

MS & IVIg as a immune modulator

Crescent



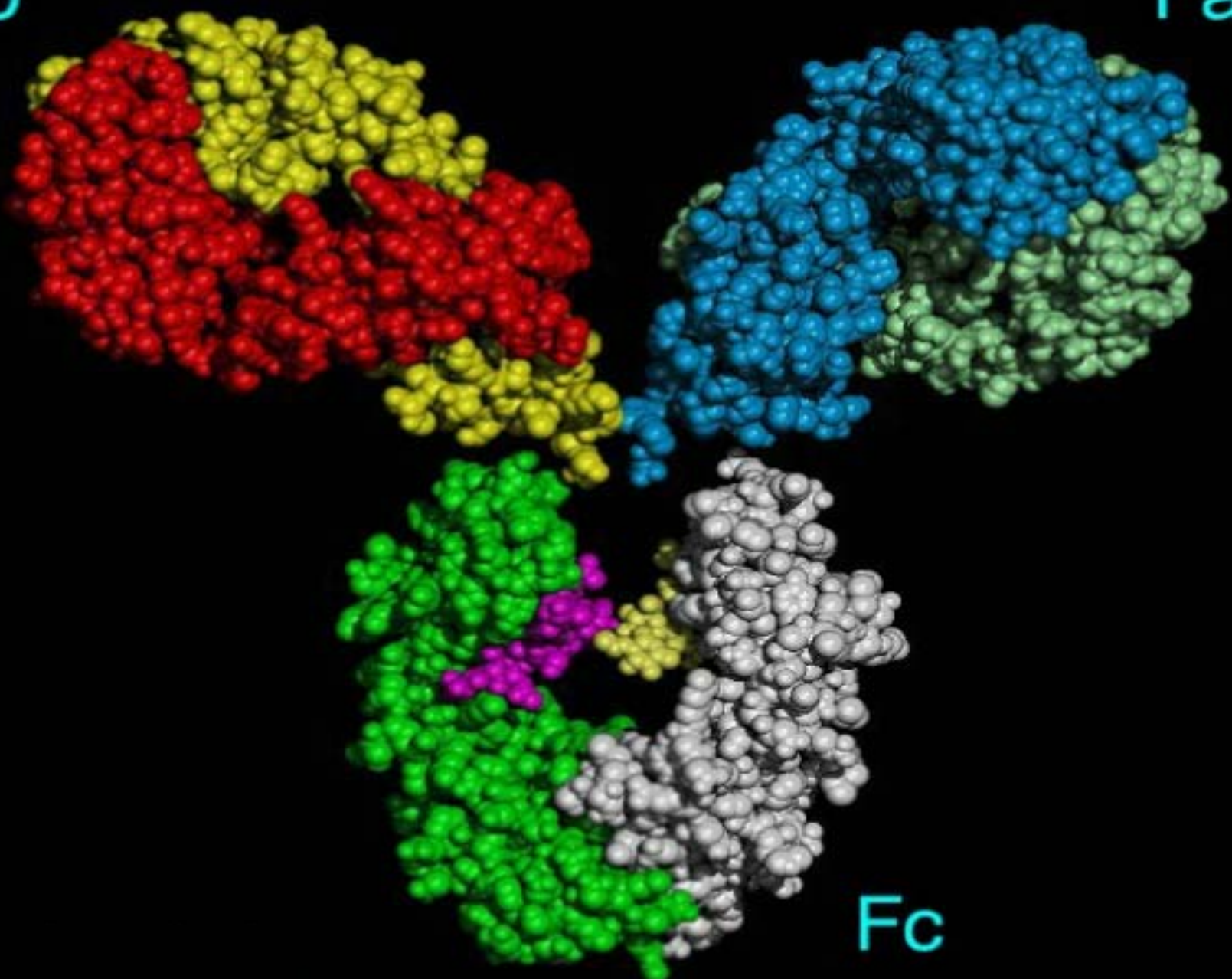
Jupiter & the Crescent Moon Presented by Imran Khan



- Jupiter

Fab

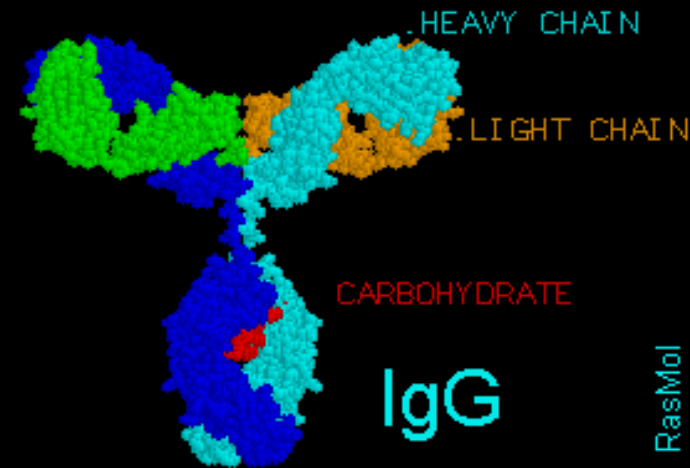
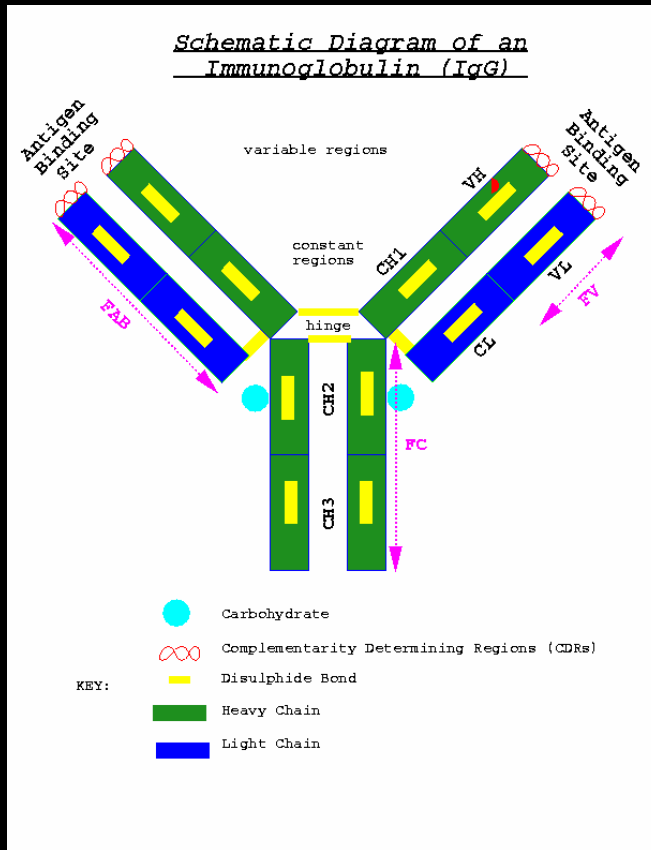
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Fc

IVIg as a Immunomodulator.

I. Khan MD

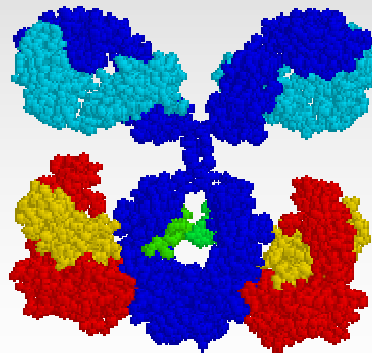


Immunomodulation action (IVIg).

The most relevant immunomodulatory actions of IVIg, operating alone or in combination, are. Inhibition of complement deposition, neutralization of cytokines, Modulation of Fc-receptor-mediated phagocytosis, and

Down-regulation of autoantibody production

"IVIg modulates the immune system, it doesn't suppress it. It appears to 'turn off' deleterious immune responses without damaging the immune system, it strengthens the immune system because it provides antibodies to infectious agents as well."



idiotype (anti-idiotype)

- Antigens (1) induce the production of antibodies (2) whose binding sites are complementary to those of the structure (1). When the binding sites of (2) are inoculated into another animal, they will induce antibodies (3) whose binding sites will be complementary to (2) and identical to the first ones (1), because they will have the same structure. These binding sites could be used as a vaccine against the antibody (1).



- **So, antibodies induced against an idiotype (anti-idiotype) would have the same structure as the original antigen, and thus could be useful as antigens to elicit an immune response against the first antigen that originate the reaction. Anti-idiotypic antibodies can be either polyclonal antibodies or monoclonal antibodies, and could be used as vaccines, specially in those cases in which getting the immunogenic proteins or codifying their genes is very complicated.**

-
- Autoimmune disease is a major women's health issue.
 - Autoimmune disease are among the 10 leading causes of death in women in every age group up to age 64.
-

- **Autoimmune disease is now the third major category of illness in the United States behind heart disease and cancer.**
 - Projected to become the number one disease category in the future.
-

Underlying cause of autoimmune diseases is the same, these chronic illnesses should be considered as a whole.

Autoimmune diseases spokesperson

- **Actress Kellie Martin** works as national **spokesperson** for the **American Autoimmune Related Diseases Association (AARDA)**.
- Honored for her efforts to raise awareness of autoimmunity and autoimmune diseases (ADs) as a major women's health issue, Martin's own education came too late. In 1998, her 19-year old younger sister, Heather, died due to a case of SLE (lupus) that was repeatedly misdiagnosed.

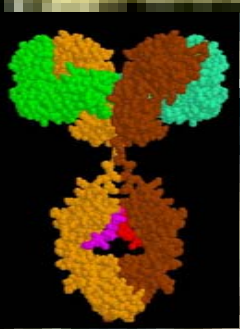


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represented by: Retna Ltd., USA

- **Worked in TV series ER**

IVIg modulates the immune system



Clin Immunol Immunopathol. 1992 Jan;62(1 Pt 2):S73-81.

Modulation of autoimmunity by intravenous immune globulin through interaction with the function of the immune/idiotypic network.

Dietrich G, Kaveri SV, Kazatchkine MD.

Institut National de la Sante et de la Recherche Medicale (INSERM), Paris, France.

“It is our view that IVIg is effective in autoimmune diseases not merely by a passive transfer of suppressive anti-idiotypes, **but rather by imposing a normal function on the defective network in autoimmune patients**”

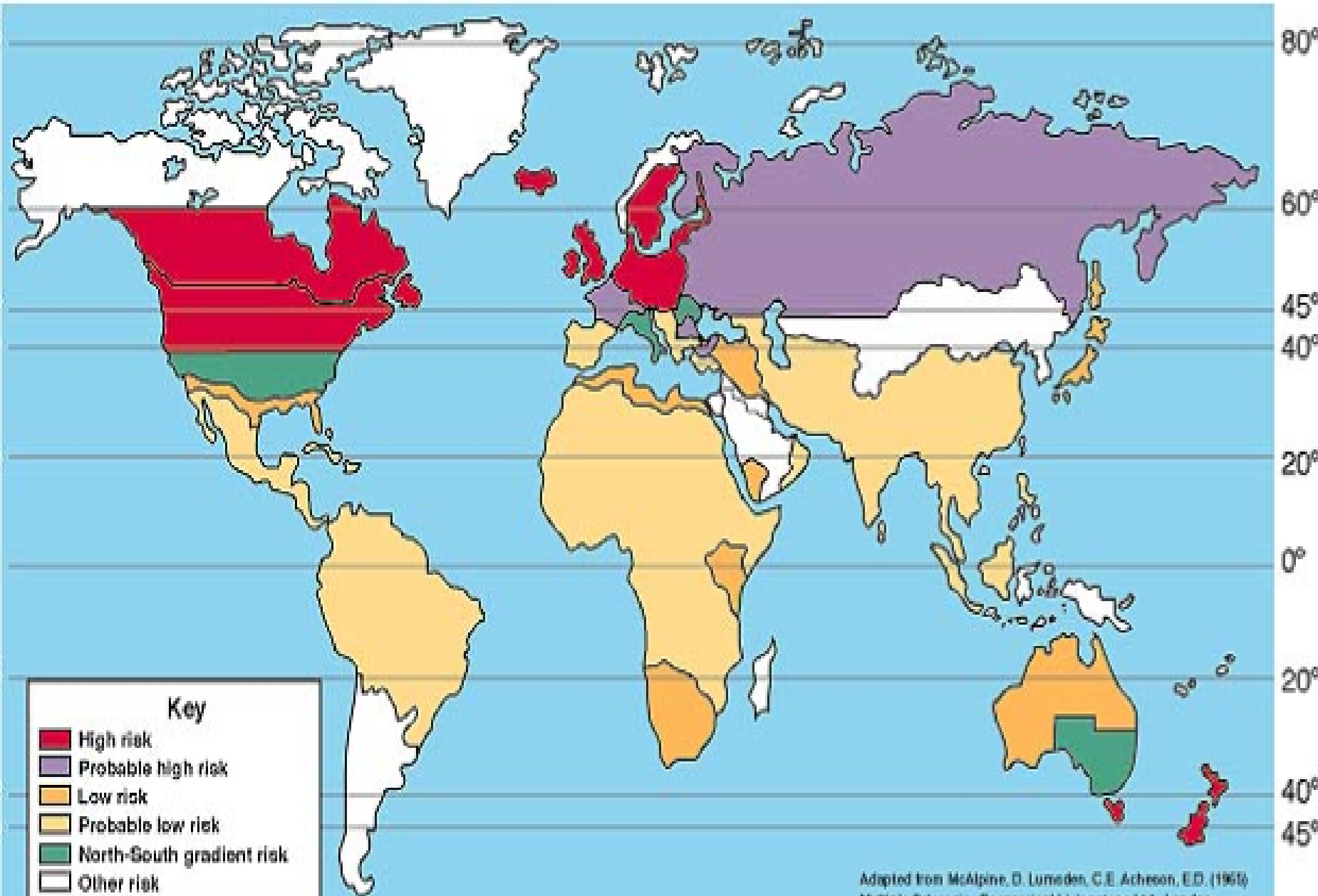
- **Antibodies that react to the antigen binding domain (CDRs) of another > antibody are typically called anti-idiotypic antibodies. .**

