gland quickly reduced by **magnetic stimulation. (**see antibiotic chapter)

Graves Disease: Graves disease in which the immune system over stimulates the thyroid gland, causing hyperthyroidism. Over-activity of the thyroid is sometimes named "diffuse toxic goiter." The thyroid gland helps set the rate of metabolism (the rate at which the body uses energy), and when it is over-stimulated, it produces more thyroid hormones than the body needs. High levels of thyroid hormones can cause difficult side effects. This is a rare disease that tends to affect women over the age of 20. The incidence is about 5 in 10,000 people.

What are the symptoms of Graves 'disease:

- Insomnia, irritability, weight loss without dieting,
- Heat sensitivity, increased perspiration,
- Fine or brittle hair, muscular weakness,

- Eye changes, lighter menstrual flow,
- Rapid heart beat, and hand tremors.

Grave's Disease is the only kind of hyperthyroidism that is associated with inflammation of the eyes, swelling of the tissue around the eyes, and protrusion, or bulging, of the eyes. Some patients will develop lumpy reddish thickening of the skin in front of the shins called pretibial myxedema. This skin condition is usually painless. The symptoms of this disease can occur gradually or very suddenly and are sometimes confused with other medical problems. Women can have Grave's Disease and have no obvious symptoms at all.

Tests: TSH level, T3, T4 and antithroid antibodies.

Treatment:

- To lower the amount of thyroid hormones produced by the body, the medication used are methimazole (Tapazole) or propylthiouracil (PTU) pills. These drugs act to prevent the thyroid from manufacturing the thyroid hormone.
- Surgery: Part or all of the thyroid gland will be removed. In most cases, people who have surgery for Graves disease will develop an under-active thyroid (hypothyroidism), and will have to take thyroid replacement hormones for the rest of their lives.
- Radioactive iodine: The iodine damages thyroid cells to shrink the thyroid gland, to reduce hormone levels. Like surgery, this condition usually leads to hypothyroidism, requiring medication for the rest of the patient's life.
- Pulse Magnetic stimulation of all swollen areas will dramatically reduce swelling in affected areas within 15 minutes.

Autoimmune Diabetes Insipidus: & DIDMOAD syndrome (diabetes insipidus, diabetes mellitus, optic atrophy, deafness). **Diabetes Insipidus** (DI) is a disorder in which there is an abnormal increase in urine output coupled with higher fluid intake and thirst. Autoimmune DI is highly likely in young patients with a clinical history of autoimmune diseases and radiological evidence of pituitary stalk thickening. Pituitary gland is the master gland which controls the body's hormones, thickening of the stalk is a indication of inflammation.Demonstration of autoantibodies against AVP-cells of the pituitary in the serum of patients with so-called idiopathic diabetes insipidus indicates an autoimmune basis of the disease. This interpretation of the new antibody results is supported by a frequent association of idiopathic diabetes insipidus with recognized auto-immune diseases. The disease can be triggered by many infections incuding Malaria, T.B. and other autoimmune diseases.

Symptoms consist of urinary frequency, frequent awakening at night to urinate (nocturia) or involuntary urination during sleep or "bedwetting". Urine output is increased as it is not concentrated normally. Instead of being a yellow color, the urine is pale, colorless or watery in appearance and the concentration (osmolality or specific gravity) is low.

Test: Autoantibodies against vasopressin (AVP)-producing cells of the human pituitary gland as well as conventional antibodies have been seen with central diabetes. MRI scan of the head will

show thickening of the pituitary stalk, (request the radiologist to focus on the pituitary stalk). Thiamine blood levels should be checked to look for a deficiency. Sed rate is elevated.

Treatment:

- Prednisone trial should resolve all inflammation and resolve the higher fluid intake.
- Desmopressin DDAVP treatment initiated leads to a normalization.
- Thiamine 75mg/day replacement if deficiency is found.
- Vibramycine 100mg twice daily for two weeks is helpful. (**read chapter 24**)
- Raise foot end of bed by 3 inches.

Rarely D.I will be associated with anemia, thiamine and thiamine pyrophosphokinase (TPKase) enzyme deficiency, diabetes mellitus, sensorineural deafness and thiamine-responsive megaloblastic anemia. If treated with Thiamine therapy started at 75 mg/day. With Thiamine replacement Insulin requirement decrease eventually stops. The macrocytic anemia improved with thiamine treatment. This syndrome is called **DIDMOAD** syndrome (diabetes insipidus, diabetes mellitus, optic atrophy, deafness).

Diabetes mellitus: Insulin dependent diabetes mellitus (IDDM or type-1) is an disease of the pancreas, resulting in a lack of insulin. Today, the autoimmunogenesis of type-1 diabetes mellitus is unquestioned. Evidence for this includes the detection of specific antibodies, an association with other autoimmune diseases. New evidence suggests that beta-cell regeneration is possible, but ongoing autoimmune damage prevents restoration of beta-cell mass. The actual trigger that leads to the loss of immunotolerance is rotavirus. The prevalence of celiac disease in children and adolescents with diabetes is elevated, suggesting that serological screening for celiac disease be performed for all children and adolescents with type-1 diabetes mellitus. Insulin is produced in the pancreas by beta cells. **The main source of energy for all cells and especially for brain cells is glucose.** Insulin is necessary for glucose to get into cells and be used for energy production. After eating, the level of glucose rises in the blood, which leads to insulin being released from the pancreas. Person with damaged, beta cells has reduced insulin. Type 2 diabetes (non-insulin-dependent diabetes mellitus) Insulin concentrations are mostly increased but peripheral tissues are resistant to insulin (insulin resistance). Beta cells are not able to increase secretion of insulin to overcome this resistance. Type-2 diabetes usually develops after 40 years of age in overweight people, lately in obese adolescents.
Gestational diabetes mellitus: or type -II is characterized by insulin resistance, have positive pancreatic islet antibodies, especially to glutamic acid decarboxylase (GAD). The following evidence exists that diabetes type-1 is an autoimmune disease:

- Association with other autoimmune diseases – pernicious anemia, Addison's disease, autoimmune thyroid disease

- Lymphocytic infiltration around the islets of Langerhans in the pancreas.
- Immunosuppressive treatment is able to delayed onset of disease.
- Autoantibody presence in serum:
- ICA (Islet cell antibodies) - against the endocrine cells in pancreatic islets.
- IAA (Insulin autoantibodies) is present.
- GAD – autoantibodies to glutamic acid decarboxylase is present.

Symptoms: Excessive urination, intense thirst, dehydration and mineral loss. Weight loss: Because of the insufficient level of insulin, glucose can not be used as a energy source.

Diagnosis: The level of glucose is measured after 12 hours of fasting (Fasting Plasma Glucose Test). If this test is not conclusive, Oral Glucose Tolerance Test may be used to confirm the diagnosis. The test called hemoglobin A1C is elevated in diabetes.

Incidence: People under the age of 40. The disease often starts in childhood and affects more Caucasians than African-Americans. The male-to-female ratio is 1:1.

Treatment:

- Insulin is used as a substitute for the lost beta cells function. It has to be used life-long, several times per day in subcutaneous injections before meals. The proper dosage of insulin and appropriate menu plans have to be determined by a doctor.
- Findings suggest that **vitamin D3** deficiency is a important pathogenic factor in type 1 diabetes, and that its supplementation should be considered not only at birth, but also at diagnosis of type-1 diabetes with the aim of protecting residual beta cells from further destruction. Cod Liver Oil supplements are helpful in preventing diabetes.
- **Yeast** is a useful supplement if taken twice a day, along with turmeric. Green tea with cloves taken four times a day will lower glucose levels. It is recommended to take some Insulin drops under the tounge and this will in turn produce your normal insulin. Consume Thymus and Pancreas from animal meat.
- **Omega-3** suplements are of benefit.

Addison Disease: Addison's is an uncommon autoimmune disease, characterized by reduced functioning of the outer layer of the adrenal gland. The adrenal glands are located on top of each kidney and produce steroids (glucocorticoid hormones). A person with Addison's disease will have a deficiency in the producing glucocorticoid hormones (GH). These hormones are named GH as they are involved in how the body utilizes and stores **carbohydrates**, protein, fat and blood sugar. The adrenal gland produces Cortisol, the production is controlled by the pituitary gland in the brain. The Pituitary produces a hormone called ACTH which stimulates the adrenals to make cortisol. (ACTH is **a**dreno**c**or**t**icotropic

hormone)

A deficiency in GH causes an increase in the release of sodium and a decreased release of potassium in the urine, sweat, saliva, stomach and intestines. These changes result in low blood pressure and increased water excretion that can in some cases lead to dehydration. The adrenal gland also plays a role in the immune response.

Majority of Addison's disease cases are caused by autoimmune process. The first case with Addison was caused by tuberculosis which remains as the commonest cause of Addison's. **John F Kennedy suffered from Addison's disease**, his political career was made possible due to administration of cortisol.

Symptoms in Addissons:

- **General weakness and becoming easily tired**.
- Dark areas of skin. Seen in the arm-pits, the nipples, **the creases of the hands**, inside the mouth, recent scars, and **elbows**.
- **Blood pressure is low** and falls when on standing which can make you dizzy.
- Nausea, vomiting and weight loss.
- Abdominal pains which wax and wane.
- Diarrhea or constipation which wax and wane.
- Cramps and pains in muscles **with craving for salty foods** and drinks.
- Menstrual periods become irregular, or stop.
- **Sudden symptoms of**, severe vomiting. diarrhea, abdominal pain, dehydration, low blood pressure and unconsciousness are caused if the level of cortisol falls this is called an **Addisonian crisis.**

Diagnosis of Addison's disease:

- Cortisol levels in the blood.
- ACTH stimulation test to check if adrenals inability to produce cortisol.
- Insulin test to check diabetese.

The treatment of Addison's disease:

- Daily dose of Hydrocortisone is 20 mg first thing in the morning and 10 mg at 6 pm.
- ACE (adrenal cortical extract). ACE is a blend of all 50 or so hormones made by the adrenal cortex and is the alternative medicince that can be used for Addisons.

Chapter 16 Autoimmune Gynecological / Obstetrics diseases.

Autoimmune Endometriosis: Endometriosis occurs when tissue lining the uterus (endometrium) is found outside the uterus. This displaced tissue develops lesions which respond to the menstrual cycle monthly. Endometrial tissue builds up, breaks down, and sheds in monthly cycles. Menstrual blood flows from the uterus and out of the body through the vagina,

but the tissue shed from extrauterine endometrial lesions has no way of leaving the body. This results in internal bleeding, and inflammation resulting in pain, infertility, scar tissue formation, adhesions, and bowel problems. Women with endometriosis frequently suffer from autoimmune inflammatory diseases, hypothyroidism, and fibromyalgia (FM), chronic fatigue syndrome (CFS), allergies and asthma. These findings also suggest a strong association between endometriosis and autoimmune disorders and indicate the need to consider the co-existence of other conditions in women with endometriosis. Women with endometriosis also have higher than expected rates of autoimmune inflammatory diseases including systemic lupus erythematosus, Sjogren's syndrome, and rheumatoid arthritis, as well as multiple sclerosis. Typically a 10-year delay between the onset of pelvic pain and diagnosis of endometriosis is seen.