Mycoplasma



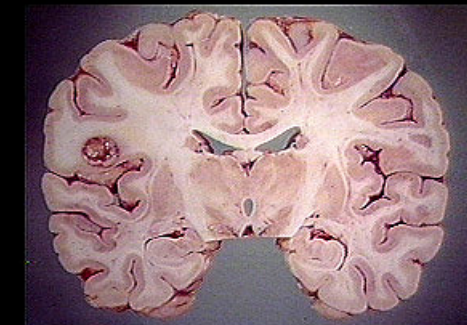
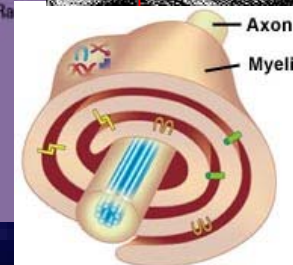
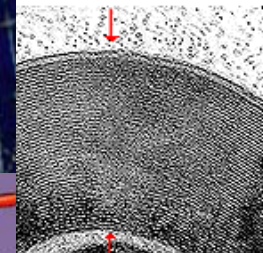
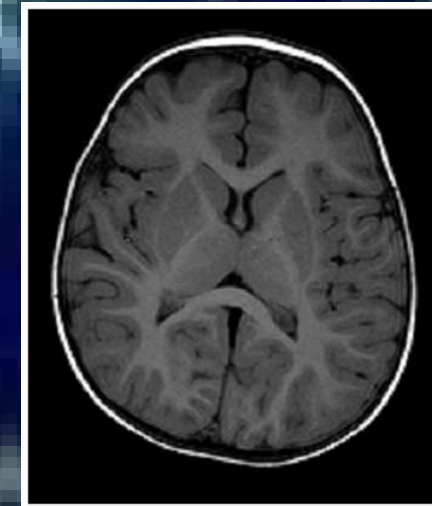
- **According to Dr Shyh-Ching Lo, senior researcher at The Armed Forces Institute of Pathology and one of America's top mycoplasma researchers, this disease agent causes many illnesses including AIDS, cancer, chronic fatigue syndrome, Crohn's colitis, Type I diabetes, multiple sclerosis, Parkinson's disease, Wegener's disease and collagen-vascular diseases such as rheumatoid arthritis and Alzheimer's.**

World Distribution of Multiple Sclerosis



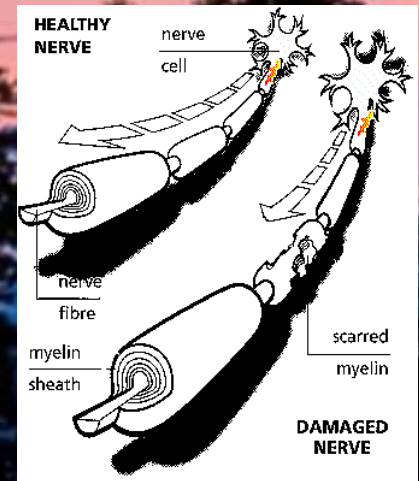
Adapted from McAlpine, D. Lumden, C.E. Achson, E.D. (1961)
Multiple Sclerosis. Reappraisal Livingstone Ltd., London

Multiple Sclerosis (MS) is an inflammatory disease of the Central Nervous System (CNS) - that's the brain and spinal cord. Predominantly, it is a disease of the "white matter" tissue.

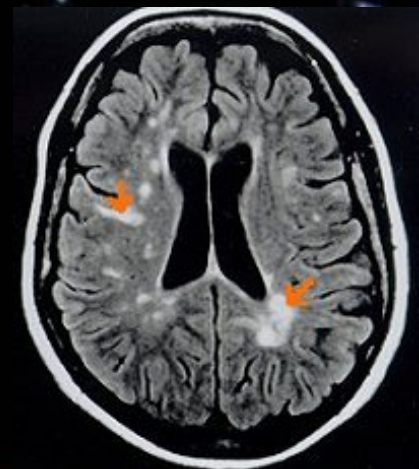


Multiple Sclerosis

In people affected by MS, patches of damage called plaques or lesions appear in seemingly random areas of the CNS white matter. At the site of a lesion, a nerve insulating material, called myelin, is lost. Clinically, MS is a hard condition to characterize because it is very unpredictable and variable.



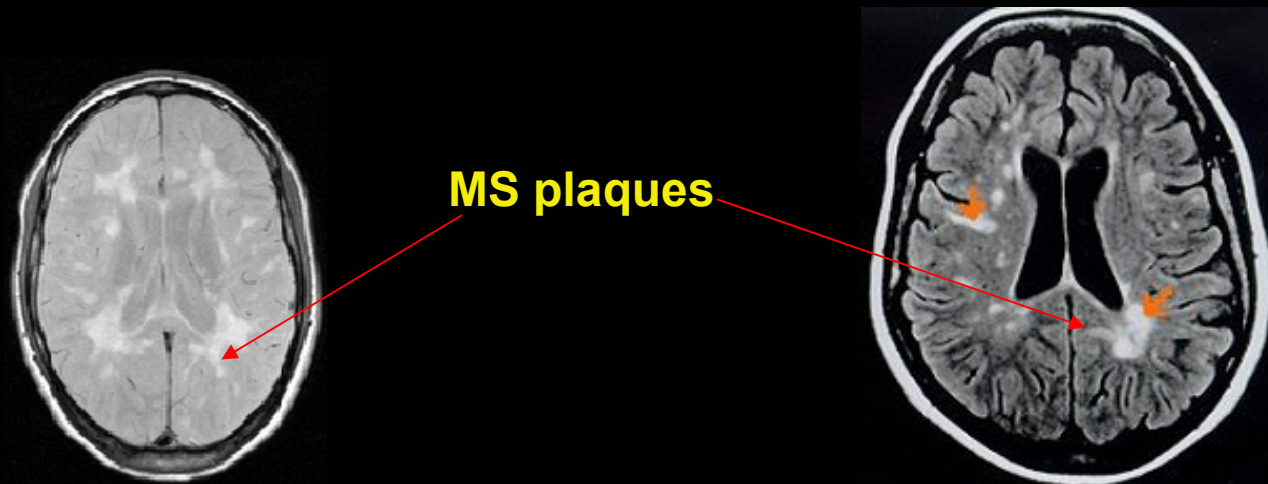
- After about ten years, approximately 50 per cent of people with RRMS go on to develop SPMS (Herndon, 2002)



Multiple Sclerosis. Neurology

Relapsing-remitting Multiple Sclerosis

Austrian Multiple Sclerosis Study Group test Immunoglobulin efficacy in a randomized, controlled 2-year trial in patients with relapsing-remitting MS.



Dr. Fazekas. "Monthly intravenous immunoglobulin (IVIg) administration to patients with relapsing-remitting multiple sclerosis (MS) improves the course of clinical disability and reduces the frequency of relapses, Treatment with IVIg resulted in **59%** lower annual relapse rate in the IVIg group than in the placebo group." **Lancet 1997;349:589-593.**

Authors concluded that monthly IVIg improved the course of clinical disability and reduced the frequency of relapses in relapsing-remitting MS.

- **Transverse Myelitis & IVIg**

- <http://www.annals.org/cgi/content/full/126/9/721>

• POSTPARTUM TREATMENT OF AUTOIMMUNE DISORDERS

• J Neurol. 2004 Sep;251(9):1133-7

• Effect of intravenous immunoglobulin treatment on pregnancy and postpartum-related relapses in multiple sclerosis.

Achiron A,

• Acute exacerbations may complicate the course of pregnancy and the postpartum period in patients with relapsing-remitting multiple sclerosis (RRMS). 108 pregnant RRMS patients.

• Group I patients were not treated,

• Group II patients were treated with IVIg 0.4 g/kg body weight/day for 5 consecutive days within the first week after delivery with additional booster doses of 0.4 g/kg body weight/day at 6 and 12 weeks postpartum (defined as 12 weeks after labor), and

• Group III patients were treated continuously with IVIg during gestation and the postpartum period (0.4 g/kg body weight/day for 5 consecutive days within the 6-8 weeks of gestation with additional booster doses of 0.4 g/kg body weight/day once every 6 weeks until 12 weeks postpartum).

• Relapse rate per woman per year for patients treated with IVIg for the whole pregnancy and postpartum period (Group III, N = 28) compared with the untreated Group I patients (N = 39) were as follows: first trimester 0.43 vs. 0.72, second trimester 0.15 vs. 0.61, third trimester 0.0 vs. 0.41, and postpartum period 0.28 vs. 1.33 ($p < 0.05$).

• Patients treated with IVIg only during the postpartum period (Group II, N = 41) also showed a decrease in relapse rate compared with untreated Group I patients, 0.58 vs. 1.33 ($p = 0.012$).

• **We conclude that in RRMS patients IVIg treatment could be considered as an optional treatment to reduce the incidence of pregnancy and postpartum-related relapses. Further randomized double-blind studies are needed to confirm our findings.**

PMID: 15372259 [

Avicenna or Ibn Cenna

Wrote the first book on medicine.

- Avicenna's *Canon of Medicine* in Europe. The Arabic text of the *Qanun* was translated into Latin as *Canon medicinae* by Gerard of Cremona in the 12th century and into Hebrew in 1279. Henceforth the *Canon* served as the chief guide to medical science in the West and is said to have influenced Leonardo da Vinci. Its encyclopaedic content, its systematic arrangement and philosophical plan soon worked its way into a position of pre-eminence in the medical literature of Europe, displacing the works of Galen and becoming the text book for medical education in the schools of Europe. The text was read in the medical schools at Montpellier and Louvain as late as 1650, and Arnold C. Klebs described it as "one of the most significant intellectual phenomena of all times." In the words of Dr. William Osler, the *Qanun* has remained "a medical bible for a longer time than any other work".

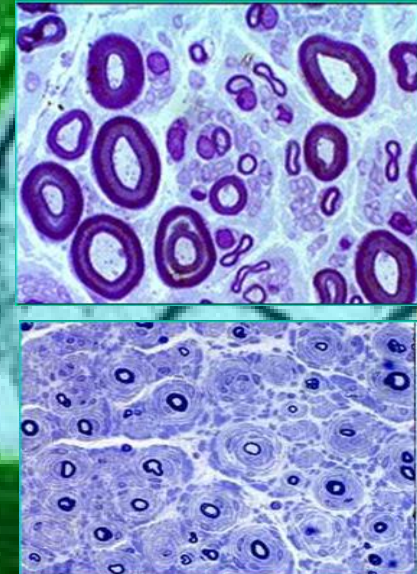
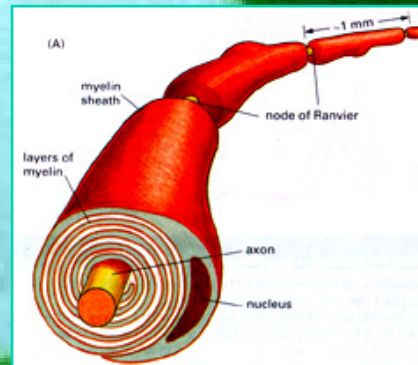


- **Ibn Sina believed that the human body cannot be restored to health unless the causes of disease is treated.**
- **So we cannot treat autoimmune diseases with pain and antidepressants.**

Chronic inflammatory demyelinating polyneuropathy (CIDP) characterized by slowly progressive weakness and sensory dysfunction of the legs and arms. The disorder, is also called chronic relapsing polyneuropathy, is caused by damage to the myelin sheath of the peripheral nerves. Although it can occur at any age and in both genders, CIDP is more common in young adults, and in men more than women. (**Under diagnosed**)

- Symptoms include tingling numbness (in the toes and fingers), weakness of the arms and legs, aching pain in muscles, loss of deep tendon reflexes (areflexia), fatigue, and abnormal sensations.

CIDP is closely related to acute Guillain-Barré syndrome and it is considered the chronic counterpart of the acute disease.



MADSAM. Neurology

- **MADSAM — Multifocal acquired demyelinating sensory and motor neuropathy. MMN and MADSAM respond to IVIG.**
- **Chronic pain, autonomic syndromes, sympathetic dystrophy**
- **Trigeminal Neuralgia (BMC Neurol. 2003 Jan 30;3(1))**

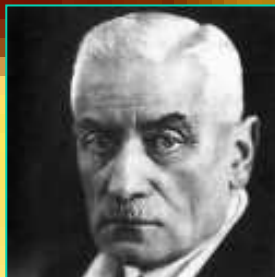
Intravenous immunoglobulin in the treatment of primary trigeminal neuralgia refractory to carbamazepine:

Onion Bulb formation in demyelination.



Guillain Barre Syndrome. Neurology

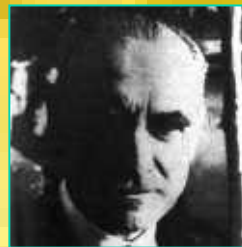
- Guillain-Barrè (ghee-yan bah-ray) syndrome is a disorder in which the body's immune system attacks part of the peripheral nervous system. The first symptoms of this disorder include varying degrees of weakness or tingling sensations in the legs or hands.
- Patients can have total paralysis. Treat with IVIG – treatment of choice.
- Usually Guillain-Barrè occurs a few days or weeks after the patient has had symptoms of a respiratory or gastrointestinal viral infection. Occasionally surgery or vaccinations will trigger the syndrome. (Usually loss of muscle reflexes, rarely increased ALS like).
- Clinical trials have demonstrated that steroid treatment is not effective but may even have a deleterious effect on the disease.
- 9,575 new U.S. cases with GBS annually, 526 to 3,830 are triggered by infection with *Campylobacter*, the most frequently isolated cause of foodborne diarrhea. Sources of *Campylobacter* include raw and undercooked poultry, raw milk, and polluted water



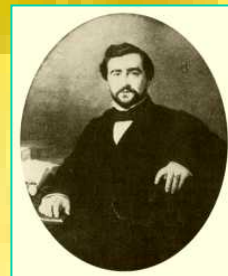
Guillian



Barre



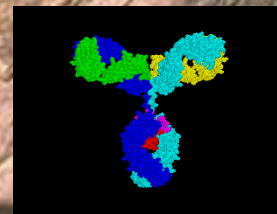
Stroh



Landry
First description
of a patient with
GBS

Mechanism of action (IVIg).

- When an IgG level is depressed, IVIG restores the level to ward off infection.
- IVIG molecules (Specially IgG) can bind and neutralize toxins .
- Following high doses of IVIG, the body tends to increase the catabolism, or breakdown, of total IgG in order to return to a normal, lower "set point" blood IgG level . Thus reducing level of circulating antibodies.



Stiff - Person Syndrome. Neurology

- Exaggerated startle suggesting abnormal brainstem function & in Hyperkplexia

- The Stiff Person syndrome is a rare disorder . In classical Stiff Man syndrome, it gradually develops and slowly progresses over several years. Patients complain of painful spasms around the back, stomach and sometimes thigh and neck. These spasms may be precipitated by unexpected events, such as a door slamming, a car backfiring or being tapped. Spasms may also be precipitated by attempts to move. As the disease progresses, there is often some degree of fixed postural abnormality, usually an arching of the lower back .
- antibody is called anti-GAD
- Abnormal axial posture, increased lumbar lordosis
- Electrical recordings from the affected muscles (termed EMG) can be useful in making the diagnosis. Here the characteristic finding is an inability of the affected muscles to relax.