In women who have endometriosis, tissue similar to the lining of the uterus the endometrium grows in other parts of the abdominal cavity. The endometrial tissue may attach itself to the ovaries, the outside of the uterus, the intestines, or other abdominal organs. Endometriosis affects an estimated eight to ten percent of reproductive age women. It may cause infertility or pelvic pain, although some women with the disease may not experience symptoms. In addition, family members of women with endometriosis have the disease. Subacute focal endometritis has been associated with cervical Ureaplasma urealyticum colonization and Chlamydia trachomatis are considered a factor in pelvic adhesions or endometriosis.

Symptoms: Women experience pelvic pain usually for about 10 years before they are diagnosed with endometriosis. In women the pain starts shortly after their first periods. The pain usually varies during the menstrual cycle. Menstrual irregularities, heavy menstrual bleeding and spotting before menstrual periods, may occur. Cramps and pain, caused by the misplaced tissue are seen during menstruation, often causing, and recurrent first-trimester miscarriages. Pain occurs during sexual intercourse. Some women have back pain.

Tests: Thyroid antibodies and thyroid blood tests (TSH, T3, T4). Anti-laminin-1 autoantibodies may be present confirming the diagnosis of endometriosis. ANA is positive. CA-125 is elevated in the blood. MRI and ultrasound will show lesions in the pelvis.

Treatment:

- Zithromax (250-mg once a day for eight days is given to all patients to clear up any infection associated endometriosis like (chlymadia). Hydrocortisone acetate 10% foam helps control pain in the vagina. In non responders Hydroxychloroquine, an immune-modifying, antirheumatic drug, is added for relief along with hormone treatments. Methotrexate has been used to help control the symptoms of pain.
- Before in vitro fertilization (IVF) Tetracycline (5%) (5-10 mL) is instilled into the endometrioma cyst and the cyst contents are sequentially aspirated and flushed with sterile saline until the aspirated fluid was clear. Saline is injected into the cul-de-sac to

dilute any tetracycline that may have leaked. The fluid is then removed. Ultrasound is performed 6 weeks later to assess the efficacy of treatment. Treatment can be repeated if the endometrioma cyst persists.

Recurrent Spontaneous Abortion: Recurrent Miscarriage Syndrome (RMS):
Recurrent miscarriage syndrome and infertility are common problems in the United States. Recurrent miscarriage affects more than 500,000 women annually. If properly screened through a protocol, the cause will be found in almost all women. The most common defect in women with RMS is a homeostasis defect associated with Antiphospholipid syndrome. Other hereditary and acquired procoagulant defects are also commonly found, if looked for. It is important to evaluate women with RMS appropriately, because if a cause for the RMS is found, most women will achieve normal-term delivery. More than 98% will have a normal term delivery with preconception aspirin (ASA) and addition of postconception heparin to be continued to term. Patients should be screened by an obstetrician or by reproductive specialists for hormonal and anatomic defects before initiating a procoagulant evaluation; if such prescreening is done, the yield of this therapy leads to an excellent outcome.

Symptoms: recurrent abortion or miscarriage.

Test: antiphospholipid, Anti nuclear, & Antigliadin antibody for celiac disease.

Treatment of the common procoagulant defects consists of preconception low-dose ASA at 81 mg/day followed by immediate postconception low-dose fractionated porcine heparin at 5000 U every 12 hours was added immediately postconception; both agents were used to term delivery. (Please also read the section of antiphospholipid syndrome). Cod liver oil 1000mg can be used along with omega-3 fatty acids as supplements.

Male -Infertility: Many infections can be present in the urinary tract, uterus, vagina and hymen. These infections can trigger autoimmune inflammatory reactions causing pain, itching and infertility. Many studies show that mycoplasma or ureaplasma are the most common cause of infertility. Fifty percent of women are infected with Chlamydia, mycoplasma or ureaplasma, and fifty percent of those with tubule blockage. **The more partners you have, the more likely you are to be infected**, although you can be infected by one contact. An infection can prevent pregnancy by blocking the uterine tubes. **The infection can produce antibodies against sperm so that they can't swim toward the egg**, antibodies can cause abortions, premature birth and low birth weight.
Some of the men are infertile as they have **antisperm antibodies**. These people have no other symptoms other then a abnormal antibody.

Symptoms: Infected people may have burning on urination, discomfort when the bladder is full, or an urgency to void. Bleeding from penis during sex.

Test: Men with a history of infertility should be tested for antisperm-antibodies.
Treatment:

- Zithromax (250-mg once a day for eight days) or Biaxin (500-mg BID for 10 days), for Chlamydia and mycoplasma infections. I recommend that both the partners have to be treated with antibiotics or failure rates will be higher.
- Treatment for men who have antisperm-antibody is to take prednisolone, 40 mg a day, for the first 10 days, then 15 mg on days 11 and 12 of the partner's cycle for 3-9 months.

Eclampsia- Preclampsia: Preeclampsia, called toxemia, is a problem that occurs in some women during pregnancy. It can happen during the second half of pregnancy with symptoms of high blood pressure, swelling of hands, feet and protein in the urine. Some of those suffering from preeclampsia can develop eclampsia which consists of additional symptoms of seizures. Eclampsia is commonly in patients with autoimmune diseases thus we present some simple ways to diagnose the patients who will develop eclampsia and provide treatment guidelines. Pre-eclampsia develops in the interaction between the placental disease and maternal responses. Pre-eclampsia probably is auto-immune, with the auto-antibodies directed against certain types of phospholipids or trophoblastic constituents. Eclampsia is defined as seizure activity or coma in an obstetrical patient with preeclampsia. Eclampsia commonly present in the third trimester of pregnancy or within the first 48 hours following delivery, rare cases can be seen prior to 20 weeks' gestation or as late as 20 days postpartum. Preeclampsia is a disorder a resulting from systematic inflammatory maternal reaction. **CRP** is a positive marker of inflammation, higher levels of CRP are present in preeclampsia than in normal pregnancy. It has been reported that in autoimmune patients platelets are presensitized or are relatively inflamed, which indicates a subgroup of women can benefit from low-dose aspirin in the prevention of thrombosis. I recommend monitoring the CRP levels late in the pregnancy which will indicate the patients most likely to develop eclampsia. Eclampsia can occur without development of preeclampsia.

Symptoms Pre-eclampsia causes placental, renal, hepatic, myocardial, cerebral and adrenal ischaemia - in all highly vascular organs. This causes Seizures, headaches, coma, renal failure abortion, heart attack, stroke to happen during eclampsia.

Tests: CRP monitoring, serum homocysteine, B-12, B-6, Folic acid levels should be done. Antiphospholipid antibodies should be checked.

For treatment:

- Fish Oil 3000mg daily should be given to all patients who have eclampsia.
- Low dose heparin or asprin to desensitize platelets. Asprin lowers the risk of complication in the mother and baby by 15%.

- Magnesium sulfate is is an anticonvulsant and helps prevent seizures and maintain uterine and fetal blood flow. Can be administered IV and IM (intrannuscular). Intravenous route is preferred over IM route as administration is controlled easily. The goals of magnesium therapy are to terminate seizures. Patient should be evaluated to assure that deep tendon reflexes are present, respirations are at least 13 breaths per min, and urine output is at least 100 mL during the preceding 3 h.When using magnesium sulfate IV, close monitoring of patient and fetus is necessary. Magnesium therapy usually is continued for 12-24 hours following delivery and may be stopped when the hypertension resolves and the patient has shown adequate urine production. Renal impaired patients should be monitored with magnesium levels, with aggressive adjustments made to achieve levels at 6-7 mg/dL.
- IVIg treatment can control all symptoms of eclampsia and is safe during pregnancy.
- For patients with elevated homocysteine use sublingual or intramuscular B6, B-12 and Folic acid replacement. Those who have antiphospholipid antibodies need subcutaneous heparin. Coumadin started at the time of preeclampsia results in normal delivery.

Chronic Pelvic pain & Pelvic inflammatory disease: Pelvic inflammatory disease (PID) is an infection of the upper genital tract in women that can include endometritis, parametritis, salpingitis, oophoritis, tubo-ovarian abscess, and peritonitis. It affects up to 1.5 million women in the United States and costs an estimated $1.06 billion each year. The etiologic agent often is never identified, but common causal agents are *Chlamydia trachomatis and, Neisseria gonorrhoeae.* Chronic pelvic pains starts with pelvic inflammatory disease, this is one of the most preventable conditions. The infection and inflammation of the female upper genital tract, is a common cause of **infertility**, **chronic pain** and **ectopic pregnancy.** Since pelvic inflammatory disease has a multimicrobial etiology including Neisseria gonorrhoeae, Chlamydia trachomatis and anaerobic and mycoplasmal bacteria, treatment of pelvic inflammatory disease should consist of broad spectrum antibiotics.

Symptoms: Lower abdominal pain, painfull menstrual cycle, fever, back pain, and vomiting, Lower genital tract infection such as vaginal discharge, bleeding, itching, and odours.

Test of Pelvic Pain: PID and may be evaluated by urine and vaginal swab testing instead of speculum and bimanual examination. Cervical or vaginal mucopurulent (green or yellow) discharge. Transvaginal ultrasound, computed tomography,and magnetic resonance imaging (MRI).The classic findings of acute PID on transvaginal ultrasound are tubal wall thickness greater than 5 mm, fluid in the cul-de-sac.

- Elevated erythrocyte sedimentation rate or C-reactive protein.
- Laboratory confirmation of gonorrheal or chlamydial infection.
- Oral temperature of 101°F (38.3°C) or greater.
- White blood cells on vaginal secretion saline wet mount.

Management:

- Cefotetan (Cefotan) 2 g IV every 12 hours or cefoxitin (Mefoxin) 2 g IV every six hours ; plus doxycycline (Vibramycin) 100 mg orally or IV every 12 hours
- Clindamycin (Cleocin) 900 mg IV every eight hours; plus gentamicin loading dose IV or IM (2 mg per kg) followed by a maintenance dose (1.5 mg per kg) every eight hours (single daily dosing may be substituted)
- Ofloxacin (Floxin) 400 mg IV every 12 hours or levofloxacin (Levaquin) 500 mg IV once daily; with or without metronidazole (Flagyl) 500 mg IV every eight hours
- Ampicillin/sulbactam (Unasyn) 3 g IV every six hours; plus doxycycline 100 mg orally for 14 days.
- Ceftriaxone (Rocephin) 250 mg IM in a single dose or cefoxitin 2 g IM in a single dose with concurrent probenecid (Benemid) 1 g orally in single dose or other parenteral third-generation cephalosporin; plus doxycycline 100 mg orally twice daily for 14 days with or without metronidazole 500 mg orally twice daily for 14 days.