Kyphosis



Lordosis

N Engl J Med. 2001 Dec 27;345(26):1870-6

Dalakas

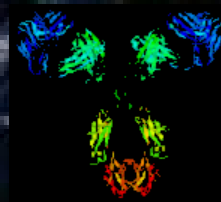


Status Spasticus a condition when a patient is twitching all over episodic opisthotonos.

Do no harm

“As to diseases make a habit of two things - to help, or at least, to do no harm.”

Hippocrates



Steroids & Cytotoxic treatment is associated with multiple Side effects.
(Immune suppression, weight gain, Gastric Ulcers, Cataracts, Skin atrophy, Hypertension, Osteoporosis, arthritis, Depression, Glaucoma, Heart disease, Myopathy, Coronary artery disease & Cushing's Syndrome.

National Institutes of Health, Bethesda, MD 20892. (Neurology. 1994 Feb;44(2):223-6.)
High-dose (IVIg) can increase blood viscosity in vitro and has been associated with thromboembolism.


Thromboembolic events were observed in two (3%) of 65 patients we treated with IVIg


Serum viscosity increased after IVIg in all the patients by 0.1 to 1.0 centipoise (cp) exceeding upper limit of normal (normal, 1.5 to 1.9 cp) and increased as high as 2.6 cp. The increase in viscosity occurred immediately after completion of the infusion, declined over 1 month


Complication from IVIG


- June 9 issue of Neurology. The report describes sixteen patients being treated at Wake Forest and several other regional medical centers who had a stroke during, or shortly after, the administration of intravenous immunoglobulin (IVIg), which is used in the treatment of a variety of neurologic and blood disorders.


Increased Viscosity what to do?


8 Glasses of Water a Day
©2002 Wendy @ <http://www.charjungle.com>



Monday 
[] [] [] [] [] [] [] [] [] []

Tuesday 
[] [] [] [] [] [] [] [] [] []

Wednesday 
[] [] [] [] [] [] [] [] [] []

Thursday 
[] [] [] [] [] [] [] [] [] []

Friday 
[] [] [] [] [] [] [] [] [] []

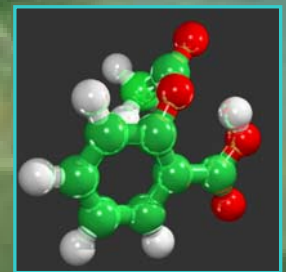
Saturday 
[] [] [] [] [] [] [] [] [] []

Sunday 
[] [] [] [] [] [] [] [] [] []

Get the "Kids And Nutrition" CD game at <http://www.nutritionproducts.net/1304> (great for fundraising too!)

Because increased serum viscosity can impair blood flow and trigger a cardiovascular or cerebrovascular thromboembolic event, IVIg should be used judiciously with monitoring of serum viscosity in elderly patients and those with **cryoglobulinemia, monoclonal gammopathies, high lipoproteins, or preexisting vascular disease.**

All the patients should drink 8 glasses of water daily for a month after the infusion. & take a aspirin daily.



aspirin

How to safely infuse IVIG

- **Use a Pump.** (To precisely control rate of infusion).
- The total dose of **2g/kg** is divided into five daily doses of 400mg/kg. (Alternate days infusion).
- Rate of infusion should not exceed 200 ml/h or 0.08 ml/kg per minute.

“IVIG in treatment of autoimmune diseases: Present status & practical therapeutic guidelines” Marino C. Dalakas MD (Muscle & Nerve 22: 1479-1497, 1999)



- You may increase the rate to 0.02 mL/kg/minute. Most patients can tolerate a gradual increase to 0.03-0.06 ml/kg/minute

• **Therapeutic dose 2gm/kg**

- **Neurology. 1994 Feb;44(2):223-6 High-dose intravenous immunoglobulin and serum viscosity: risk of precipitating thromboembolic events.**
- **Dalakas MC.**

Common Side effects IVIG

Infusion rate-related

Headache

Backache

Myalgia

Pyrexia

abdominal pain

chest tightness

hypotension or hypertension

Thrombophlebitis

- Independent of infusion rate
- Fatigue urticaria
- Anaphylaxis (IgA deficiency)
- Aseptic meningitis (Migraine)

- Eur Neurol. 2003;50(3):172-5. Therapy with intravenous immunoglobulins: complications and side-effects.

Wittstock M,

. Published data about prevalence of adverse effects range from 5%

FDA approved uses of IVIG

- Primary agammaglobulinemia
- Chronic lymphocytic leukemia
- Common variable immunodeficiency
- HIV X-linked agammaglobulinemia (<13 age)
- Bone marrow transplantation (allogeneic) (>21)
- Idiopathic thrombocytopenic purpura
- X-linked hyper-IgM deficiency
- Kawasaki syndrome



I.T.P. (Thrombocytopenia)

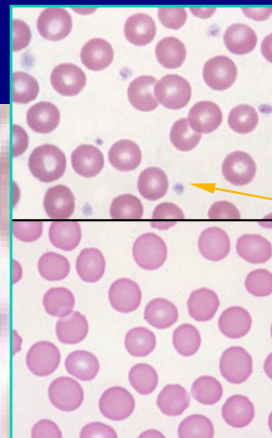
- *The effect to increase the platelet count in patients with immune/idiopathic thrombocytopenic purpura was first reported in a study by Professor Paul Imbach, M.D., University Children's Hospital, Switzerland, published in 1981 in the journal Lancet ("High-dose Intravenous Gammaglobulin for Idiopathic Thrombocytopenic Purpura" – Lancet I, 1228-1230, 1981). This study was the first to show*
- *a benefit of IVIG application in an autoimmune disease and was the first proof of an immunomodulatory role of IVIG*
- *ITP affects approximately 100,000 people in the United States, and its cause remains unknown in most cases. ITP occurs most frequently in children and young adults. Pregnant women are especially susceptible.*



Fetal Alloimmune Thrombocytopenia

- **Alloimmune thrombocytopenia is a serious fetal disorder resulting from platelet-antigen incompatibility between the mother and fetus. The diagnosis is usually made after the discovery of unexpected neonatal thrombocytopenia. Approximately 10 to 20 percent of affected fetuses have intracranial hemorrhages**
- **The neonates, however, are either born with evidence of profound thrombocytopenia or develop symptomatic thrombocytopenia within hours after birth. Affected infants often manifest generalized petechiae or ecchymoses over the presenting fetal part. Hemorrhage into viscera and bleeding following circumcision or venipuncture also may ensue. The most serious complication of neonatal alloimmune thrombocytopenia is intracranial hemorrhage, which occurs in 10-20% of infants**
- **The recurrence risk of neonatal alloimmune thrombocytopenia is extremely high and approaches 100%**
- **Treatment with IVIG**

Platelets are tiny cells which circulate in blood and function is to take part in the clotting process. Inside each platelet are many granules, containing compounds that enhance the ability of platelets to stick to each other and also to the surface of a damaged blood vessel wall.



Upper panel: normal platelet count.
(Blue cells)

Lower panel: severe thrombocytopenia.

Hemolysis

- **Effect of IVIG on Jaundice and Hemolysis:**
- Twenty neonates made up the treatment and the remaining 20 the control groups.
- The increase in bilirubin levels during the first 10 days of life was significantly lower in IVIG-treated neonates than the control group (1-tailed $P=0.004$).
- IVIG-treated neonates needed virtually no phototherapy when compared to the controls (0% vs. 35%) (2-tailed $P=0.008$).
- The neonates (7 from the control group) required a mean of 4 day course of phototherapy (Range:2-6 days).
- Of these neonates requiring phototherapy, 6 were Rh- and 1 ABO-incompatibles. These differences were significant comparing to the respective Rh- and ABO-incompatibles of the treatment group. (Fisher exact test: 1-tailed P -value: 0.007, 2-tailed P -value: 0.007, respectively.).
- Neonates treated with IVIG also showed shorter duration of hospitalization. No side effects of IVIG therapy were observed.
- Irn J Med Sci 2000; 25(3&4):129-133.
- The increase in bilirubin levels during the first 10 days of life was significantly lower in IVIG-treated neonates than the control group (1-tailed $P=0.004$).
- **IVIG-treated neonates needed virtually no phototherapy when compared to the controls (0% vs. 35%) (2-tailed $P=0.008$).**



Myelofibrosis

- Arch Pediatr. 1996 Jan;3(1)
Myelofibrosis regressing under corticotherapy and intravenous immunoglobulins in an infant Pilorget H, Bangui A, Adam M, Leverger G.
- Lupus. 1997;6(4):408-11. **Successful treatment of early secondary myelofibrosis in SLE with IVIG.** Aharon A, Levy Y,

- **Fibrosis regression induced by intravenous gammaglobulin treatment**
- **1: Ann Rheum Dis. 2003 Feb;62(2):175-7. H Amital¹, E Rewald²**
- **Methods: Eight patients with excess fibrotic reaction in the course of diverse diseases were analysed; Results: Fibrotic excess was reduced in all the patients by IVIg treatment. In five patients the disease as a whole benefited from the infusion of immunoglobulins.**
- **Conclusion: IVIg may enhance resorption of fibrosis and promote healing in patients with fibrotic associated disorders.**

Interstitial pulmonary fibrosis, high power. During active disease, there is frequently an inflammatory cellular infiltrate consisting mainly of lymphocytes and macrophages with many neutrophils; these cells are present in the interstitium and in the airspaces

Multifocal Motor Neuropathy Neurology

- (MMN) slowly progressive asymmetrical weakness and muscle atrophy, accompanied by cramps, fasciculation's. Weakness more pronounced than atrophy in muscles. As MMN progresses, atrophy is prominent. Disease begins in arms. The striking clinical feature is the multifocal distribution of the weakness, which, in the beginning, may be localized within the territory of individual peripheral nerves. The affected nerves are not palpably enlarged, as in patients with hereditary neuropathies (Two or more nerves involved). Sed rate may be elevated.
- Patients do not show upper motor neuron involvement as in ALS.
- Conduction block in motor nerves is hallmark of MMN. Motor conduction block (MCB) is failure of a nerve action potential to propagate a segment of intact myelinated nerve fiber. MCB leads to reduction of the amplitude and the area of (CMAP) after stimulation of the nerve proximal to the affected segment. The CMAP is normal distal to the affected segment. In MMN motor conduction block occurs most frequently in the ulnar and median nerves, both proximally and distally. MCB also occurs also in acute and chronic compressive neuropathies, Guillain-Barre syndrome, and CIDP

Human immunoglobulin (HIG) is the treatment of choice for MMN based on the results of two independent trials

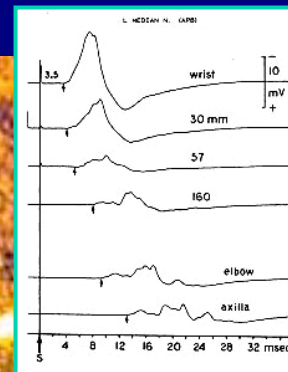
Patient trying to extend fingers



Patient trying to make a Fist.



Conduction Block



Dermatomyositis or Polymyositis Rheumatology

- The diseases differ in that dermatomyositis is accompanied by a skin reaction that is manifested as a rash, commonly seen over the face, chest, and knuckles.

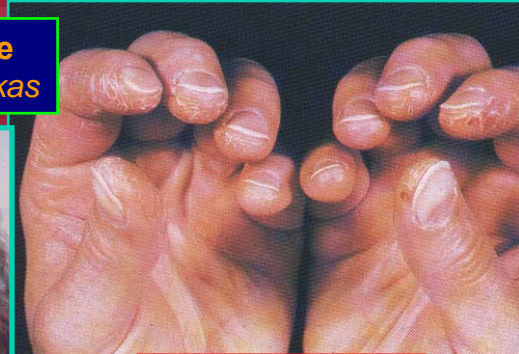
NEMJ Volume 329:1993-2000 December 30, 1993 Number 27 **A Controlled Trial of High-Dose Intravenous Immune Globulin Infusions as Treatment for Dermatomyositis** *Marinos C. Dalakas*

Results The eight patients assigned to immune globulin had a significant improvement in scores of muscle strength ($P < 0.018$) and neuromuscular symptoms ($P < 0.035$), whereas the seven patients assigned to placebo did not. With crossovers, a total of 12 patients received immune globulin. Of these, nine with severe disabilities had a major improvement to nearly normal function.

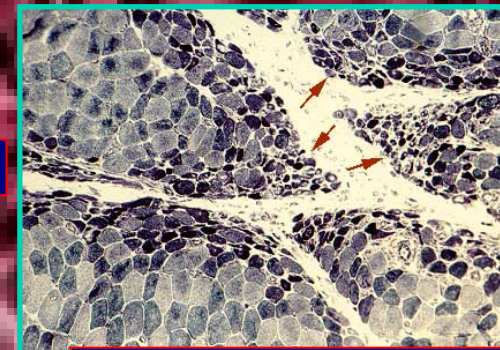
Conclusions **High-dose intravenous immune globulin is a safe and effective treatment for refractory dermatomyositis.**



Periorbital Rash



Machinist hands



Perifascicular atrophy

CPK & Sedrate elevated.

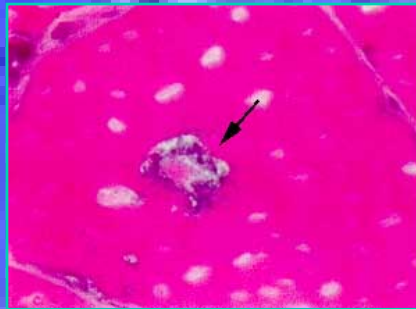
Patients have difficulty rising from a sitting position, climbing stairs, lifting objects, or reaching overhead. In some cases, distal muscles (those not close to the trunk of the body) may also be affected later in the course of the disease. Trouble with swallowing (dysphagia) may occur. Very rarely, the muscles ache and are tender to touch. The disease may be associated with other collagen vascular, autoimmune or infectious disorders Is there any treatment?

Myositis (IBM).^{Neurology}

- **Inclusion body myositis, a inflammatory myopathy. Refractory polymyositis upon reevaluation, has been diagnosed as (I.B.M.). Weakness affects the distal flexor muscles of hands and quadriceps muscles more severely**



Eosinophilic Inclusions



Rimmed Vacuole



I.B.M Patient



Muscle Atrophy

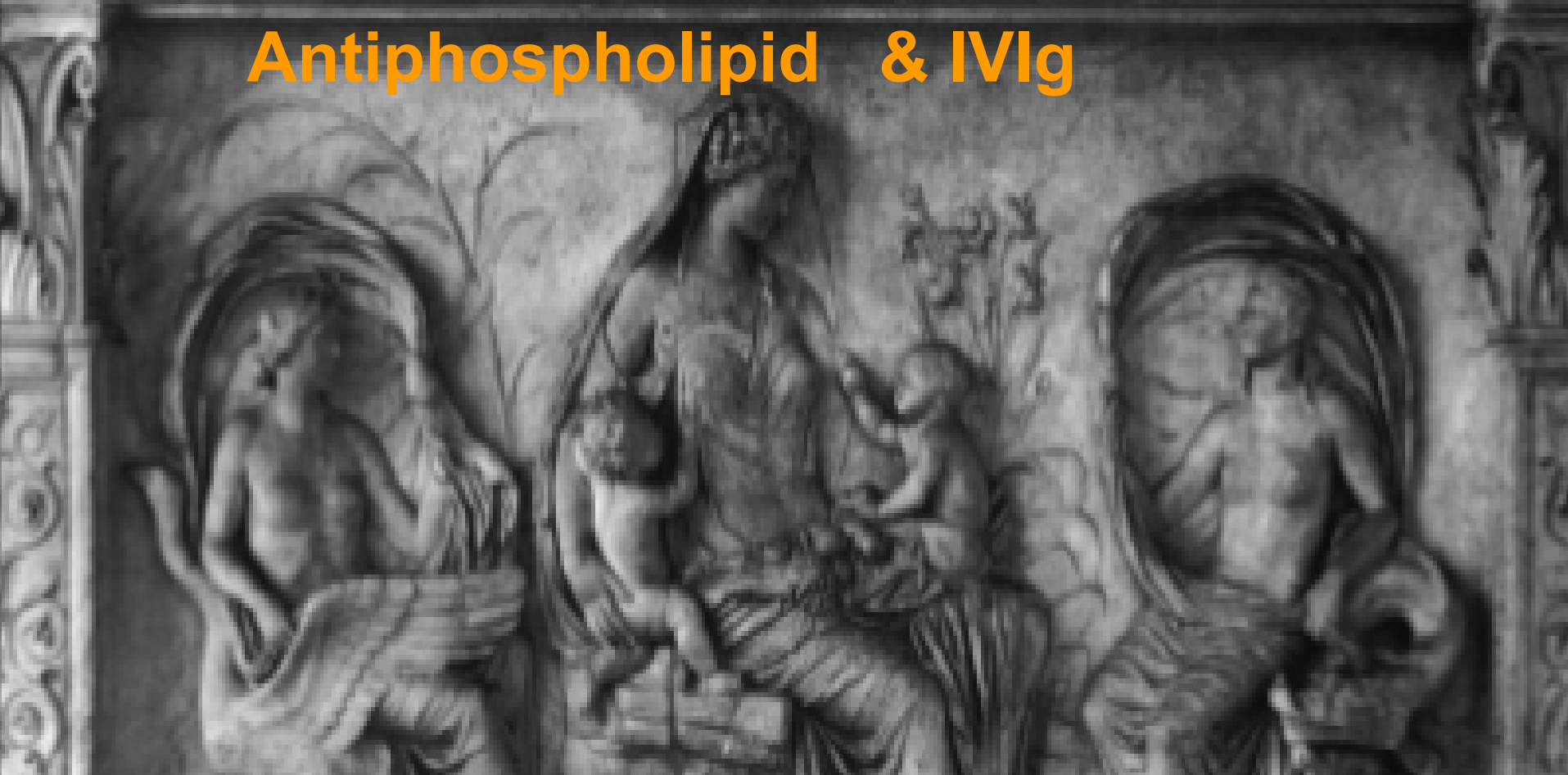
• Anticardiolipin antibody syndrome

- PATIENT(s): Forty-seven women were enrolled in the study. The mean age of the women was 37 years (range, 28-45 years),
- . Immunologic abnormalities included antiphospholipid antibodies (32%), antithyroid antibodies (53%), antinuclear antibodies (28%), antiovarian antibodies (2%), increased natural killer cells (40%), increased immunoglobulin (Ig)M level (28%), and increased CD4/CD8 T-cell ratio (15%).
- Treatment with IVIG at a dose of 0.2 g/kg within 2 weeks of attempted conception. Once conception was achieved, IVIG treatment was continued on a monthly basis at the same dose through 26-30 weeks of gestation.
- Of the 47 women, 36 received initial IVIG treatment, and 24 subsequently became pregnant. Of these women, 20 continued IVIG treatment through 26-30 weeks of gestation, and **19 (95%)** had a successful term pregnancy.
- . Of the 11 women who refused IVIG therapy, **7 became pregnant, and all 7 miscarried.**
- Low-dose IVIG therapy is beneficial for older women with immunologic abortion. The optimum duration of IVIG treatment in these women requires further study

Successful treatment of immunologic abortion with low-dose intravenous immunoglobulin. Stricker RB, Fertil Steril. 2000 Mar;73(3):536-40.

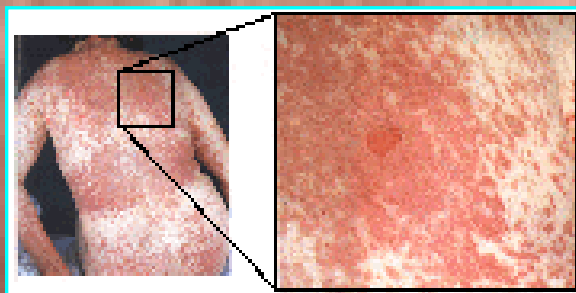


Antiphospholipid & IVIg

- 
- **Patients with Antithyroid antibodies, CD15, CD16, NK Cells & infertility. Am J Reprod Immunol. 1996 Apr;35(4):363-9. & 1996 Aug;31(1-2):125-41. 86.3% of women with elevated NK cells who received the IVIg and anticoagulation therapy had a successful pregnancy outcome;**
 - **Am J Reprod Immunol. 2001 Dec;46(6):399-404. 16 Patients Treated with IVIg become Fertile..**
 - **Aspirin & heparin effective in 70% of patients, rest 30% respond to IVIG.**

Steven Johnson Syndrome & Toxic Epidermal Necrolysis

- Pediatrics. 2003 Dec;112(6 Pt 1):1430-6. Use of intravenous immunoglobulin in children with stevens-johnson syndrome and toxic epidermal necrolysis: seven cases. Metry DW, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis are the most severe cutaneous reactions that occur in children. **We review 28 previous reports in which IVIG** was used in pediatric patients with SJS and toxic epidermal necrolysis and discuss our experience in 7 children with SJS, in whom **no new blisters developed within 24 to 48 hours after IVIG administration and rapid recovery ensued**



• **Steven Johnson**

Toxic Epidermal Necrolysis

Arch Dermatol. 2003 Jan;139(1):26-32.

- **Treatment of toxic epidermal necrolysis with high-dose intravenous immunoglobulins: multicenter retrospective analysis of 48 consecutive cases.** Prins C
- **OBJECTIVE:** To evaluate the effect of high-dose intravenous immunoglobulin (IVIG) in toxic epidermal necrolysis (TEN), parameters that may affect response to treatment, and the effect of different IVIG batches on Fas-mediated cell death. **DESIGN:** Multicenter retrospective analysis of 48 consecutive TEN patients treated with IVIG. **SETTING:** Fourteen university hospital dermatology centers in Europe and the United States. **PATIENTS:** Forty-eight patients with TEN (skin detachment >10% of their body surface
- **CONCLUSIONS:** Early infusion of high-dose IVIG is safe, well tolerated, and likely to be effective in improving the survival of patients with TEN. We recommend early treatment with IVIG at a total dose of 3 g/kg over 3 consecutive days (1 g/kg per day for 3 days).

Dermatology. 2003;207(1):96-9.

Effect of high-dose intravenous immunoglobulin therapy in Stevens-Johnson syndrome: a retrospective, multicenter study. 12 SJS patients (mean age 44 years) were treated with IVIG at a mean dose of 0.6g/kg/day for an average of 4 days. An objective response to IVIG infusion was observed in all patients within a mean of 2 days, and **the overall survival rate was 100%**. Total skin healing occurred, on average, within 8.3 days

Int J Dermatol. 2004 Nov;43(11):847-51. (IVIG in TEN) Al-Mutairi N, Arun J, Osama NE average total body surface area involvement was 57.5% (30-90%). 12 Patients treated 100% survival.



Atopic Dermatitis or Eczema



- In atopic dermatitis, the skin becomes extremely itchy. Scratching leads to redness, swelling, cracking, "weeping" clear fluid, and finally, crusting and scaling. In most cases, there are periods of time when the disease is worse (called exacerbations or flares) followed by periods when the skin improves or clears up entirely (called remissions).
- U.S. health insurance companies spend more than \$1 billion per year on atopic dermatitis.



copyright 1998 Arthur C Huntley MD



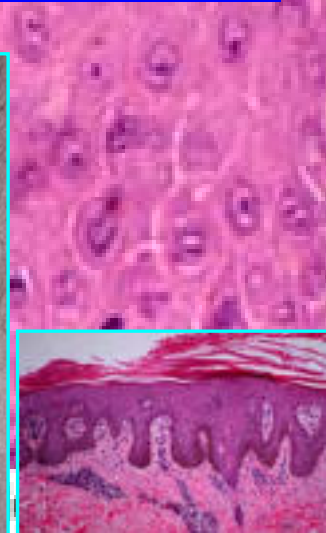
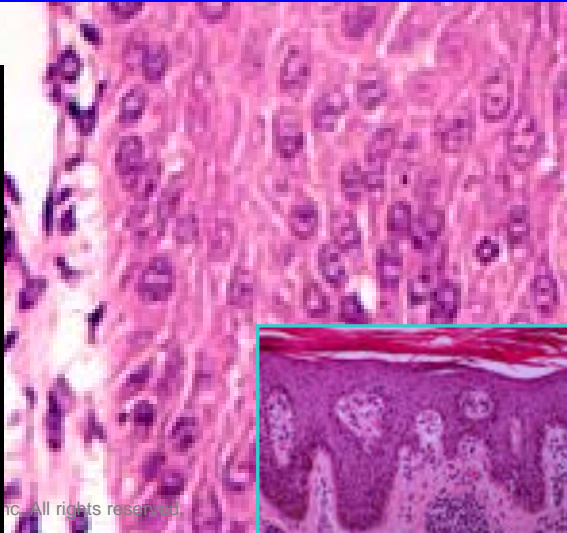
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Psoriasis

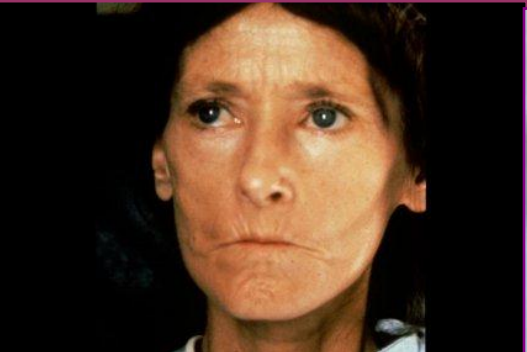
- **Psoriasis** is an immune-mediated, genetic disease manifesting in the skin and/or the joints. It affects more than 4.5 million people in the United States. In plaque psoriasis, the most common type, patches of skin called "lesions" become inflamed and are covered by silvery white scale
- U.S. health insurance companies spend more than \$1 billion per year on atopic dermatitis.
- Between \$1.6 billion and \$3.2 billion is spent per year to treat psoriasis



Scleroderma



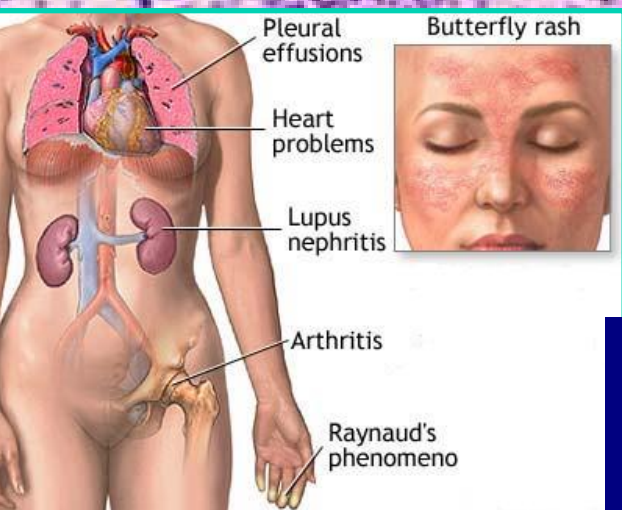
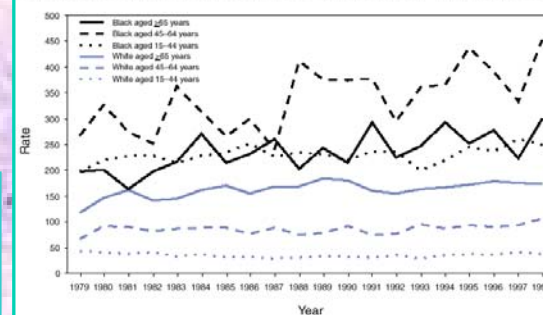
- Br J Dermatol. 2003 Dec;149(6):1276-81
- Scleromyxoedema: treatment of cutaneous and systemic manifestations with high-dose intravenous immunoglobulin.
Kulczycki A We report a series of three consecutive patients with scleromyxoedema treated with high-dose intravenous immunoglobulin (hdIVIg). Each of the three patients had relatively low levels of a highly basic IgG-lambda paraprotein, and each has demonstrated a sustained response of both their cutaneous and extracutaneous disease to hdIVIg



Lupus or S.L.E. Rheumatology

Mortality Rate

FIGURE 1. Systemic lupus erythematosus death rates* among females, by age group and race — United States, 1979–1998



ANA (Anti Nuclear Antibody)
Increased C.R.P. & Sed rate

Lupus (SLE) is an autoimmune disease that can affect virtually any system in the body. Think of it as a 'self-allergy' where the body attacks its own cells and tissues, causing inflammation, pain, and possible organ damage.

Lupus. 1999;8(9):705-12.