Chapter 17 Respiratory autoimmune Disorders

Asthma: Asthma starts like an allergic disease and with repeated exposure to allergens turns into an autoimmune disease, it affects the small airways (bronchioles) that carry air in and out of the lungs. The airways can become inflamed, swollen and constricted (or narrowed), with excess mucus being produced. Asthma can affect anyone, at any age, anywhere. An asthma 'attack' consists of a wheezing or whistling noise in the chest, coughing and difficulty breathing that occur when the airways become narrowed, inflamed and blocked by plugs of mucus. Recently, chronic **Chlamydia pneumoniae** infection has been suggested as a cause for adult-onset asthma. Higher levels of C-pneumonia are found in children with recent asthma attacks. Allergic form of asthma can be triggered by any food including carrots, by metal dust in nickel cobalt and even dust mites. In a group of children with asthmatic mothers, those exposed to cats were more likely to wheeze as compared to those with no cat exposure. The risk of wheezing increased in each of the five years of the child's life. By the third year, the risk of wheezing doubled, and by the fifth year it tripled. Children of asthmatic mothers become more readily sensitized to cat allergens.

Tests: In infants with asthma, Umbilical **erythema** (**Red Umbilicus**) can be a sign of food intolerance specially an allergy to milk. Test for food and milk allergies should be done. In children with bilateral otitis the common cause of asthma is milk allergy. Tests for Mycoplasma pneumonia antibody need to be done in adults. Test for antigliadin antibodies and anti-H.Pylori antibodies

Treatment of asthma:

- In infants with the red umbilicus, otitis media (ear infections) and those that show allergies to milk, all milk products should be removed. They can be given soy milk. This will resolve the asthma issue. In resistant cases patient will need to be placed on gluten

free diet please see the celiac disease section. In adults a search should be done for Mycoplasma and then 4 weeks course with oral doxycycline (100 mg twice daily), azithromycin (1000 mg once weekly), or erythromycin (1000 mg daily) be given. If a mild benefits is seen in asthmatic patients then minocycline 100 mg daily may be used for additional two weeks. Antimicrobial therapy appeared to "cure" or significantly improve asthma in approximately one half of treated adults.

- Clarithromycin, 500 twice a day for two weeks can be used for Chlamydia.
- A new protocol which recommends **Azithromycine 1000mg taken once a week for ten** weeks has been found useful in patients with Astma due to Mycoplasma.
- Intravenous Magnesium sulphate infusion 40 mg/kg doses (maximum 2 g) can cause bronchodilation in treatment of severe asthma, 2.5 mg nebulised salbutamol mixed with either 2.5 mL isotonic magnesium results in an enhanced bronchodilator response in treatment of severe asthma.
- People with asthma are sensitive to pollen concentration and carbon dioxide (CO2) concentration. CO2 concentration is higher at night under trees and lower altitudes. Classrooms may have higher concentration of CO2.
- Nebulized MgSO4, particularly in addition to a beta2-agonist, in the treatment of an acute asthma exacerbation appears to produce benefits with respect to improved pulmonary function and may reduces the number of hospital admission.
- 2 g of IV or 40 mg/kg magnesium sulfate improves pulmonary function when used with standard therapy in patients with very severe, acute asthma.(specially in children)
- Children with cat allergy & asthmatic symptoms triggered by a cat should **avoid cats**.
- In rare cases where asthma is still not controlled a course of IVIg can be used.
- The allergen causing asthma should be avoided. Steroids, inhalers and epinephrine are used for long term asthma management.

Sarcoidosis: Sarcoidosis is a multi-systemic disease in which the immune system starts to attack multiple organs. This over-reaction by the immune dysfunction is characterized by the formation of granulomas (inflammatory masses) in the affected organs. Granulomas are clumps formed by cells of the immune system lumping together. Granulomas can appear on the walls of the alveoli (small air sacs in the lungs) or on the walls of the bronchioles (breathing tubes in the lungs). Current estimates show that over 50 percent of people with sarcoidosis will get well within a year without treatment. The disease has remitting and relapsing periods just like any other autoimmune disease. It closely resembles tuberculosis, berylliosis (metal poisoning caused by inhalation of beryllium dusts). The resemblance to TB causes one to think that sarcoidosis is triggered by a infectious organism like TB. Following BCG vaccination cases of sarcoidosis have been reported and mycobacterium DNA & antibodies have been found in sarcoidosis. Once thought to be a rare disease, with better diagnostic procedures and sarcoidosis is becoming commonly recognized. With a high incidence of lung involvement sarcoid is believed to be caused by a toxin that is inhaled. There is a genetic predisposition that makes some people more

susceptible to sarcoidosis. Excessive exposure to sunlight and high vitamin-D levels can cause the chronic inflammation in sarcoid.

Symptoms of sarcoidosis: Many patients have no symptoms, and the diagnosis is made almost accidentally through routine testing or x-rays.

- Fatigue, weakness, fever, abdominal pain and weight loss.
- Dry cough (without sputum), shortness of breath, or mild chest pain.
- Scaly rash, red bumps in legs, fever, sore eyes, swelling of the ankles.
- Seizures, poor school performance, facial paralysis, double vision and headaches. Growth failure, diabetes insipidus (excessive urination), and lack of sexual maturation.
- **Sunlight can aggravate all the symptoms.**

Sarcoidosis diagnosis:

- **Calcium** levels are elevated especially during attacks.
- Angiotensin-converting enzyme (**A.C.E**) level, which are elevated.
- A biopsy of affected organ can be done to confirm the diagnosis,
- **Kveim Test**, a reaction appearing 4 wk after intradermal injection of sarcoid spleen or lymph node extracts, is **positive in 50 to 60%** of patients.
- MRI/CT/Gallium scans & bronchoscopy can be abnormal in sarcoid.

Treatment for sarcoidosis

- Doxycycline 100mg twice a day for two weeks, then three a week for a year.
- Minocycline 200mg at least three times a week long term clears up skin lesions.
- Ketoconazole an antifungal is useful in long term treatment especially if the calcium levels are elevated at a dose of 600-800mg.
- Hydroxychloroquine 200 mg bid is more effective than corticosteroids for treatment of disfiguring skin.
- Prednisone dose is10 to 20 mg/day. For a prompt effect use Prednisone 40 mg/day or methylprednisolone 48 mg/day is used, such doses are poorly tolerated by many patients.
- Those patients who cannot tolerate prednisone need a trial of methotrexate starting at 2.5 mg/wk and increasing in increments of 2.5 mg/wk to a total of 10 to 20 mg/wk as tolerated by a WBC > 4000/mm^3. After 8 wk of methotrexate, the corticosteroid can be reduced and then often discontinued. Serial blood counts and liver enzyme tests should be performed every 6 wk.
- Inhaled steroids may help suppress active lung sarcoid while causing few side effects.
- Methotrexate at12.5 mg to 20 mg per week for at least 6 months also helps is clearing up the skin lesions.
- Angiotensin Receptor Blocker can be used to reduce sensitivity to sunlight and to help people return to a normal lifestyle. (**COZAAR**).

- Removing vitamin D from food products helps. Particularly check the labeling on milk, breakfast cereals, diet supplements and vitamin preparations. Natural medications can also a significant source of Vitamin D, and, in the absence of a reliable list of ingredients, such medications should be discontinued. After Vitamin D has been removed from the diet, sunlight remains the major catalyst leading to the proliferation of sarcoid granuloma
- The patient should wear sunglasses in all but the darkest of indoor environments. If there is a need to venture outdoors then thick clothing must cover all exposed skin, mandating the use of gloves and hats, and dark sunglasses. The patient should be instructed to stay indoors for the duration of any therapy aimed at inducing remission.

Amyloidosis: Amyloidosis occurs when substances called amyloid proteins build up in body's organs. Amyloid is an **abnormal protein** produced by B-cells in the bone marrow that can be deposited in any tissue or organ. Amyloid is a inflammatory disease and has been reported as a low grade B-cell lymphoma of **m**ucosa-**a**ssociated **l**ymphoid **t**issue (MALT) type. Amyloidosis frequently affects the **brain heart, kidneys, liver, spleen, nerves** and **gastrointestinal tract**. Amyloidosis occours in many autoimmune diseases incuding **SLE, arthritis, myeloma and people on dialysis.** Usually seen in men over the age of 40.

The most common type of the disease, primary systemic amyloidosis, is a bone marrow disorder. Other types that come from the liver are considered familial, or inherited. In still other cases, amyloidosis may occur as a result of kidney disease in people who have undergone long-term dialysis therapy.

Symptoms:

- Severe fatigue, Weakness
- Weight loss, Difficulty swallowing, Diarrhea
- Shortness of breath
- Numbness or tingling in hands or feet
- An enlarged tongue (**macroglossia**)
- Skin changes
- Swelling of ankles and legs
- An irregular heartbeat

Tests: Bood or urine tests may detect an abnormal high protein levels. Rectal biopsy by a needle to remove a small sample of tissue

Treatment:

- Minocycline or Doxycycline daily for two weeks, then one daily for a year.
- Rituximab was given to act on B-cells, interfering with their production of autoantibodies. In patients with amyloidosis, Rituximab was given to kill progenitor B-cells of the small clone terminating in amyloid-producing plasma cells.
- **Peripheral blood stem cell transplantation.** Peripheral blood stem cell transplantation involves using high-dose chemotherapy and transfusion of previously collected immature blood cells (stem cells) to replace diseased or damaged marrow. These cells may be your

own (autologous transplant) or from a donor (allogeneic transplant). Autologous transplant is currently the preferred standard.

- **Medicines.** Magentic pulse therapy accompanied by electronic pulsar therapy, consumption of olive oil, using turmeric daily one to two teaspoons. Steroid pulses can be used the amount infused is 1000 mg every week for a month and then twice a month for two to three months.