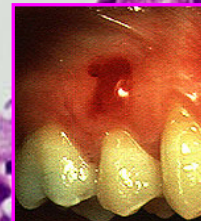
A study of 20 SLE patients with intravenous immunoglobulin--clinical and serologic response

Department of Medicine and the Research Unit of Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, and Sackler Faculty of Medicine, Tel-Aviv University, Israel.

OBJECTIVE: To test the clinical response of systemic lupus erythematosus (SLE) patients to intravenous immunoglobulins (IVIg), and whether the clinical response of IVIg treatment in SLE is accompanied by modification of SLE-associated autoantibodies/antibodies (Abs) and complement levels. **METHODS:** Twenty SLE patients were treated with high-dose (2 g/kg) IVIg monthly, in a 5-d schedule. Each patient received between 1-8 treatment courses. They were evaluated for the clinical response, Systemic Lupus Activity Measure (SLAM) score before and after IVIg, levels of antinuclear antibody (ANA), dsDNA (double-stranded DNA), SS-A or SS-B, ENA (extractable nuclear antigens), C3 and C4 levels before and after the treatment, and before and after each treatment course. **RESULTS:** A beneficial clinical response following IVIg treatment was noted in 17 out of 20 patients (85%)

Pemphigus.

- Any non healing skin, gum or eye lesion should be considered as Pemphigus.
- **Consensus Statement on the Use of Intravenous Immunoglobulin Therapy in the Treatment of Autoimmune Mucocutaneous Blistering Diseases** A. Razzaque Ahmed, MD, DSc; Mark V. Dahl, MD; for the Consensus Development Group *Arch Dermatol.* 2003;139:1051-1059. .



Gum lesion of Pemphigus



Non healing skin lesion

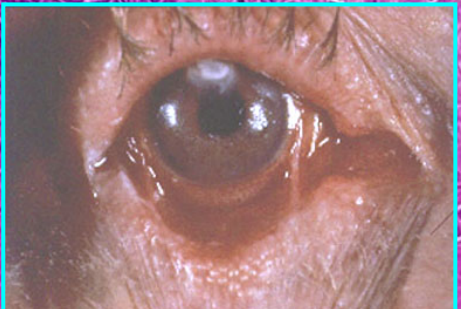


Pemphigus vulgaris is an autoimmune disorder, where the body's immune system attacks some of the proteins in the skin. Pemphigus usually occurs in middle-aged or older people

Pemphigoid.

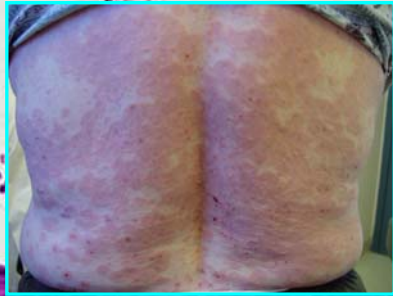


- Involves Cornea, Iris, Conjunctiva, Lens.
- Patients have been described with eye **irritation**, excessive tearing, and foreign body sensation where the eye symptoms preceded the appearance of mouth and skin lesions. Blisters can involve the skin surface of the eyelids
- Ophthalmology. 2004 Jul;111(7):1380-2. In 8 patients who completed the protocol, progression of the disease was not observed (Sami N)

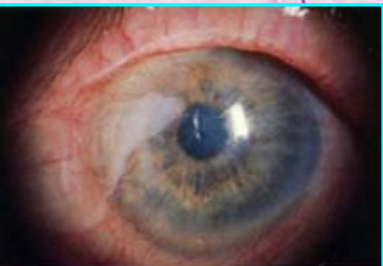
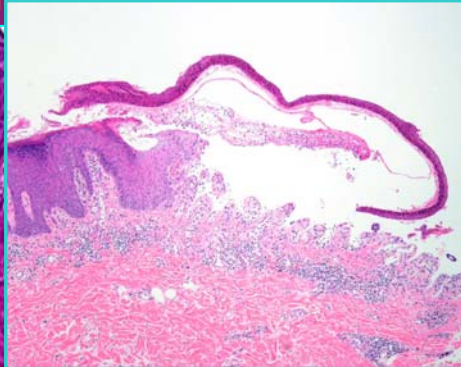


Cicatricial pemphigoid

Ocular cicatricial pemphigoid is a chronic, progressive, auto-immune disease characterised by shrinkage of the conjunctiva, entropion, trichiasis, xerosis and, finally, reduced vision from corneal opacification. The long-term prognosis without IVIGS is always very poor.



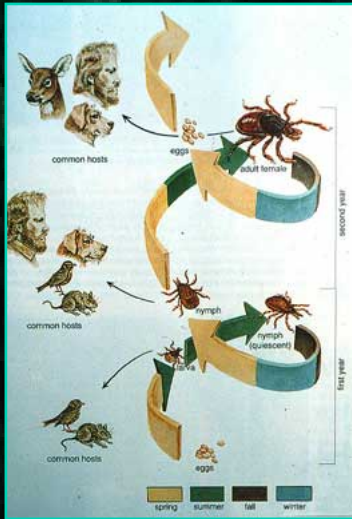
Bullous Pemphigoid



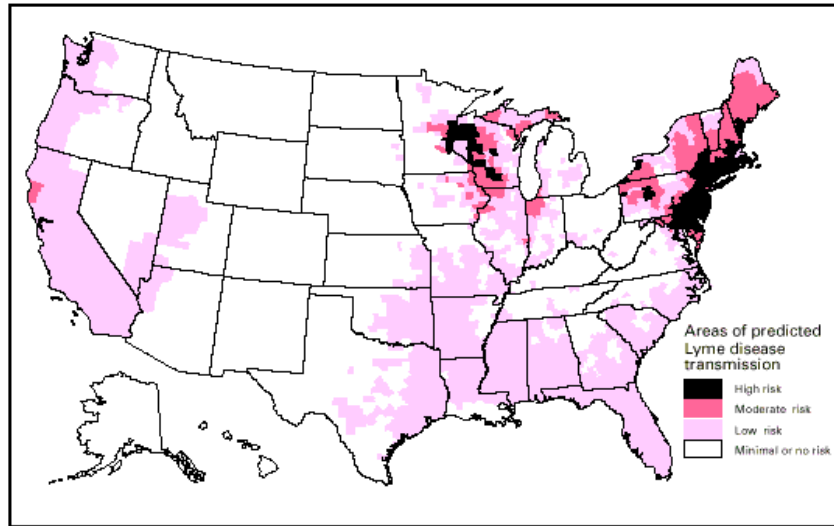
Symblepharon, corneal and conjunctival keratinisation, neovascularisation and pannus. Note the central dimple.

Lymes Disease

Infectious Diseases, Neurology, Internist, Family Physician



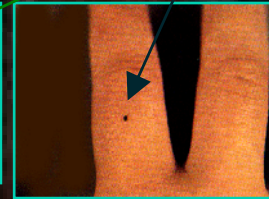
National Lyme disease risk map with four categories of risk



Note: This map demonstrates an approximate distribution of predicted Lyme disease risk in the United States. The true relative risk in any given county compared with other counties might differ from that shown here and might change from year to year. Risk categories are defined in the accompanying text. Information on risk distribution within states and counties is best obtained from state and local public health authorities.



Target lesion on skin after bitten by Deer tick.



Life cycle of Deer Tick

Borrelia burgdorferi
Cause of Lymes



- Endemic or 'hot spots' in the Berkshire range, on Cape Cod, Martha's Vineyard, Nantucket
- Two Controlled Trials of Antibiotic Treatment in Patients with Persistent Symptoms and a History of Lyme Disease
Dr. Klempner says, that researchers should investigate autoimmune and other processes to determine whether they play a role in a least some of the symptoms of chronic Lyme disease.

New England Journal of Medicine . vol. 345(2): July 12, 2001.

In chronic Lyme Disease the patient is sterile (No *Borrelia*) so the chronic sickness is a autoimmune process. Treat with IVIG.

Hepatitis C Patients & IVIG



- **Need 2gm/kg infusion.**

- Multiple problems autoimmune in nature causing chronic neuritis, neuropathy are treated.

- BioDrugs. 2004;18(1):63-70.

Intravenous Immunoglobulin Plus Interferon-alpha in Autoimmune Hepatitis C.

Malaguarnera M, Guccione N, Musumeci S, Bregna A, Motta M, Di Fazio I.

Institute of Internal Medicine and Geriatrics, University of Catania, Catania, Italy.

Post Polio Syndrome

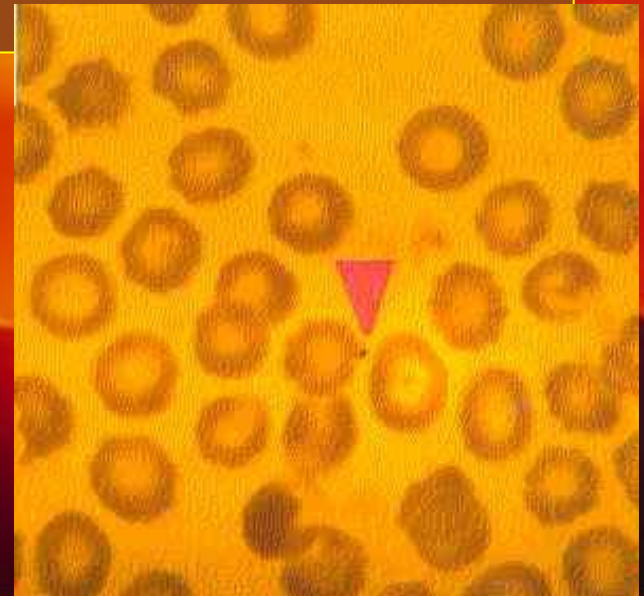


- Sixteen patients with a history of acute polio and progressive symptoms of muscle weakness, which are typical for post-polio syndrome, were treated with immunoglobulin intravenously. Their high levels of pro-inflammatory cytokines in cerebrospinal fluid (CSF), indicating an ongoing inflammatory process, were dramatically reduced after treatment. When treated with a standard regimen of immunoglobulin intravenously, given daily on three consecutive days, the expression of CSF proinflammatory cytokines was dramatically reduced to almost zero
- Prior poliomyelitis – Ivlg treatment reduces proinflammatory cytokine production.
Gonzalez H, Khademi M, Andersson M, Piehl F, Wallström E, Borg K, Olsson T.
Journal of Neuroimmunology (2004). In press.

Chronic Fatigue Syndrome

- **CFIDS** Chronic Fatigue & Immune deficiency syndrome.
- **Approved for use in UK & Canada.**
- Am J Med. 1990 Nov;89(5):561-8.
A double-blind, placebo-controlled trial of intravenous immunoglobulin therapy in patients with chronic fatigue syndrome. Lloyd A, Hickie I, Wakefield D, Boughton C, Dwyer J
- **CONCLUSION:** Immunomodulatory treatment with immunoglobulin is effective in a significant number of patients with CFS
- 6 Million patients in USA mostly women.
Clin Infect Dis. 2003 May 1;36(9):e100-6. Epub 2003 Apr 22.
Successful intravenous immunoglobulin therapy in 3 cases of parvovirus B19-associated chronic fatigue syndrome. Kerr JR,

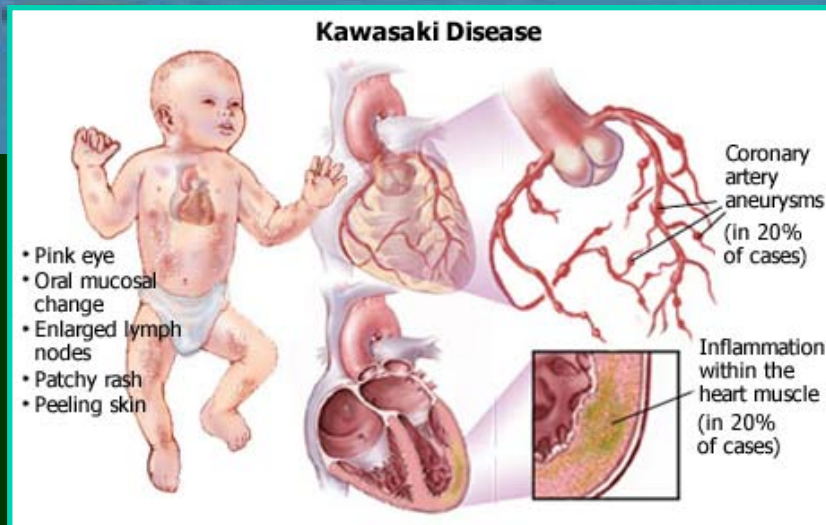
In summary, a multi-drug resistant cluster of canine chronic fatigue syndrome showed complete clinical and hematological remission 7 days after treatment with **thiacetarsamide sodium**, an organic trivalent arsenical given intravenously in low dosages (0.1/mlk/Kg/day) for 3 days. Severe skin lesions were associated with CFS-related symptoms, presence of micrococci-like organisms in the blood, high muscle enzymes and the recovery of two vancomycin-resistant strains of *Staphylococcus xilosus* from drinking water and a lesion.



Kawasaki Disease

Pediatrics & Cardiology

- **Red Tongue.**
- **Elevated CRP.**
- **Cardiac aneurysms.**
- **Fever, Red Eyes,**
- **Enlarged Lymph Nodes**
- **IVIG is the treatment of choice.**
- **Kawasaki disease should be treated with IVIG (3 gm/kg single dose) within 10 days of onset of symptoms.**



Red Tongue

Rash



Swollen hands



Peeling skin

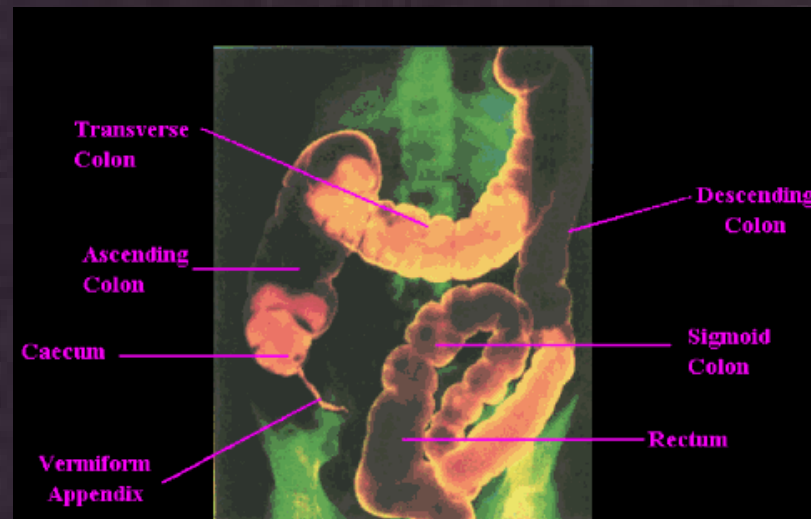


Ulcerative Colitis & Crohn's

- **Am J Gastroenterol. 1992 Jan; 87(1): 91-100.**
Intravenous immunoglobulin therapy for active, extensive, and medically refractory idiopathic ulcerative or Crohn's colitis.

Levine DS, Fischer SH, Christie DL, Haggitt RC, Ochs HD.

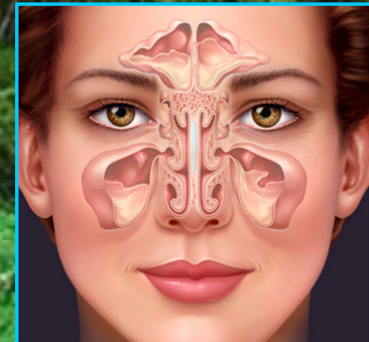
- **For all 12 patients, statistically significant reductions were achieved in the colitis activity score and daily prednisone dose.**



Second screen of a slide showing large intestine structure

Sinusitis – ENT

- Sinusitis is an inflammation of the mucosal surface of the paranasal sinuses.
- Symptoms of acute sinusitis are confused with an upper respiratory infection. In the diagnosis consider Immunodeficiency states.
- Immunodeficiency evaluation in patients with recurrent sinusitis, otitis, cellulitis or pneumonia is indicated including total immunoglobulin levels .
- Intravenous gammaglobulin is appropriate in patients who have recurrent sinusitis with appropriate immune deficiencies.



Common Variable Immune Deficiency

- (CVID) is a disorder characterized by low levels of serum immunoglobulins (antibodies) and an increased susceptibility to infections. In some patients there is a decrease in IgG and IgA; in others, all three (IgG, IgA and IgM) of immunoglobulins may be decreased .
- The presenting features of most patients with CVID are recurrent infections involving the ears, sinuses, nose, bronchi and lungs. Recurrent lung infections cause scarring of these structures and results in bronchiectasis. Patients who have received complete immunizations against polio, measles, diphtheria and tetanus will usually have very low or absent antibody levels to one or more of these vaccines.
- Treatment Most patients with immunodeficiency and arthritis respond favorably to treatment with gamma globulin.

- **Below-normal levels of IgG and IgA**
- **Zero-to-slightly-low levels of IgG**
- **low-to-normal IgM levels**
- **whether B cells produce antibodies following a common vaccination like a tetanus shot**
- **How well the T cells are working**
- **gastrointestinal infections if there are digestive symptoms**

• IgG SUBCLASS DEFICIENCY

- Recurrent ear infections, sinusitis, bronchitis and pneumonia are the most frequently observed illnesses in patients with IgG subclass deficiencies. Both males and females may be affected
- Selective IgG1 subclass deficiency is very rare. IgG2 subclass deficiency is the most frequent subclass deficiency in children, while IgG3 subclass deficiency is the most common deficiency seen in adults. IgG4 deficiency most often occurs in association with IgG2 deficiency



Selective IgA Deficiency

Selective IgA Deficiency (1/600) is the severe **deficiency** or total absence of the **IgA** class of immunoglobulins in the blood serum and secretions . **Most common immune deficiency. blood product that contains IgA, an allergic reaction may result. Although allergic reactions to IgA are very uncommon, it is important that every patient with Selective IgA Deficiency is aware of the potential risk of transfusion reactions if they receive blood or blood products .**

The diagnosis of Selective IgA Deficiency is usually suspected because of either chronic or recurrent infections, allergies, autoimmune diseases, or chronic diarrhea An occasional patient may also have IgG2 subclass deficiency and associated antibody deficiency.

Some patient with IgA deficiency also have IgG2 subclass deficiency with a deficiency of antibody production. In these individuals, the use of replacement gamma globulin may be helpful in diminishing the frequency of infections (Arch Pediatr. 2001 Jun;8(6):629-33.)

IgA deficiency patients are at increased risk of autoimmune diseases and they benefit from IVIg.

Vasculitis & IVIG

Wegener's Granulomatosis

Polymyalgia Rheumatica

Behcet's Disease

Takayasu's Arteritis

Rheumatoid Vasculitis

Polyarteritis Nodosa

Churg-Strauss Syndrome

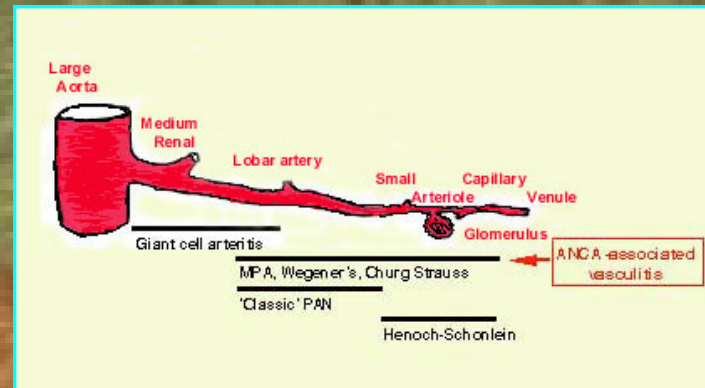
Microscopic Polyangiitis

Giant Cell Arteritis

Cryoglobulinemia

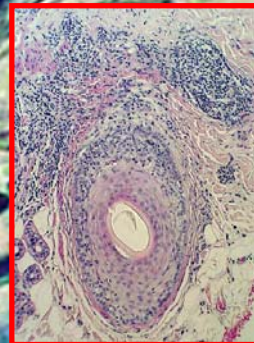
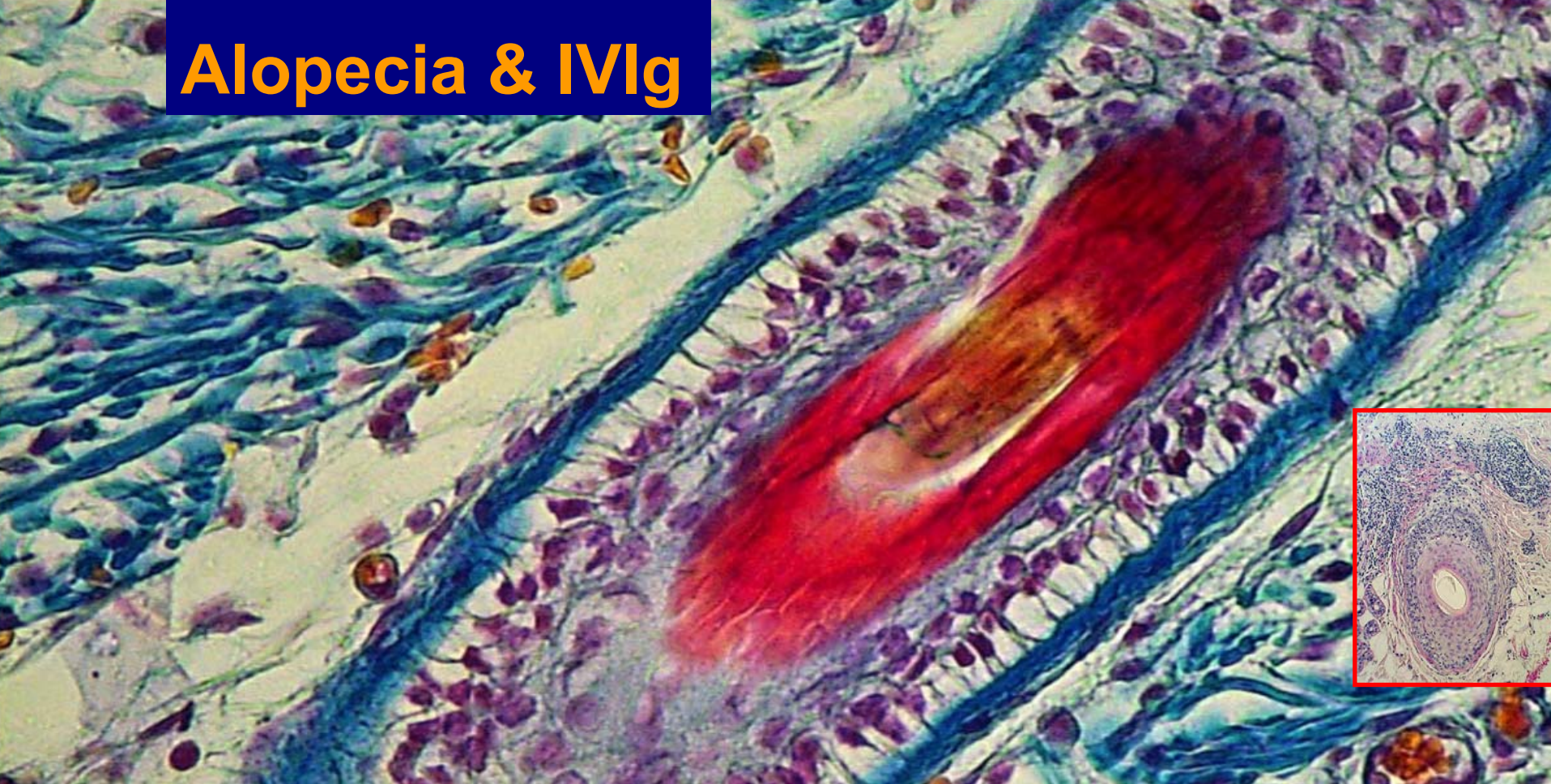
Central Nervous System Vasculitis

Buerger's Disease



• Splinter hemorrhages

Alopecia & IVIg



- Asian Pac J Allergy Immunol. 1999 Mar;17(1):59-62. Effect of IVIG on the hair regrowth in a common variable immune deficiency patient with alopecia universalis.

Boonyaleepun S,

- Br J Dermatol.1994 Nov;131(5):735-Alopecia areata responding to immunoglobulin, with varying response to different preparations.

Ostlere LS, Harris DW,

- Inflammation in hair follicle

Sjogren's & IVIG

- **Neurology. 2003 Feb 11; 60(3): 503-5.**
Benefit of IVIG for long-standing ataxic sensory neuronopathy with Sjogren's syndrome. IV immunoglobulin.

Takahashi Y, Takata T, Hoshino M, Sakurai M, Kanazawa I. (IVIG) was given to five patients with severe disabilities for an average of 12 years. Four patients showed remarkable improvement, two of whom responded after the first course.

- **Ann Rheum Dis. 1995 Nov; 54(11): 936.**
Successful application of high dose intravenous immunoglobulins in Sjogren's syndrome associated arthritis.



Urticaria.

- Br J Dermatol. 1998 Jan;138(1):101-6.

Intravenous immunoglobulin in autoimmune chronic urticaria. O'Donnell BF,

Ten patients with severe, autoimmune CU, poorly responsive to conventional treatment, were treated with IVIG 0.4 g/kg per day for 5 days. The outcome on cutaneous wealing and itch was monitored using urticaria activity scores, visual analogue scales and autologous intradermal serum tests. **Clinical benefit was noted in nine of 10 patients: three patients continue in prolonged complete remissions (3 years follow-up)**

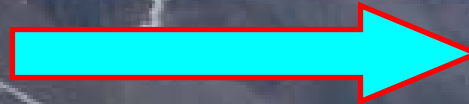


- **Urticaria**
- **Greaves MW, O'Donnell BF. Related Articles, Links**
Not all chronic urticaria is "idiopathic"!
Exp Dermatol. 1998 Feb;7(1):11-3.
- **30% of the total in which the disease is caused by the presence of IgG autoantibodies against the high affinity IgE receptor (FcepsilonR1alpha)**

Vitiligo



FROM here

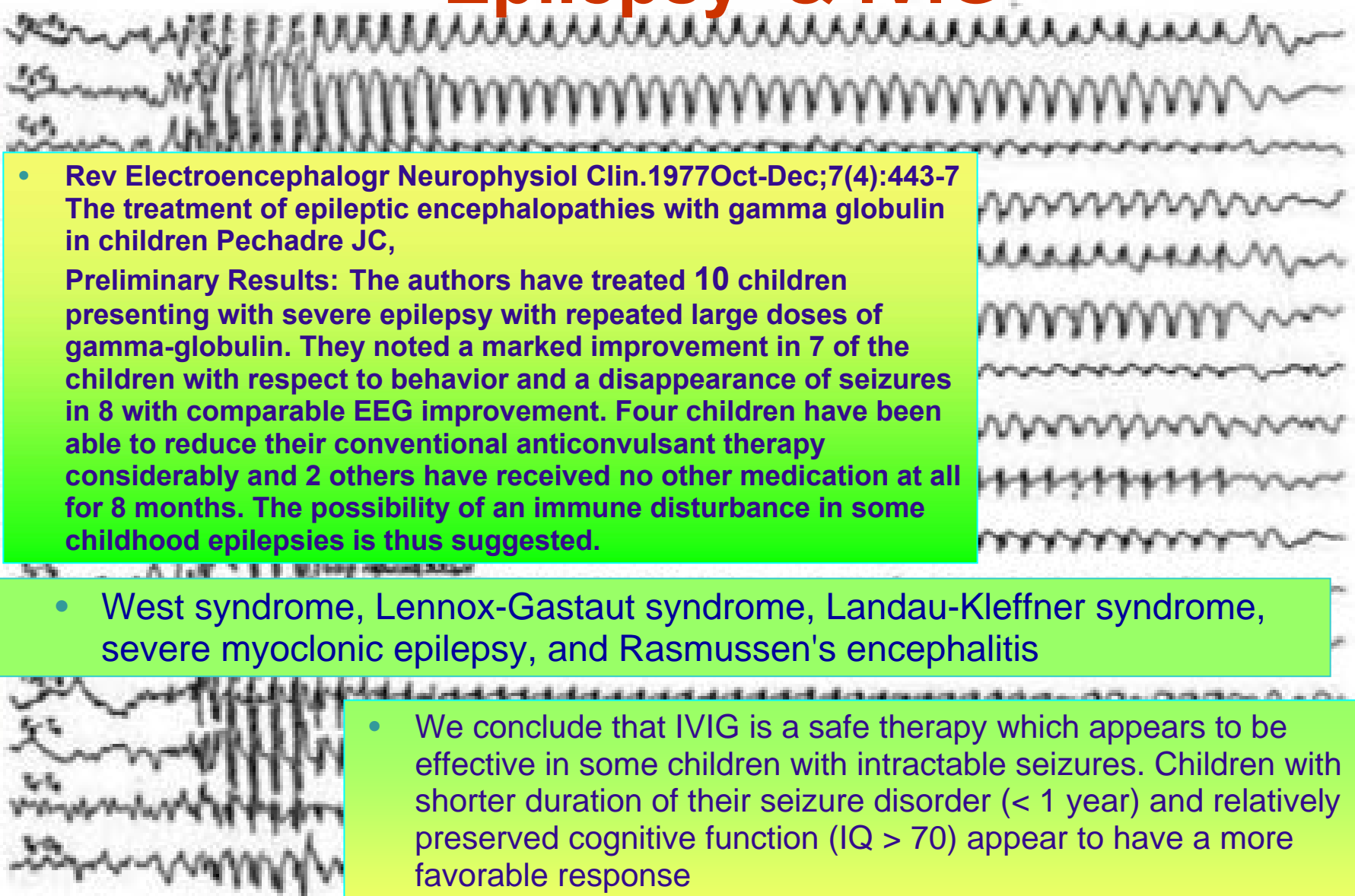


To This

- The cutaneous autoimmune diseases most closely linked to CVID are vitiligo and alopecia areata. Eight cases of vitiligo with CVID, including our own, have been reported. In all the cases, the depigmented lesions had the typical morphology and symmetrical distribution. Two of the previous patients were described as having extensive vitiligo, although the actual body surface areas involved were not disclosed. A progressive course appears to be the rule in CVID-associated vitiligo. With our patient and two others, treatment of CVID with intravenous immunoglobulins (IVIg) led to improvement in their general health, but failed to reverse the depigmentation.