Interstitial lung disease (ILD,

Interstitial lung disease (ILD) comprises more than 200 disorders characterized by diffuse inflammation and **scarring** of the lung. Some of these are Bronchiolitis obliterans and organizing pneumonia (BOOP). Diffuse alveolar damage (DAD) adult respiratory distress syndrome (ARDS). Air in supplied to the lungs by the wind pipe called trachea which divides into smaller air pipes, the most tiny air pipe is called a bronchiole which takes air to the tiny air sacs called alveoli. The lung has millions of these tiny air sacs (alveoli). The tissue between the air sacs of the lungs is called the interstitium. In ILD there is inflammation in the walls of alveoli and loss of alveolar blood flow due to inflammation in the tiny blood vessels called (capillaries). Inflammation in these parts of the lung may heal or may lead to permanent **scarring** of the lung tissue. Once **scarring** of the lung tissue develops, the condition is called **pulmonary fibrosis**. Fibrosis and scarring, in the lung tissue, causes permanent loss**,** of that tissues ability to transport oxygen. The walls of the bronchioles (small airways) also get inflamed, it is called bronchiolitis. Some of these autoimmune lung diseases have different names. Diffuse alveolar damage (DAD), adult respiratory distress syndrome (ARDS). The progression of these diseases is through stages named (exudative, proliferative, and fibrotic) that correlate with the time rather than its specific cause. Except for asthma all these diseases cause fibrosis.
ILD is a clinical challenge because the disease spectrum can range from mild disease that is responsive to medications to progressive loss of pulmonary function and death. Corticosteroids and cyclophosphamide result in clinical improvement in a subset of patients. **The names of some of these diseases are:**

- Usual interstitial pneumonitis (UIP), Nonspecific interstitial pneumonitis (NSIP)
- Bronchiolitis obliterans-organizing pneumonia (BOOP)
- Respiratory bronchiolitis associated interstitial lung disease (RB-ILD)
- Desquamative interstitial pneumonitis (desquamative IP)
- Lymphocytic interstitial pneumonitis (LIP)
- Acute interstitial pneumonitis, Farmer's lung, Honeycomb lung
- Acute interstitial pneumonia (Hamman-Rich syndrome, idiopathic ARDS)
- Alveolar proteinosis, pulmonary phospholipoproteinosis
- Asbestosis, Berylliosis, Hard-metal pneumoconiosis
- Coal worker's pneumoconiosis (black lung disease)
- Connective tissue disease-associated interstitial lung disease
- Desquamative interstitial pneumonia (DIP), Hypersensitivity pneumonitis (HSP)
- Systemic lupus erythematosus (lupus lung), Mixed connective tissue disease
- Lymphocytic interstitial pneumonia (LIP)

- Nonspecific interstitial pneumonia (NSIP)
- Pigeon breeder's disease , Pulmonary alveolar microlithiasis
- Eosinophilic granuloma (EG), histiocytosis X (HX), or Langerhans granulomatosis
- Pulmonary fibrosis, Respiratory bronchiolitis
- Respiratory bronchiolitis-associated interstitial lung disease (RB-ILD)
- Rheumatoid lung, Sarcoidosis, Polymyositis, Dermatomyositis, Scleroderma lung
- Silicosis, Pneumoconiosis ,Smoker's bronchiolitis
- Usual interstitial pneumonia (UIP) and IgA deficiency triggered ILD

The causes of these diseases are diverse from those that involve mining or expose workers to asbestos or metal dusts can cause pulmonary fibrosis. Workers doing these kinds of jobs may inhale small particles (like silica dusts or asbestos fibers) that can damage the lungs, especially the small airways and air sacs, and cause **scarring** (fibrosis). Agricultural workers also can be affected by exposure to organic substances, such as mold, hay, fumes and chemicals. Exposure to radiation can trigger these diseases & almost any medication can cause ILD except for aspirin.

Symptoms of ILD:

- Shortness of breath (dyspnea) on exercise, cough and fatigue.
- Dry rales ("Velcro" crackles) may be present on chest auscultation.
- Wheezing is not seen.**UNCOMMON**
- Signs of advanced disease include increased dyspnea and a fast heart rate (tachypnea), blue color of the skin (cyanosis) and digital clubbing.
- Advanced disease in children may result in weight loss or failure to thrive.

Tests for ILD:

- CT scan can determine the type of ILD present.
- Pulmonary Function Tests, the breathing test results are abnormal in ILD. Arterial Blood Gas: test measures the amount of oxygen and carbon dioxide in the blood. The results may be normal or show a reduced oxygen level.
- Bronchoscopy involves inserting a tube through the nose into the trachea (windpipe) to see the airways. In bronchoalveolar lavage, a small amount of sterile saline is placed in one area of the lung and then withdrawn. This fluid contains cells that will be analyzed under the microscope. People with chronic obstructive pulmonary disease have very high titers of antibodies to chlamydia, showing infection with that germ and anti-Ro/SSA antibodies are also seen frequently.
- **IgG levels and IgG sub-class levels need to be done on all patients.**

Teatment for ILD:

- **Azithromycine** 500mg twice a day should be given on alternate day for a week and if there is any benefit then can be continued for two to three weeks. Those patients not responding to Azithromycine should try **Doxycycline** 100mg daily for two weeks.
- Hydroxychloroquine is used in ILD, especially in pediatric patients, because of its relatively low toxicity. Among cytotoxic agents, cyclophosphamide, azathioprine and methotrexate are used most frequently. Although cyclophosphamide is often the drug of

choice as adjunctive therapy to corticosteroids in adults, a higher than expected sterility rate limits its usefulness in children.

- Intravenous pulse cyclophosphamide 10-30 mg/kg every 3-4 weeks, and 2-4 mg/kg/day of cyclosporine-A is also used for a complete list of drugs and side effects see the treatment section of CIDP.
- For patients with low IgG levels or low IgG-subclass levels use - IVIg at 200mg/kg/month to 400mg./kg/month for four months to two years as needed.
- Lung transplant is to be avoided as the disease can develop in the transplant tissue.
- Corticosteroids have emerged as primary pharmacologic therapy. Steroids have been used with varying degrees of success to treat ILD hypersensitivity pneumonitis and other forms of ILD. About 50% of patients have responded to steroids.

Chapter 18 Renal autoimmune Disorders

Autoimmune Interstitial Cystitis: Interstitial cystitis (IC) is a condition that results in recurring discomfort or pain in the urinary-bladder and the surrounding pelvic region. IC is often associated with diseases such as allergies, irritable bowel syndrome, fibromyalgia, inflammatory bowel disease (Crohn's disease and ulcerative colitis), systemic lupus erythematosus, and Sjogren's syndrome (dry eyes). The symptoms vary from case to case and even in the same patient. People may experience mild **discomfort, pressure, tenderness, or intense pain in the bladder and pelvic area**. The prevalence of allergies in IC is reported to be between 40 and 80% of patients. Usually the symptoms follow a remitting and relapsing course. Interstitial Cystitis patients are wrongly treated for what their doctors assume must be bladder infections, urethritis, or "emotional" problems. Repeated symptoms of pain and urgency, suggesting a urinary tract infection, are a hallmark of IC.

Symptoms

- Bladder spasms which are very painful, bladder frequency, bladder pain, low bladder capacity, and incontinence.
- (Urgency), a frequent need to urinate or (frequency),
- While urinating very little urine may be passed.
- Women's symptoms often get worse during menstruation. Rarely painfull menstruation or pain during intercourse is reported.

Test: Check CRP to see if it is elevated. ANA antibodies may be positive; **urine analysis does not show a infection** but inflammatory cells are seen.

Treatment:

- Doxycycline 100 mg twice a day taken on daily for 3 weeks a week has been reported to help in controlling the symptoms of IC. Both partners have to be treated or the treatment will not work. A trial of prednisone is used to control IC.
- Alcohol, tomatoes, spices, chocolate, caffeine, citrus drinks, artificial sweeteners and acidic foods may irritate your bladder. Try removing these from your diet.
- Using a TENS ("transcutaneous electrical nerve stimulation or frequency stimulator) unit helps improve the blood flow to the bladder.

Henoch-Schonlein purpura: Henoch-Schonlein purpura (HSP) is the most common type of vasculitis (inflammation within the blood vessels) diagnosed in childhood and is rarely seen in adults. The main clinical manifestations of HSP include purpura (small blue spots over the skin), arthritis, abdominal pain, gastrointestinal bleeding, and **nephritis** (inflammation of the kidney). The symptoms are caused by inflammation of the blood vessels resulting from IgA -antibody deposits in blood vessel walls. The mean age of children affected by HSP is 5 years, and majority of children affected with HSP are younger the ten years old years old. HSP is most common from September to January and frequently follows a sinus infection. It has been attributed to pharyngitis caused by Streptococcus, hepatitis B infection, varicella, mycoplasma, herpes simplex virus, **Helicobacter pylori**, human parvovirus B19, and Coxsackie virus. H-pylori antibodies have been reported in HSP patients frequently. Higher levels of H-Pylori antibodies are seen during new attacks of HSP. In a study new attacks of HSP were treated by 1mg/kg/day of prednisone for two weeks. In about 84 patients none ever had any kidney involvement later on. HSP is generally benign and self-limited condition seen in children; and more severe in adults.

Diagnosis: Urine and blood test may show elevated CRP, Elevated BUN (Blood urea nitrogen), Serum IgA is often elevated.

Treatment: Prednisone 1mg/kg/day for two weeks. NSAID can be used if needed. In difficult cases Dapsone 100mg daily for two weeks will give prolonged remissions. The condition is self limiting and repeat attacks are usually not seen. We recommend you to follow the diet guidelines in the diet section. For adults please see the treatment guidelines below in autoimmune glomerulonephritis.

Glomerulonephritis Autoimmune: Each kidney contains approximately one million miniature filtering units, called nephrons. Each of these is made up of a glomerulus, a collection of capillaries (tiny blood vessels) that filters the blood. Inflammation of these filtration units is termed glomerulonephritis (GN). When GN develops as a long term condition, it is associated with an autoimmune reaction. This is where the body attacks these filtering units, in the kidneys. In such cases, symptoms of renal failure appear gradually over time. Injury to the abdomen or back may be triggering these diseases. Steroids given at the time of injury may prevent the

development of these conditions. There are several types of GN but treatment is the same. It can be associated with hepatitis-C virus.

Symptoms of Glomerulonephritis:

- Feeling of tiredness, shortness of breath, a loss of appetite and high blood pressure.
- Fluid retention causes swollen feet and puffiness of the face and around the eyes.
- Urine is passed less frequently and may appear frothy, cloudy or blood-stained and dark in color.

Diagnosis of Glomerulonephritis: Urine and blood tests show elevated ESR, serum creatinine is elevated, MRI scan of the kidney shows enlargement of the kidneys and occasionally a kidney biopsy, may also be performed to establish the diagnosis and the severity of the problem. Serum C-reactive proteins levels are elevated, antineutrophil cytoplasmic antibodies (ANCA) are usually present. Antibodies against hepatitis-C virus need to be measured.

Treatment of Glomerulonephritis: If the inflammation is only mild, treatment with **doxycycline 200 mg once a day can decrease protein in the urine** it acts as a metalloproteinase inhibitor in glomerulonephritis. More severe cases may require a combination of antibiotics, corticosteroids and immunosuppressant drugs.