- Spickett G, et al. Alopecia totalis and vitiligo in common variable immunodeficiency. *Postgrad Med J* 1991;67:291-4.

Epilepsy & IVIG



- Rev Electroencephalogr Neurophysiol Clin.1977Oct-Dec;7(4):443-7
The treatment of epileptic encephalopathies with gamma globulin in children Pechadre JC,

Preliminary Results: The authors have treated 10 children presenting with severe epilepsy with repeated large doses of gamma-globulin. They noted a marked improvement in 7 of the children with respect to behavior and a disappearance of seizures in 8 with comparable EEG improvement. Four children have been able to reduce their conventional anticonvulsant therapy considerably and 2 others have received no other medication at all for 8 months. The possibility of an immune disturbance in some childhood epilepsies is thus suggested.

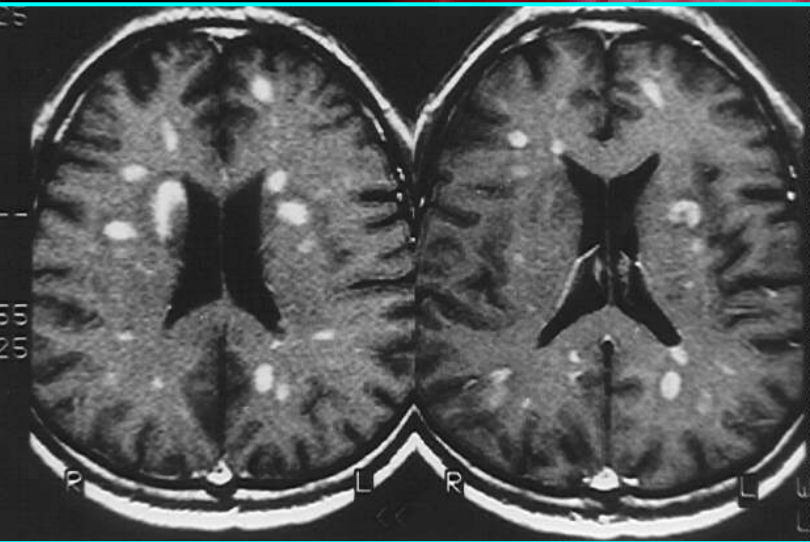
- West syndrome, Lennox-Gastaut syndrome, Landau-Kleffner syndrome, severe myoclonic epilepsy, and Rasmussen's encephalitis

- We conclude that IVIG is a safe therapy which appears to be effective in some children with intractable seizures. Children with shorter duration of their seizure disorder (< 1 year) and relatively preserved cognitive function (IQ > 70) appear to have a more favorable response

- Eur Arch Psychiatry Neurol Sci. 1986;236(2):119-22. Treatment of idiopathic West and Lennox-Gastaut syndromes

Fig. 23-3. Petit mal absence, age 8. Two slow waves, the attack begins.

A.D.E.M (Acute disseminated encephalomyelitis)



- **Pediatr Neurol. 1999 Aug;21(2):583-6. Intravenous immunoglobulin therapy in acute disseminated encephalomyelitis.**
 - **Nishikawa M,**

Three children ranging in age from 2 to 5 years with acute disseminated encephalomyelitis (ADEM) were successfully treated with high-dose intravenous immunoglobulin (IVIG). Their symptoms were somnolence, fever, headache, vomiting, and resting tremor. In all of these patients, it was difficult to distinguish the condition from viral encephalitis before analyzing the myelin basic protein. ADEM was diagnosed because of increased levels of myelin basic protein in their cerebrospinal fluid and abnormal high-signal intensity on T2-weighted magnetic resonance imaging. All patients were given IVIG at a dose of 400 mg/kg/day for 5 consecutive days. **The patients rapidly regained consciousness in 14 hours, 2 days, and 4 days and** demonstrated a complete clinical improvement within 18 days, 10 days, and 7 days of the initiation of the treatment, respectively. IVIG may prove useful as an alternative treatment to corticosteroids for ADEM.

PANDAS

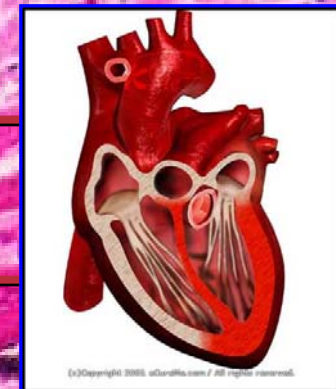
Susan J Perlmutter, Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood . **OCD and tic disorders & autism** THE LANCET • Vol 354 • October 2, 1999; pp1153-1159



Myocarditis

- **METHODS AND RESULTS:** Ten patients were treated with high-dose intravenous immune globulin infusions (2 g/kg). All were hospitalized with NYHA class III to IV heart failure, left ventricular ejection fraction (LVEF) < 0.40, and symptoms for < 6 months at the time of presentation. One patient died before the completion of therapy. The remaining 9 were discharged, and LVEF was reassessed 12 months after therapy. LVEF improved from 0.24 +/- 0.02 (mean +/- SEM) at baseline to 0.41 +/- 0.04 at follow-up (P = .003). All 9 patients improved functionally to NYHA class I to II, and there have been no subsequent hospitalizations for heart failure during the course of follow-up. **CONCLUSIONS:** In this series of patients with new-onset dilated cardiomyopathy treated with high-dose immune globulin, LVEF improved 17 EF units. *Circulation*. 1997 Jun 3;95(11):2476-8.
- **Gamma-globulin treatment of acute myocarditis in the pediatric population**
- NA Drucker, **BACKGROUND:** Myocardial damage in myocarditis is mediated, in part, by immunological mechanisms. High-dose intravenous gamma-globulin (IVIg) is an immunomodulatory agent that is beneficial in myocarditis secondary to Kawasaki disease, as well as in murine myocarditis. Since 1990, the routine management of presumed acute myocarditis at Children's Hospital, Boston, and Children's Hospital, Los Angeles, has included administration of high-dose IVIg. **METHODS AND RESULTS:** We treated 21 consecutive children presenting with presumed acute myocarditis with IVIg, 2 g/kg, over 24 hours. By 1 year after presentation, the probability of survival tended to be higher among IVIg-treated patients (.84 versus .60, P = .069). We observed no adverse effects of IVIg administration. **CONCLUSIONS: These data suggest that use of high-dose IVIg for treatment of acute myocarditis is associated with improved recovery of left ventricular function and with a tendency to better survival during the first year after presentation.** *Circulation*, Vol 89, 252-257, Copyright © 1994 by American Heart Association

Cardiac autoimmune diseases.



ALS + Gulf War Syndrome

- **Experimental Clinical Study on ALS Infections**

High Frequency of Systemic Mycoplasmal Infections in Gulf War Veterans and Civilians with Amyotrophic Lateral Sclerosis (ALS)

Journal of Clinical Neuroscience 2002

We have found that mycoplasmal infections in GWI, CFS, FMS and RA can be successfully treated with multiple courses of antibiotics, such as doxycycline, ciprofloxacin, azithromycin, clarithromycin or minocycline. Multiple treatment cycles are required, and patients relapse often after the first few cycles, but subsequent relapses are milder and most patients eventually recover. GWI patients who recovered from their illness after several (3-7) 6-week cycles of antibiotic therapy were retested for mycoplasmal infection and were found to have reverted to a mycoplasma-negative phenotype [42,43].

Garth Nicholas MD

Myasthenia Gravis (Grave). Neurology

- Myasthenia gravis is a chronic disorder characterized by weakness and rapid fatigue of any muscles under your voluntary control. It results from a breakdown in the normal communication between nerves and muscles.
- The muscle weakness improves with rest. Myasthenia may cause difficulties with speech, chewing, swallowing and breathing, as well as weakness of limbs.
- Myasthenia can affect any age, but it's more common in women younger than 40 and in men older than 60. Treatments are available to control myasthenia gravis and relieve symptoms.

Diagnosis By

- 1 Tesson Test by using edrophonium
- 2 Acetylcholine receptor antibodies.
- 3 EMG/NCV There is a decrement of amplitude on repetitive stimulation.

Crescent helping treat autoimmune diseases.

Myasthenia is the culprit of changing ptosis (dropping of an eyelid), diplopia (double vision), focusing problems, eyestrain, generalized fatigue including breathing.

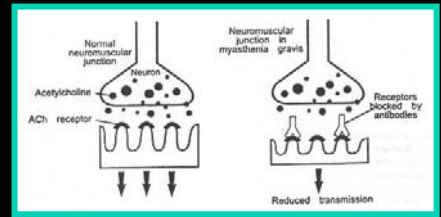
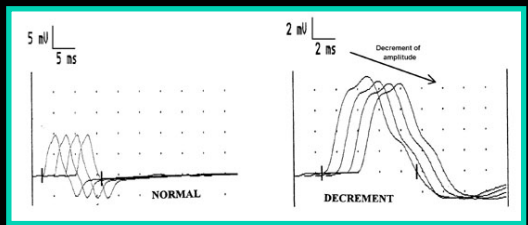
36,000 cases in USA



One Eyelid Involved



Both eyelids affected

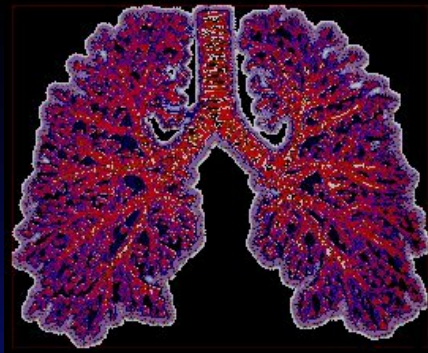


- **Lambert Eaton Myasthenic Syndrome**



- **Muscle Nerve. 2000 Nov;23(11):1767-72.
Chronic multiple paraneoplastic syndromes. Kleopa KA,**

A patient presented with symptoms of limbic and brainstem encephalitis, motor and sensory neuronopathy, cerebellar dysfunction, and highly positive anti-Hu antibodies. He also harbored P/Q-type calcium channel antibodies and manifested the Lambert-Eaton myasthenic syndrome (LEMS). Small-cell lung cancer was found, and he received both antineoplastic therapy and intravenous immunoglobulin (IVIg). Remission of the malignancy was achieved. Although the anti-Hu-related manifestations improved after therapy, LEMS has persisted, leading to IVIg dependency. Copyright 2000 John Wiley & Sons, Inc.



IVIg Steroid-Sparing Effects in Asthmatic Patients

- J Allergy Clin Immunol. 1999 May;103(5 Pt 1):810-5.
Effect of intravenous immunoglobulin on steroid consumption in patients with severe asthma: a double-blind, placebo-controlled, randomized trial.

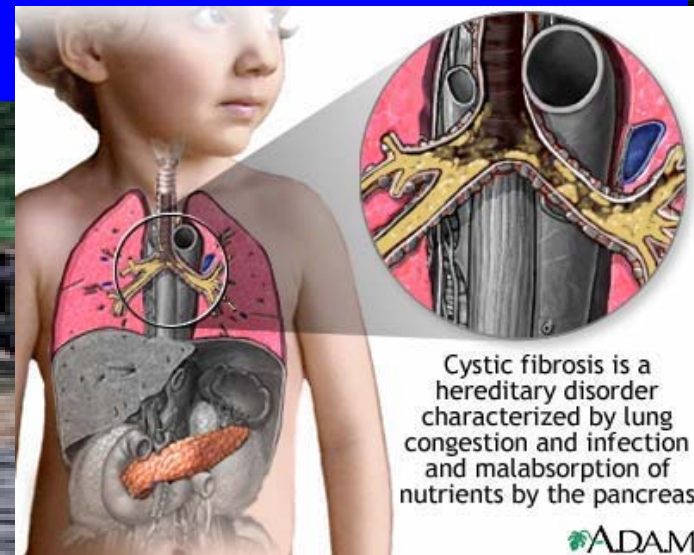
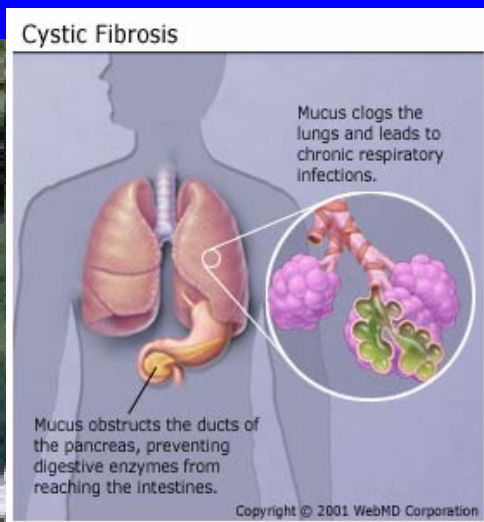
Salmun LM, IVIG may be a useful steroid-sparing agent in patients with severe asthma requiring high doses of oral steroids.