- If Hepatitis –C virus is found then treatment with interferon-α (3 million units subcutaneously, 3 times per week) and ribavirin (500 mg orally, twice a day) for 48 weeks is recommended which may resolve the GN.
- For rapidly progressive glomerulonephritis patients IVIg is used at a dose of 400mgkg for 5 days. Based upon tests can be repeated once every 4 weeks. The repeat dose is usually 400mg/kg single infusion only.
- For a complete list of drugs please see the treatment section under CIDP, fish oil supplements are useful in IgA type nephropathy..

Chronic Autoimmune Prostatitis (CAP), Nonbacterial Prostatitis, Chronic Pelvic Pain Syndrome:

Prostatitis is and affects prostate gland in men around ages 19-91. The prostate is a gland that is just below a man's urinary bladder. It surrounds the urethra like a donut and is in front of the rectum. The urethra is the tube that carries urine out of the bladder, through the penis and out of the body. The prostate gland makes a fluid that provides nutrients for sperms. This fluid makes up most of the ejaculate fluid.

Prostatitis can cause diverse symptoms. Urination becomes difficult, painfull & frequent. There is a feeling of a fever, low-back and groin pain (the area where the legs meet your body). It make one less interested in having sex or unable to get an erection or maintaining one. Prostatitis is easy to confuse with other infections in the urinary tract.

More than 90 percent of men with prostatitis meet the criteria for chronic autoimmune prostatitis and chronic pelvic pain syndrome. In a study using a needle biopsy for culture of prostate tissue, it was found that there is frequently an occult bacterial prostatitis, especially in men with

leukocytes in prostatic secretions. Some studies have noted increased uric acid levels in prostate secretions in men with chronic autoimmune prostatitis. Benign prostatic hypertrophy is essentially a inflammation causing swelling and in reality is C.A.P. The cause of prostate cancer is chronic inflammation, which can easily be prevented by proper anti-inflammatory treatment.

Symptoms:

- Painful ejaculation or pain in the penis, testicles or scrotum.
- Low back pain, rectal pain, and pain along the inner aspects of the thighs.
- Irritative or obstructive urinary symptoms and decreased sex drive or impotence.
- These patients do not have recurrent urinary tract infections.
- Patients may have a tender prostate.

Tests for CAP: No bacteria will grow on any culture, but leukocytes may be found in the prostatic secretions. Urine cultures are negative after prostate massage. The premassage urine has fewer than 10 white blood cells per high-power field, and the postmassage urine contains more than 10 to 20 white blood cells per high-power field. PSA (prostate specific antigen) can be elevated. ESR & CRP are elevated.

The treatment for CAP:

- Given the high rate of clandestine or hidden prostatic infections**, an antibiotic trial is reasonable**, to see if the patient responds clinically. *Chlamydia trachomatis*, *Ureaplasma urealyticum* and *Mycoplasma hominis* have been identified as potential pathogens, treatment should cover these organisms.
- Doxycycline (Vibramycin) 100mg/daily or minocycline (Minocin) 100mg/twice daily for 14 days, or erythromycin at 500 mg four times daily for 14 days.
- Hot sitz baths and nonsteroidal anti-inflammatory drugs (NSAIDs) may provide some symptom relief. Some men may notice aggravation of symptoms with intake of alcohol or spicy foods and, if so, should avoid them. In men with irritative voiding symptoms, anticholinergic agents such as oxybutynin (Ditropan) or alpha-blocking agents such as prazosin (Minipress), Hytrin may be beneficial.
- To achieve remission bolus therapy with cyclophosphamide and prednisolone is recommended. Please see dose guidelines in the CIDP treatment section.
- Bicycle seats are very important to prevent further injuries of the prostate. The most common bicycling associated urogenital problems are nerve entrapment syndromes presenting as genitalia numbness, which is reported in 50-91% of the cyclists, followed by erectile dysfunction reported in 13-24%. The best seat is without the hard nose. Other less common symptoms include prolonged erection (priapism), penile thrombosis, and infertility, blood in the urine (hematuria), and torsion of spermatic cord, prostatitis and elevated serum PSA. Symptoms are avoided by a flat seat, which does not have the nose.
- Untreated prostate disease will turn into Prostate cancer. In ealrly stages antibiotics, Cod Liver Oil supplements & doxycycline can help control the cancer.

Wegener's involving the urinary tract (Orchitis-ureteral stenosis-pseudotumor of the bladder): Wegener granulomatosis (WG) can present with urinary system involvement. WG needs to be diagnosed and treated quickly. If proper anti-inflammatory treatment is not provided, then kidney failure and vasculitis can affect other organs very quickly. Usually middle aged men are the main targets. Past history of arthritis, skin rash, **runny nose** and **asthma**, helps to diagnose Wegeners disease. Rarely WG can cause a **facial paralysis** and **sudden onset** of **hearing loss**. Respiratory tract **infections** can trigger **relapses** in patients. Treatment with trimethoprim-sulfamethoxazole (**Septra**) is beneficial in preventing relapses.

Symptoms: Acute urinary retention related to **prostatitis**, inflammation of the **testicle** (**orchitis), difficulty in passing urine** due to ureteral stenosis accompanied by pain in the penis, bladder pseudo-tumor (inflammation causing the appearance of a bladder tumor) and causing blood in the urine, with penile ulceration. Some people experience narrowing of the trachea. The symptoms can include voice change, hoarseness, shortness of breath, or cough. Fever and night sweats may occur. Fever may signal an infection, often of the upper respiratory tract.

- **Sinus involvement**: A common sign of the disease is almost constant runny nose or other cold symptoms that do not respond to treatment. A hole may develop in the cartilage of the nose, which may lead to collapse (called saddle-nose deformity). The eustachian tubes, which are important for normal ear function, may become blocked, causing hearing loss with a feeling of a blockage or fullness in the ear.
- **Lungs:** Cough, hemoptysis (coughing blood), shortness of breath, and chest discomfort.
- **Musculoskeletal system**: Pain in the muscles and joints.
- **Eyes:** Redness, burning, or pain. Double vision or reduced vision.Conjunctivitis (inflammation of the conjunctiva) Swelling of the eye muscles or Myositis
- **Skin lesions**: Small red or purple raised areas or blister-like lesions, ulcers, or nodules.

Test: anti-neutrophil cytoplasm antibody (ANCA) is positive, biopsy of the bladder or skin has vasculitis. ESR & CRP are elevated. Protein in the urine and serum creatinine is elevated.

Treatment: Early high-dose steroids accompanied by Cytoxan should be used as first-line therapy to avoid unnecessary surgery. Septra (Co-trimoxazole (800 mg of sulfamethoxazole and 160 mg of trimethoprim) given twice daily for 24 months to prevents relapses in patients. For other drugs please see the CIDP treatment guidelines.

IgA nephropathy: The most common cause of reanl failure all over the world is IgA nephropathy. In this diseases which usually targets young adults and may follow streptococcal infection accompanied by tonsillitis. Removal of tonsil in early stages will resove the condition. IgA nephropathy is now the most common cause of glomerulonephritis in the world Henoch-Schönlein purpura (HSP), a systemic illness, has been closely linked to IgA nephropathy. Other systemic diseases in which mesangial deposits of IgA are regularly observed include systemic lupus erythematosus, hepatitis, dermatitis herpetiformis, and ankylosing spondylitis.

The association of some cases of IgA nephropathy with syndromes that affect the respiratory tract or gastrointestinal tract, such as celiac disease, led to the suggestion that IgA nephropathy is a disease of the mucosal immune system. This concept is also supported by the clinical observation that hematuria worsens during or after upper respiratory tract or gastrointestinal tract infections. Serum IgA levels are elevated in approximately half of patients with IgA nephropathy, but that increase is unlikely to play a role in the pathogenesis of the disease, as markedly elevated IgA levels are observed in patients with AIDS who do not have IgA nephropathy. However, IgA is probably accumulated and deposited because of a systemic abnormality rather than a defect intrinsic to the kidney. IgA nephropathy is more common in males than in females

Symtoms of IgA nephropathy: Gross hematuria has also followed tonsillectomy, vaccinations, strenuous physical exercise, and trauma. episodic gross hematuria and persistent microscopic hematuria. Recurrent macroscopic hematuria, usually associated with an upper respiratory tract infection, or, less often, gastroenteritis, Mild proteinuria is common. Hypertension.
However, IgA nephropathy and gluten hypersensitivity are associated, and withdrawal of gluten from the diet of these patients has resulted in clinical and immunological improvement of the renal disease.

Tests of IgA nephropathy: Sed rate will be elevated, CRP is high, urine proteins elevated.
Treatment: Remove tonsils, use ceftriaxone, doxycycline, steroid pulses 500mg I/V weekly.

Chapter 19, What is IVIG (Intravenous Immunoglobulin)

1. What is IVIG or Intravenous Immune Globulin?

IVIg is a human blood product formed by taking antibodies from the plasma of about 20,000 donors and then mixing them together. These antibodies are processed through filters and chemical treatment to remove viruses. Then the product is sold as IVIg. IVIg is a collection of antibodies consisting mainly of IgG (immunoglobulin-G)
These antibodies have proven effective in the treatment of all immune system disorders, including nearly all autoimmune conditions example CIDP, GBS, MS, OCD, PANDAS, Alzheimers... The sooner you can treat the patient with IVIg the better the results. There is a short window of opportunity usually within the first 18 months after the diagnosis during which you see the most benefits of IVIg. Treatment with IVIg within the window period is likely to halt the progress of the disease.
Following exposure to toxins and poisonous chemicals including carbon monoxide the body's immune system mounts an attack on the body. This autoimmune attack is halted by IVIG. No matter what the problem is in the immune systeam IVIg will fix it.

2. How does IVIG work?

For immune deficiency where the body does not make enough antibodies, IVIG supplies them.
For autoimmune disorders like GBS & CIDP, there is a abnormal antibody (autoantibody) being formed which is inactivated by IVIG.
Antiidotype antibodies are normal antibodies which are produced in the absence of any antigen. They are capable of inactivating many different types of antigens.
Patients with autoimmune disorders like CIDP are deficient in antiidotype antibodies. IVIG supplies these antibodies.

3. How long does it take for IVIG treatment to have a effect?
Patients may see a response in 24- 48 hours. Some patients will have to wait 3-4 weeks to see any effect after IVIg infusion. In a few persons no effects may be seen following IVIg. If 4-5 cycles of IVIg do not show any response then one has to try a different approach like plasmapheresis, antibiotics, cytotoxic or immune suppressants.

4. Why is IVIG so expensive?
The plasma donors are paid then the plasma is sent to processing centers for mixing, antibody removal, chemical treatment and filtration to remove viruses. This is followed by the products to be freeze dried. All this ends up for IVIG to be priced at $ 48 to $ 80 a gram. A single infusion costs about $9k for a adult. For a child the cost is lower as a small dose is used. IVIg is much cheaper in China($20 gram) and the surrounding countries of Pakistan ($30 gram) and India.

5. How is IVIG administered?
IVIG is mixed in a bag and a tube runs from it to a vein usually in the arm. The recommended way to infuse includes a pump. Usually it is given at a rate of 100 cc/ hour to 200 cc/ hour. The rate is reduced for any problems such as headaches, rash, fatigue, hypertension or hypotension. For an adult's infusion is usually given over 5 to 6 hours. IVIg can also be given subcutaneously and in children it has been given orally.

6. What are the common side effects OF IVIG?
Some times patients get a headache which is commonly seen in females with a history of Migraines. Patients may experience fatigue which is similar to getting Flu, resulting from antibodies interaction. Some patients get a rash and its recommended they take Benadryl or even steroids as a premediction to avoid the rash. A severe headache with a stiff neck after IVIg may be due to aseptic meningitis. Variation in blood pressure, shortness of breath can also be seen. Remember there are lots of antibodies and some may result in odd reactions. Some patients have developed Giant Cell Myocarditis which will promptly get better if aziathoprine is given.

7. How can one reduce the side effects of IVIG?
Remember to drink eight glasses of water a day for hydration before starting the treatment and continuing this a month after the last infusion. Some doctors recommend taking a baby aspirin to prevent thrombophelebitis. Patients need to check with their doctors if they can use aspirin and should not take this if they are on coumadine or have bleeding disorders. Patients should not take asprin, if they have a history of gastric ulcers. Use premedication to help reduce side effects. Some recommend that one should take Tylenol or other NSAID for prevention of headaches and pains. Use a benadryl capsule for a skin rash and this will help you to relax during the treatment. Using low dose prednisone will reduce side effects like headaches.

8. Where is the IVIG treatment given?
IVIG can be given at home, in a clinic, hospital or patients office.

9. What is the frequency of the IVIG treatment in autoimmune diseases ?

Usually a dose of 2 grams per kilogram is divided into four doses and 500mg/kg is infused daily for 4 days. This is followed by a monthly infusion of 500mg/kg. It is recommended that young women and older men take this on alternate days.
In immune deficiency a lower dose is used depending on the IgG level in the person. Usually the dose is 100-200mg/kg/ month.

10. What are the differences in brands of IVIG?
Generally the difference is in the amount of IgA content and weather the IVIg contains sucrose, glucose or some other sugar as a stabiliser. Some IVIg products have Glycine while another one has no preservatives. In general all the IVIg products work about the same.

11. What is a recall OF IVIG?
A recall happens when someone reports defects, side effects of a particular IVIg batch. Then the FDA may issue a warning or a recall. This may also depend on contamination.
A recall may be followed by shortage of the product in the market. Recently consumer demand for IVIg is surpassing production.

12. Where can I find out about recalls of IVIG?
The FDA in the US maintains a current list of blood-product recalls on its site. This is because its members use so many different types of blood products, and generally store them in quantity. Look under Biologics and then recalls near the middle of page.
http://www.fda.gov/cber/recalls.htm
13. Who is a good provider for IVIG?
Choose someone who knows about IVIG. Who has 10 years of experience with IVIg.

14. What is the recommended dose as compared to age?
Children can tolerate a higher dose and the whole 3g/kg dose has been given without side effects as a single infusion. Young adults up to 25 years of age can tolerate 1g/kg as a single infusion. Up to age 50 only 400mg /kg is recommended in one day.
Some over 75 year old patients we recommend not to infuse more then 400mg/kg in one week.

15. What is the right IVIG product for me?
Patients with congestive heart failure or compromised renal function tolerate a product with a low osmolality and low volume; Patients who are diabetic should receive a product containing no sugars; Patients receiving products with sucrose may be at a higher risk for renal failure; Patients with immunoglobulin A (IgA) deficiencies should only receive products with the lowest amount of IgA or they could have anaphylactic reactions. In IgA deficiency I would recommend using the subcutaneous route which will eliminate any chances of a allergic response. Patients with small peripheral vascular access or a tendency toward phlebitis may want to avoid preparations with a low pH.

16. I have no more veins left. How can I get IVIg?
IVIg can be delivered by the subcutaneous route if venous access is a problem. This is the preferred way of delivery for a immune deficient patient and children. It is also the best way to infuse if a patient has IgA deficiency.

17. IVIG and vaccination issue.
IVIG prevents vaccinations to take any effect in your body.
Immunizations should not be given for at least 1 month before -- and preferably 3 months after a course of IVIG. While on IVIg you may not need routine flu shots, as you are getting the antibodies from the IVIg.

18. IVIg and blood tests:
The ESR will usually go up after an IVIg treatment in the range of 80mm-100mm/hour. This elevation is considered normal following IVIg infusion.

Chapter 20- How to take care of pain and stiffness:

Pain and stiffness are one of the most common problems in patients suffering from autoimmune diseases. These symptoms are seen in nearly all autoimmune diseases and specially Fibromyalgia and Stiff Person Syndrome. Stiffness begins secondary to stress, exposure to cold, vitamin deficiencies and poor posture. Repeatedly doing the same task will also cause stiffness, lifting of heavy weights without stretching will result in stiffness. We have seen how a cat stretches after it gets up. That is what all of us need to do every morning. Stretching helps reduce stiffness. Children cry at night because they are getting stiff due to the cold. Thus need an extra cover. Sitting in front of a air conditioner or cold air draft will cause stiffness. Stretching is very important and if you cannot lift your arm ask someone to help you stretch. In a few days you will be able to do this yourself.

Remember to take a hot shower after wakening up to reduce stiffness. Heat helps to relax the muscles. If the muscles remain stiff a short massage is helpful. Massage will reduce inflammation if done correctly. Light massage and cupping can be used to ease pain.

Correct the vitamin deficiencies like **B-12 Cynocobalamine**, B-1 (Thiamine), and B-6 (Pyridoxine). Too much pyridoxine is toxic to the human nerves and thus should not be taken in large doses. In any person with chronic stiffness, calcium, **magnesium**, **iron**, thyroid functions and the vitamin levels need to be. If any of the hormone, mineral or vitamin levels are low then the treatments will not work. Do not depend on tests for B-12 deficiency. If the patient is clinically anemic by looking in their conjectival area give them sublingual or injectable B-12.

I.V.I.g reduces stiffness as seen in the treatment of stiff person syndrome. Colostrum is the milk secreted after the delivery of a baby. Bovine colostrum taken at a dose of 500mg to 1000mg twice a day will also reduce stiffness. As stiffness is reduced then the pains go away. One becomes more active and feels youthful. We recommend that anyone with stiffness should use colostrum. Muscles become soft without any stretching, muscles spasms also become less.

For stiffness and pain in the body use a icepack rub it on the painful area then stretch that area by moving your extremities. This is followed by applying a hot towel on the same area, (moisten a towel with hot water and apply it over the stiff area).

In acute injuries seen in athletes require quicker treatments, in such situations a simple injection of lidocaine or just a needle insertion will relive the pain. This procedure can be done on any muscle in the body. Usually one milliliter (ml) or 1 cubic centimeter (cc) of lidocaine is injected into the painfull area, followed by stretching of the muscle for pain relief. This is a quick way to relive headaches and joint pains. If the lidocaine injection is not available just rub lidocaine or find a cream containing camphor/menthol combination, rub the cream over the painfull area to relive pain.

Myofacial pain syndrome is defined by the presence of trigger points. Trigger points are located within taut bands of muscle, whereas tender points are not. Palpation of trigger points often reproduces the pain radiation pattern experienced by the patient and can elicit a twitch in the muscle. The pain elicited on palpation of a tender point is localized to the area under palpation and does not elicit a jump or twitch. Lastly, trigger points often have a nodular texture described as similar to rubber, whereas tender points cannot be palpated.
Myofacial pain syndrome is a commonest cause of pain all over the world. This pain will cause tightness in the muscle, and the muscle loses its stretch reflex. If the trigger point in the affected area of the muscle is inactivated by a lidocaine injection, the muscle reflex will return instantly. To complicate the situation, Myofacial pain syndrome may occur in patients with fibromyalgia. The pain of fibromyalgia is widespread, and associated with tender areas. Myofacial pain arises from trigger points in patient muscles, which can be felt like a small bump under the skin. Patients refer to them as knots universally in America and U.K. The diagnosis of Myofacial pain syndrome should be considered when, by history, the patient's pain pattern is limited to a particular region over time.

One cubic centimeter of lidocaine injected into a trigger point or tender point will relive pain. Sometimes a few repeate injections are needed. Some physicians use B-12 and prednisone which provides long term relief. Not more then 10 cc of lidocaine should be given in one setting as chances of arrhythmia tend to increase when a doseof 10- 20 cc is given. When giving trigger points make sure the person has normal B6, B-12 levels or the injection may not work. I have seen patients with severe knee arthritis who came to the clinic in a wheel chair. After the trigger point injection they walked out of the clinic.
If spasticity is causing a problem then Botox can be injected in the affected muscle, to relive spasms for a few months.
Usually heavy lifting, repeated exercises, poor eating habits (less fat in the meals) will cause muscle spasms. Proper nutrition combined with muscle stretches should make muscle pain a thing of the past.
Muscle stimulators and TENs unit work wonders for chronic pain and stiffness, incuding stiffness in the chest, abdomen and urinary bladder.
Magnesium Phos a homeopathic remedy at 30 X potency mix a few dros in water and take it daily which will help pain and spasms in the back. Magnesium supplements, iron supplements will also help spasms.

Chapter 21-Getting around managed care.

Every insurance company and state funded plans in western countries follows similar health guidelines. FDA guidelines are global and followed all over the world.

I.V.I.g. is approved by FDA for immune deficiencies and two autoimmune diseases which are thrombocytopenia and Kawasaki disease. I.V.I.g is not FDA approved for the treatment of any other autoimmune disease. If an insurance carrier denies you for I.V.I.g treatment saying it is not F.D.A. approved try the following:

If you have Fibromyalgia, Chronic fatigue or infertility you may be denied by the insurance company to obtain IVIg treatment. To get IVIg obtain some simple blood tests like **IgG levels and IgG subclass levels**, if they come out low then submit this information to the insurance carrier saying you have immune deficiency and that is a approved condition by the FDA for treatment with IVIg. This immune deficiency is a covered benefit of your policy.

Suppose you have SLE, arthritis or P.A.N.D.A.S or any other disorder including infertility and you need IVIg. You can get this approved by submitting it under the ICD9 code *autoimmune disorder unspecified*. With the submitting papers add your any abnormal antibody level like ANA, Rheumatoid factor, raised A.S.O. titer and this will result in an approval of IVIg treatment.

If you need specific help, submit a question to www.cidpusa.org you will have to pay $10.

Disability how to get it: This is mainly aimed at the United States Social Security and Disability Act (SSI). One has to remember that disability is a **Legal issue** and not a medical one. The person has to show why they cannot be employed in a regular job. The date of payments begins from the day you applied. Thus if it takes three years for you to get a approval and numerous application SSI will have to start reimbursements from the day you first applied.

The autoimmune diseases are invisible. Thus the doctor or judge cannot see them.. If you provide completes paperwork of your diagnosis, blood tests, doctors reports you will get the award sooner. So remember its the paper work that makes the difference. If they send you for evaluation to a doctor, go and explain all your problems. That is not a place to cry, unless you are trying to get a mental disability. You hae to convience the examining doctor that you are sick and that you are not fit for any job. Once a woman came to my clinic she was well dressed, with a full makeup, when questioned how had she come to clinic? She replied “I drove here”. That answer coupled with the fact that she was asking for a lot of valium from her doctors made me think she was not disabled, and that is what I wrote on her evaluation. Another gentleman came to clinic and had fresh paint on his shoes and hands and wanted a temporary certificate for disability, ofcourse he did not get one.

There are many tests that a doctor is trained which can get you a wrong label of malingering. This is a word used in medicine to say that the patient in reality is fakeing a medical disorder. In my own eluations and of some unpublished studies, whenever this diagnosis of malingering was used after a few years the patient was found to have a real disorder. One of these tests is used

when a doctor is testing strength. Whenever a doctor asks you push against him try your full strength, even if you feel week don't let go, if you do let go suddenly the doctor is trained to call this a "**Give Away Sign**", meaning that you are malingering. Some doctors **push on your head** and then ask you does that increase your pain? If you say yes they again are taught that this is really due to malingering. **It's the training that is wrong**, the answer in this case should be that the preassure you are placeing on my scalp causes the pain there but it has no effect on my neck pain. Don't pretend to say that you have pain when in fact you don't, because a well trained neurologist will catch you and you will get the lable.

For autoimmune diseases your abnormal tests results like a weakly positive ANA, reduced IgG subclass antibody reports and submit the package. If you get denied apply again most people get approved on the thirds or fourth attempt. If it takes longer to get disability you still get paid, S.S.I. payments are calculated from the time you fist filed the application.

Chapter 22- (MMM) Mold, MSG, & MadCow

MOLD: We have tried to raise the awareness of Mold causing a autoimmune reaction and resulting in chronic sickness which can be simply treated with complete remission with proper medical help. Mold can be prevented. An environment with high humidity attracts mold and prevention from this becomes a key. Ventilation of areas that develop high humidity is important.

Mold exposure. The major presentations are headache, general debilitating severe pains, nose bleeding, fevers with body temperatures up to 40 degrees C (104 degrees F), cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, vertigo, dizziness, and in some cases, seizures. Although sleep is commonly considered a restorative process that is important for the proper functioning of the immune system, it could be disturbed by mycotoxins. Most likely, mycotoxins exert some rigorous effects on the circadian rhythmic processes resulting in sleep deprivation to which an acute and transient increase in NKC activity is observed. Depression, psychological stress, tissue injuries, malignancies, carcinogenesis, chronic fatigue syndrome, and experimental allergic encephalomyelitis is induced at very low physiological concentrations by mycotoxin-induced NKC activity. Chronic exposures to toxigenic mold could lead to abnormal NKC activity with a wide range of neurological consequences, some of which were headache, general debilitating pains, fever, cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, and seizures. Yellow Rain which is a mixture of Mycotoxins and chemicals was used as a chemical-biological agent in Southeast Asia in the l970's. Russia used Yellow Rain against Afghanistan and Southeast Asia. Yellow rain can be used to clear out an area of local people and within 24 hours occupying forces can move in to inhabit the area. Yellow Rain loses all toxic effects within 24 hours after being exposed to oxygen. Trichothecene mycotoxins are noted for their marked stability in environmental conditions. On a weight-for-weight basis, they are less toxic than other toxins

such as ricin, botulinum, and staphylococcal enterotoxin B, but trichothecene mycotoxins are proven lethal agents in warfare. Symptoms include vomiting, pain, weakness, dizziness, ataxia, blindness, anorexia, diarrhea, bleeding, skin redness, blistering, and gangrene, as well as shock and rapid death. Sensitive immunoassays and chemical procedures are available for the identification of trichothecene mycotoxins in biological samples.

MSG syndrome: Monosodium glutamate (MSG) syndrome is the main cause of obesity the world over. It is a glutamate based salt and causes severe neurological, muscular inflammatory disease, in which the muscles swell up, the hair fall out and the body gains weight. It also triggers autism and may even be involves in multiple sclerosis. Gelatin contains MSG and the MMR vaccine contains MSG.

Symptoms that MSG can bring on: Reported MSG reactions, which can occur as a result of consuming even small amounts (much less than the 1/2 gram), include migraines; hives; mouth eruptions; numbness; tingling; swelling of mucous membranes in the oral, gastrointestinal or reproductive tract; asthma; runny nose; insomnia; seizures; mood swings; panic attacks; diarrhea; and cardiac irregularities.

MSG by any other name is just the same. "monopotassium glutamate," "autolyzed yeast," "hydrolyzed soy protein" and "sodium caseinate" are examples of ingredients that always contain MSG. It is also called the chiniese salt.

- In Japan, MSG is labeled as ▫▫▫▫
  In China, MSG = Ajinomoto
  In the Phillipines, MSG = Vetsin
  In Thailand, MSG = phong churot
  In Germany, MSG = Natriumglutaminat
  In Europe - MSG = E621, but also avoid E620-625 as they also contain glutamate

But how does MSG cause obesity? Like aspartame, MSG is an excitotoxin, a substance that overexcites neurons to the point of cell damage and, eventually, cell death. Humans lack a blood-brain barrier in the hypothalamus, which allows excitotoxins to enter the brain and cause damage, according to Dr. Russell L. Blaylock in his book Excitotoxins. According to animal studies, MSG creates a lesion in the hypothalamus that correlates with abnormal development, including obesity, short stature and sexual reproduction problems.

Mad Cow an autoimmune disease: Prof Alan Ebringer, an expert in auto-immune diseases at King's College, London, challenged the accepted mainstream scientific theory that CJD and BSE in cattle are caused by rogue "**prion**" proteins. His research suggested that BSE was caused instead by **acinetobacter** a common microbe in sewage and the soil.

He said it was this **microbe**, not the "**prion**" agent which was passed on to cattle in inadequately processed **animal feed** mixed with faeces contained in internal organs of dead animals. This feed

was sold as animal protein in "winter food" for livestock. Animal waste containing faeces was known in the trade as "**green offals**", he said. People could also be infected by these bacteria in the environment. "If we are right, **the cattle kill was unnecessary**," Prof Ebringer said.

Prof Ebringer and Prof John Pirt, a worldwide authority on the role of bacteria in diseases, said their work had shown that CJD and BSE could be caused in genetically susceptible people and animals when their own bodies produced fierce antibodies which then attacked the invading acinetobacter bacteria and damaged healthy tissue too. In effect, healthy tissue was destroyed by a heavy burst of "**friendly fire**" from the body's defence mechanisms.

Prof Ebringer and Prof Pirt from Kings College London rejected the prion protein theory championed by the Nobel prizewinner, Prof Stanley Prusiner, of California University, and generally accepted as the most likely cause of scrapie, BSE and CJD. They said that Prof Prusiner's theory which he will explain to the inquiry in June - was flawed. "The prion theory is not compatible with current concepts of molecular biology and postulates the existence of novel particles which cause neurological damage," they said in their statement to the inquiry. "**The auto-immune theory is compatible with the current concept of molecular biology** and proposes that BSE or scrapie is produced by a mechanism involving 'molecular mimicry' between common bacteria and nervous tissue."

Dismissing research showing how BSE could be caused by injecting infected brain tissue from cattle into other animals, they said the work was deeply flawed since none of the material used was "pure" BSE prion protein but a mixture including normal brain tissue.They argued that acinetobacter microbes in normal brain tissue caused similar brain damage to that attributed to the prion protein. By failing to separate the two ingredients, scientists had no way of proving that prion protein was to blame. They said: "It has been known for over 120 years that, if one injects brain tissue into another animal, a neurological disorder develops three to six weeks later and it is known as **'experimental allergic encephalomyelitis'**.
This research showed that the infected cows were being fed contaminated meal, which had caused Mad Cow crisis in UK. (From UK news)

Chapter 23-Joint- replacement & inflammation: When an arthritic joint is removed, it is replaced with prosthesis an artificial joint typically made of a metal piece such as various alloys that fit closely into a sturdy plastic segment. These materials eventually erode, releasing tiny metal and plastic particles that enter the joint space. Some artificial joint recipients **experience chronic inflammation** as a result, leading to pain and loosening of the joint, which may require another replacement. The immune systeam looks at the new joint as a target to eliminate.
The inflammatory response results when the body senses a foreign intruder. One of the ways the immune system tries to eliminate the intruder is by calling in cells to fight. Everyone who receives a new joint has some inflammatory response, and everybody sheds tiny particles of the device into the joint space.

The most common complication of hip replacement surgery is an inflammatory reaction to tiny particles that gradually wear off of the artificial joint surfaces and are absorbed by the

surrounding tissues. The inflammation may trigger the immune cells to eat away some of the bone, causing the implant to loosen. To treat this complication, one can use anti-inflammatory medications or recommend revision surgery (replacement of an artificial joint). The anti-inflammatory treatment recommended by is omega-3 fish-oil 2-3 grams daily or asprin.

In some cases autoimmune disorders like Parkinson hae been triggered after joint replacement.

Implants and autoimmune disease experts from medical reports: Danish women with cosmetic breast implants experienced higher overall mortality compared with women in the general population owing in part to a 3-fold increase in suicides**.**
A group of 18 patients had developed symptoms of their disease after they had received implants. Six had autoimmune disease (systemic lupus, 2 patients; rheumatoid arthritis, 2 patients; multiple sclerosis in 1 patient; and Raynaud's disease, 1 patient). Twelve had rheumatic disease (fibromyalgia, 10 patients; inflammatory arthritis, 2 patients). All 100 patients were extensively evaluated pre- and postoperatively by interviews, clinical assessment, 45% of the 75 questionnaire responders felt that their implants had caused permanent health problems and 56% felt that they had not been given adequate informed consent by their original physicians. Studies show a association between extracapsular silicone from ruptured silicone breast implants and Fibromyalgia. If this association persists in other studies, women with silicone gel breast implants should be informed of the potential risk of developing fibromyalgia if their breast implants rupture and the silicone gel escapes the fibrous scar capsule.Women with silicone breast implants often report severe pain and chronic fatigue. Rupture of the implant is associated with an increase in symptoms of pain and chronic fatigue.

Autoimmune diseases have many causes. One mechanism by which infection is linked to the initiation of autoimmunity is termed molecular mimicry. Molecular mimicry describes the phenomenon of protein products from dissimilar genes sharing similar structures that elicit an immune response to both self and microbial-proteins. Molecular mimicry is the mechanism by which infections trigger autoimmune diseases.

Joint replacement is completely possible, I have treated many end stage joint patients who were able to walk independently without any assistance. This is done with a combination of antibiotics like Vibramycine, magnetic pulser , using turmeric daily with cod liver oil.

Chlamydial: Chlamydia infections are among the most common human infections. Every year, in millions of humans, they cause infections of the eyes, the respiratory tract, the gental tract, joints, and the vasculature. Chlamydia is intracellular resident so **it is difficult to detect in blood samples**. Chlamydia grows, in susceptible host cells that include mouth and vagina-epithelial cells, blood vessel-endothelial cells, heart muscle cells, and within monocytes and macrophages, reducing their survival while causing various autoimmune diseases. **Chlamydia infections often**

precede the initiation of autoimmune diseases and Chlamydia is often found within autoimmune lesions. Chlamydia has been suspected in the etiology and pathogenesis of autoimmune diseases.

Mycoplasma is a microorganism which lack a cell wall can invade every human tissue and then they compromise the immune system, permitting opportunistic infections by other bacteria, viruses, fungi and yeast. *Mycoplasma*, *Chlamydia*, *Borrelia*, *Rickettsia* and other pathogens can also damage and kill nerve cells resulting in degeneration of the nervous system. Patients with hidden infections, caused by mycoplasma, can be treated using antibiotics effective. Mycoplasma infections are usually difficult to detect. If the patient is suffering from the **cold agglutinin syndrome** then there is a simple blood test by taking a tube with EDTA in it, mix some of the patient's blood and place the tube on ice. If sand like particles form then cold agglutinins due to Mycoplasma are present. Once diagnosed, the Mycoplasma can be effectively treated, by using low dose **Doxycycline**. The treatment has to be **long term**, in selected cases. Double-blind clinical studies, sponsored by the National Institutes of Health, indicate that some antibiotics are effective in treating Rheumatoid Arthritis. Other, recent studies by Garth L. Nicolson, show that in addition to Rheumatoid Arthritis, other autoimmune diseases, can be treated with antibiotics to suppress chronic bacterial infections, and antivirals to suppress chronic viral infections. Patients with such infections gain significant benefits by undergoing therapies against chronic bacterial and viral infections.

Colostrum: This is the premilk secreated after pregnancy and is rich in growth factors and IgG. Taken daily it is helpful in autoimmune diseases and reduces muscle stiffness. The recommended dose is 1000mg daily. The best way to take them is by opening the capsule under the tounge and swallowing it.

Exercises: Which will help your immune functions.

Erectile dysfunction & Pelvic Floor excersise or pubococcygeal muscle (PC muscle) exercise: As age advances and autoimmune diseases become active it may be difficult to maintain an erection. This can be helped by a simple exercise. The women can do this do make the vaginal muscles tighter. Try going to the bathroom to urinate and then try stopping the urination mid stream. Remember the muscle that you used to stop the urination. Then contract this muscle when you are resting or in bed. Try holding this PC muscle in a contraction for five to fifteen minutes on a daily basis. This exercise can be repeated during sex to enhance the erection. This exercise will also help avoid rectal prolaspe and heal piles. To maintain an erection a rubber band type ring can be placed over the penis or you can stretch it around the testicles. It will work both ways.

Eye Muscle Exercise: Eyes need to be moved in every direction up, down sideways and in rotatory movements for five to ten minutes daily. This will increase the size of eye muscles and the hollows under the eyeballs will become filled and you will look younger.

Exercise to improve walking: While sitting try standing up without support and repeat this ten to twenty times this will make the knee muscles stronger and improve your steps.

Vertigo execrcise: If you have vertigo then sit on the side of the bed and move your neck and body from one side of the bed to the other. Do this for ten times. Then you lay down in bed with your head turned down toward the right side and sit up, then lay down with your head on the left side side and sit up. Reap this for five or six times. Doing this on a daily basis will stop vertigo.

Teeth whitening by Oil swishing is done in the morning by taking a tea spoon of oil in your mouth, then you swish the oil around the teeth in the front and back, you keep doing this for 15 – 20 minutes. The oil will change its color to whitish and then you can spit it out. Brush your teeth, gums and tongue lightly after this with baking soda. We recommend using mustard oil, olive oil or canola oil for this procedure. The current research shows that inflammation of the gums can triiger autoimmune diseases and is responsiable for heart diseases and strokes. I recommend that all the people should regularly use oil swishes to remove active gum disease.

A daily exercise program of 20-30 minutes daily should be done, to keep your immune functions in top shape. This can include brisk walking, in the winters and hot summers people living in USA can walk in the shopping malls.

Chapter 24) - Managing antibiotics in autoimmune diseases.

This is the most important chapter in this whole book. Medicine is an art, you have to practice it. I have seen that in some autoimmune patients when you first start antibiotics, they experience some side effects. These are usually reported as worsening of the original disease, some people experience arthritis, fatigue, palpitations, drowsiness and many other symptoms. In my opinion, if the patient experiences many side effects from a medicine, then the particular antibiotic is a good suite for their disease. These side effects are the result of a herheximer reaction. As the antibiotic is given then large number of organisms began to die. The death of the organisms triggers multiple immune reactions and causes these symptoms.

To succeed in using antibiotics one has to reduce the symptoms of the herheximer reaction. This is done by reducing the dose of the antibiotic. If you were giving 100mg twice a day (bid) then you can reduce it to 100mg daily, and then see if the adverse symptoms become less. If the symptoms did not become less then you can administer the antibiotic on alternate days. I frequently see patients who had been doing well on the antibiotic and then stopped it; this was followed by all the disease symptoms returning. In such cases the antibiotic should be continued either daily or on alternate days for several months. To reduce the reaction from the drug

increases your water intake. You can also take lemon juice to help overcome the problem. Yogurt should be taken daily when on antibiotics to replace the good bacteria in your colon. To see you do not get a herx reaction start with a low dose of the prescribed antibiotic. Some patients can only take 50mg Doxycycline.

In patients suffering from chronic diseases like arthritis, vasculitis it is necessary to treat the patients sometimes for many years. Antibiotics can be continued on alternate days like Monday, Wednesday and Friday every week. In this pattern one can continue the antibiotics for over a year. I will discuss specific treatments for some common diseases below. In some patients the course of the antibiotics has to be two years. If the patient is not seeing any benefit then it is best to try electronic pulser units along with the antibiotic. Since this is a new way to treat infectious diseases please obtain the electronic treatment guide from our website.

Let's take the case of Multiple Sclerosis that is caused by Chlamydia. Some researchers have recommended the following protocol below. By following this most patients will benefit. The frequency of the medicine can be increased if you do not see a response especially in overweight patients. In non responders patients ceftriaxone, chloroamphenicol can be tried.

- N-acetyl cysteine (NAC) 600mg -1200mg twice daily, should be taken daily until the infection is cleared it is available in a Health Food Store. Start with 600mg once daily then slowly increase it to 600mg twice daily.

- After one week start Doxycycline 100mg at night with water. If you tolerate the medicine increase the dose to two capsules one in the morning and one at night. Take this for two weeks and then change to 100mg on Monday, Wednesday and Friday. It should be continued for a year.

- One week after starting Doxycycline start Azithromycin 250mg daily Monday, Wednesday, Friday if the person tolerated it well continue this for 12 months.

- Two weeks after starting Doxycycline start Metronidazole 400mg Tuesday, Thursday, if the patient tolerated it well, then after two to three weeks change to 400mg three times daily once a week like on Fridays only for a year.

- Turmeric daily one tea spoon twice daily, yogurt take twice daily while you are on antibiotics.

- B-12 replacement is given intramuscular or sublingual weekly supplement for two years.

- Vitamin D 4000 units or Cod Liver oil should be given in winter months. Switch to fish oil or flax seed oil 3 grams daily in the summer months.

- Alpha lapoic acid, L-carnatine can also be used as supplemts with vitamin C & E.

TOXIC INGREDIENTS TO AVOID:

Women are being systemically poisoned all over the world; there is an organized effort to put toxins in their make up. Young girls are given toxic makeup and soon this will trigger acne, hair products will trigger hair loss. Lipsticks and deodorants will cause poisoning from lead and aluminum. Vaccines are full of chemicals, mercury, allergens and we need to try are best not to take these especially the Flu shots, tetanus shots and makeup. In Rajasthan India no one gets vaccination and there are no illnesses. Only the very old dies there no deaths are reported in young people and no breast cancer is seen. Holding a polythene bag in your hand is toxic, drinking in a polythene container is toxic, and all the drug delivery systems in a hospital are based upon PVC. (Good luck try to stay away from plastics).

Crystalline Silica: - "Crystalline Silica is present in some personal care products and toiletries. It's been incriminated as a cause of lung cancer in both animal studies and human."

Dioxin: - Dioxin-treated paper containers transfer dioxins to the product itself. "The Health Protection Branch of Canada has reported dioxin levels in the parts per trillion ranges in several samples of **milk and cream packaged** in bleached milk cartons manufactured in the United States. Dioxin has migrated from the cartons to the milk. U.S. milk products are probably contaminated with dioxin. **Dioxin's carcinogenicity is up to 500,000 times more potent than that of DDT."**

Formaldehyde: - Is used as a disinfectant, germicide, fungicide, and preservative. It is found in **cosmetics** and personal care products. Found in milk cartons in Pakistan.

Isopropyl Alcohol: -Implicated in mouth, tongue, and throat cancers. A colorless, volatile, flammable liquid produced by the fermentation of yeast and carbohydrates. Alcohol is used frequently as a solvent and is also found in cleaning agents, cosmetics and personal care products, perfumes and rubbing alcohol, beverages and medicine.

Lye: also known as Sodium Hydroxide or Potassium Hydroxide. A highly concentrated watery solution of sodium hydroxide or potassium hydroxide. Lye is combined with animal fats to make bar soaps, which may corrode and dry out the skin. It is found in toothpaste, eye drops, and other personal care products.

Good Luck and wishing you a healthy future. It was the American training that opened my mind.

Acknowledgements

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Due to space limitations we could not provide all the refrences on which the materials of this book are based. The vast majority of the materials in this book come from research publications at the National Library of Medicine in Washington DC.

I am a medical scientist and love to help other people. I am deep into medical research and have developed electrical devices to treat many untreatable medical disorders. I have researched and found treatments for nearly all autoimmune diseases. I can treat autism, epilepsy completely at times without drugs. I have written a book called, “the Flame within” which is a treatment guide to 101 autoimmune diseases.

Thanks to my parents that they send me for the best training in the world, I trained at Royal Postgraduate Medical School in London and Institute if Neurology in London. I also trained at National Institutes of Health in Bethesda, where I was appointed by the President of USA and served under the Surgeon General of USA.

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