Mazer and Gelfand published the results of an open-label study in **8 children**. These children had steroid-dependent asthma (normal pulmonary function maintained only if taking oral steroids), but **2 of the patients had steroid-resistant asthma** (poor pulmonary function despite treatment with oral steroids). All patients were followed up as inpatients for at least 6 months, and their therapies were optimized before initiation of IVIG therapy. Each received monthly infusions of 2 g/kg of IVIG for 6 months. All patients had significant decreases in asthma symptom scores, and they were weaned to lower daily prednisone doses after 1 month of therapy.

Cystic Fibrosis

- **1: Arch Dis Child. 2004 Apr;89(4):315-9.**
- **Intravenous immunoglobulin for cystic fibrosis lung disease: a case series of 16 children. (Balfour-Lynn IM)**
- **16 children for monthly IVIG, at a dose of 1 g/kg on two successive days for the first dose, followed by 1 g/kg monthly as a 12 hour infusion, with corticosteroid and antihistamine cover**
- **CONCLUSION: We suggest that an trial of IVIG in may lead to significant benefit**
- **J Pediatr. 1989 Feb;114(2):309-14.**

Intravenous immune globulin treatment of pulmonary exacerbations in cystic fibrosis



Organ Transplant & IVIG

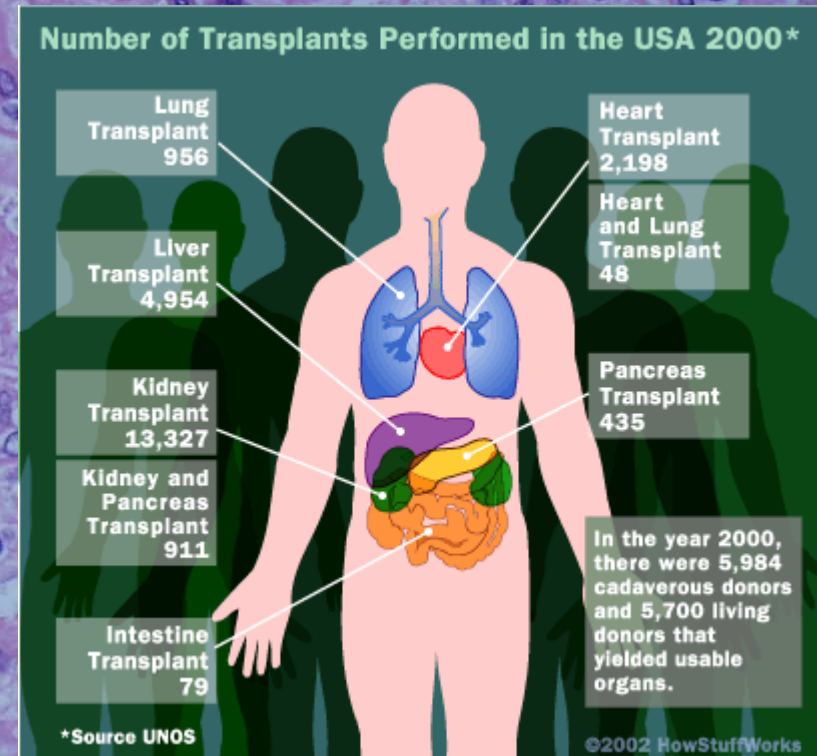
IVIG stops tissue rejection between unmatched donors.

IVIG can be used to treat rejection reaction in transplanted organs.

IVIG prevents CMV infection

In 2003 Duke could have used IVIG in the mismatched organ transplant.

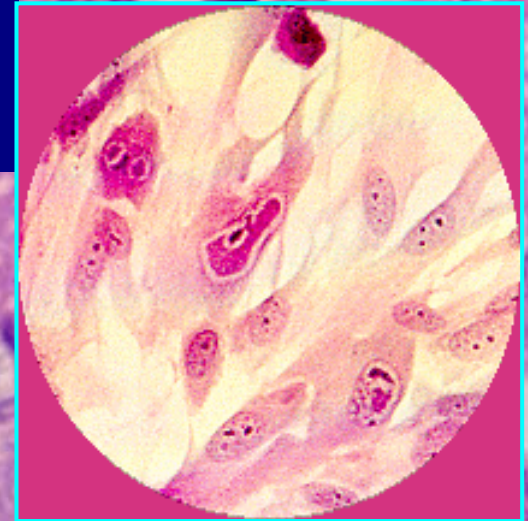
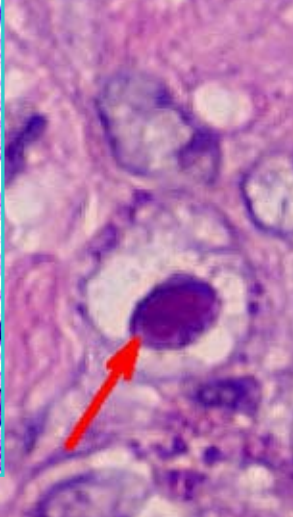
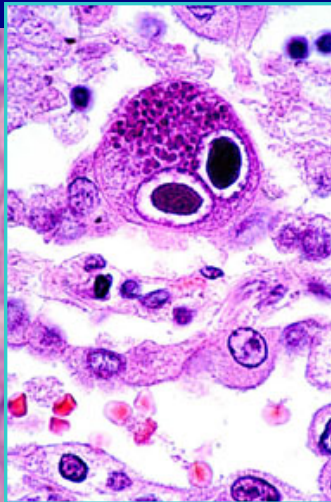
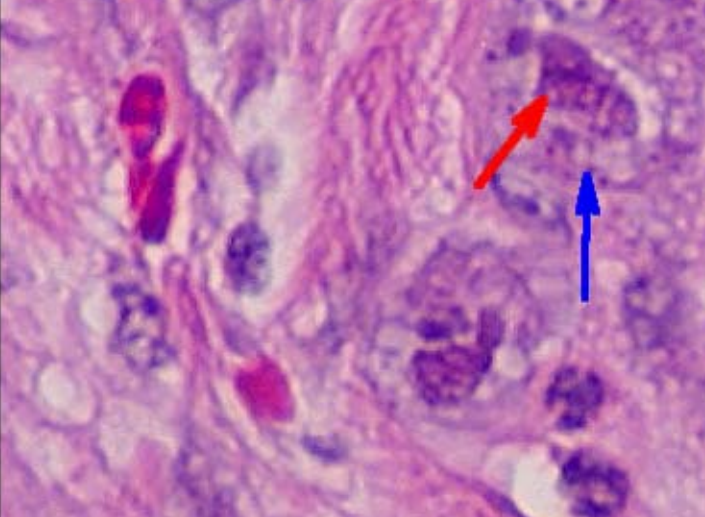
Most of unusual complications following transplant can be stopped by IVIg



Organ Transplant & CMV

- Transplant Proc. 2002 May; 34(3): 812-3. Sechet A,
- Prevention of cytomegalovirus infection and disease in high-risk renal transplant recipients with polyvalent intravenous immunoglobulins.

• "owl-eye" inclusions



- Clin Transplant. 2000 Feb;14(1):19-27. Cytomegalovirus immune globulin after liver transplantation: a cost-effectiveness analysis. Arbo MD, \$66,200 gained/yr

Autoimmune diabetes mellitus

- Clin Exp Rheumatol. 1996 May-Jun; 14 Suppl 15: S99-102.

Immunoglobulins in children with autoimmune diabetes mellitus. Heinze E.

In this paper we review the results of **six studies**, published between 1985 and 1993, which report on immunoglobulin treatment in children with idiopathic diabetes mellitus (IDDM). A total of **77 children** with newly diagnosed IDDM were infused with **high dose gammaglobulin**, while **56 patients were not infused** and served as controls. Clinical outcome as judged by the rate of induction and duration of remission, insulin requirement, metabolic control (HbA1c) and C-peptide were determined. Side effects of treatment with 0.4 g gammaglobulin/kg bw/day were minimal, and were remarkable with 2 g/kg bw/day as single doses. No significant differences between the treated and control IDDM children were observed in metabolic control or C-peptide release, while the **insulin requirement was significantly less in 2 studies during immunoglobulin therapy**. **In all 6 studies a subgroup of patients showed some benefit from treatment, with higher rates and longer durations of remissions and preserved C-peptide release.** However, no guidelines can be offered at this point for those patients who may possibly benefit from immunoglobulin therapy.



Narcolepsy + Cataplexy

- **Ann Neurol. 2004 Nov 23;56(6):905-908 Successful management of cataplexy with intravenous immunoglobulins at narcolepsy onset.**

Dauvilliers Y, Hypocretin/orexin deficiency appears to be a consistent feature of narcolepsy with a putative autoimmune mechanism involved. We treated four hypocretin/orexin-deficient narcolepsy patients with intravenous immunoglobulins .Three patients received the treatment within a few months after acute onset of narcolepsy. A clear improvement in the frequency and severity of cataplexy was obtained with a benefic effect up to 7 months without any anticataplectics drugs at follow-up. Our findings point to the importance of early diagnosis of narcolepsy, which once treated quickly may modify its long-term outlook. Ann Neurol 2004;56:905-908.

- **People with narcolepsy often:**
- **a) fall asleep during the day at inappropriate times**
- **b) have episodes of muscle weakness brought on by emotions such as laughing**
- **c) have nightmares just when they start to fall asleep.**
- **d) have feelings of paralysis during sleep**

Recurrent *Clostridium difficile* infection



Neutrophils *C. difficile*

The image shows a microscopic view of a tissue sample. On the left, there are several neutrophils, which are white blood cells with multi-lobed nuclei. On the right, there are numerous Clostridium difficile bacteria, which are rod-shaped and often appear in chains. The background is a light, yellowish color, likely representing the surrounding tissue or mucus.

- Leeds Teaching Hospitals Old Medical School, Leeds LS1 3EX, UK.

Mark.Wilcox@leedsth.nhs.uk

In the three successfully treated cases, CDD resolved within 11 days.

CONCLUSIONS: Intravenous immunoglobulin is useful for the treatment of intractable and severe CDD

Glomerulonephritis

Jpn J Infect Dis. 2004 Oct;57(5):S17-8.

Intravenous immunoglobulin (IVIg) therapy in MPO-ANCA related polyangiitis with rapidly progressive glomerulonephritis in Japan.

Muso E, Ito-Ihara T, Ono T, Imai E, Yamagata K, Akamatsu A, Suzuki K.

Division of Nephrology, Kitano Hospital, The Tazuke Kofukai Medical Research Institute, Osaka, Japan. muso@kitano-hp.or.jp

For 30 antineutrophil cytoplasmic antibody (ANCA) related rapidly progressive glomerulonephritis patients intravenous immunoglobulin (IVIg) (400 mg/kg/day) was administered for 5 consecutive days before or along with conventional immunosuppressive therapy in Japan.

- Twenty patients were treated with IVIg before the start or newly increase of conventional therapy and evaluated the independent effect of this therapy. In these patients, just after IVIg, significant decrease of CRP was noted with improvement of elevated serum creatinine in 12 out of 19 patients (63%). In the analysis of the overall outcome of 30 patients, at 3 months after IVIg and following conventional therapy,
- no patients showed renal death except 4 for whom hemodialysis had been started before IVIg. At 6 months, renal survival rate were 92% (newly renal death 2 out of 26) and 2 patients died due to cerebral bleeding (survival rate was 93%). No fatal infection was noted. IVIg might be the potent inducible therapy which can be promoted before the beginning of conventional immunosuppressant treatment for relatively aged and lower immunopotent MPO-ANCA patients in Japan.

PMID: 15507757 [PubMed - in process]

Carbon Monoxide Poisoning

- CO poisoning is the leading cause of injury and death by poisoning worldwide, with about 40,000 people treated in the U.S. annually. Brain damage occurs – days to weeks later – in half of the patients with a serious case of CO poisoning.
- A team led by Stephen R. Thom, MD, PhD, Professor of Emergency Medicine and Chief of Hyperbaric Medicine, at the University of Pennsylvania School of Medicine, report this week online in the Proceedings of the National Academies of Sciences, that CO causes profound changes in myelin basic protein (MBP) – a major protein constituent of myelin, the protective sheath surrounding neurons. Using an animal model, they showed that the CO-induced changes in MBP set into motion an autoimmune response in which lymphocytes, triggered to eliminate altered MBP, continue to attack normal MBP. Thom says that overall this work suggests that the 50 percent or more of patients who develop brain damage following severe CO poisoning may do so, in large part, due to an autoimmune reaction. The body simply does not know when to stop attacking what it now views as an invader. "This opens up a lot of possibilities, such as treatment with immunosuppressant agents, in conjunction with standard hyperbaric oxygen therapy," he says. "Until our study elucidated this immune response, we had no motivation to think along those lines."
- Penn colleagues on the paper are: Veena M. Bhopale, Donald Fisher, Jie Zhang, and Phyllis Gimotty. This study was funded by the National Institutes of Health.



The Best Kept Secret

- In 1920, Hans Gerhard Creutzfeldt described the first case of a progressive mental and neurological disturbance in a 23 year old woman. Alfons Maria Jakob described another three cases of defects in the motor systems one year later. In 1922 the eponym 'Creutzfeldt-Jakob disease' (CJD) was first used to describe a number of degenerative central nervous system diseases (1-4).

In 1950s, a peculiar disease known as 'kuru', in the Eastern Highlands of Papua New Guinea has been discovered and turned out to be due ingesting brain tissue of dead relatives for religious reasons. The neuropathological similarity between kuru, CJD, and scrapie (which is a disease affecting sheeps discovered 1973 with higher incidence in the UK) was discovered (3-6).

In 1960s, the term transmissible spongiform encephalopathy was applied after the discovery of the transmissible ability of both kuru and CJD diseases to chimpanzees (5, 7).

For years it was thought that the disease is caused by 'slow' or 'unconventional' viruses causing amyloidoses of the nervous system. In 1976 Daniel Carleton Gajdusek was awarded the first Nobel prize for his work on 'slow virus' infections theory (8).

1980s the term 'prion' was used to designate a small proteinaceous infectious particle that was resistant to inactivation by most of the procedures that modify nucleic acids, and to distinguish the agent from virus and viroids. These protein particles are the causative infectious agents for the prion diseases. This theory, also known as the 'protein-only' hypothesis and has been under criticism for years (5).

- “The best-kept secret in this field is that [prions] in any form have never shown infectivity,” said the head of Yale University’s surgery department to the United Press International’s Steve Mitchell.”

Mad cow Disease



- Could mad-cow disease be caused not by prions, but by a simple bacterium?
- Alan Ebringer, a professor of immunology at King's College, London, possibility that mad-cow disease,, are the result of the body's own immune response to a bacteria called *Acinetobacter*.
- *Acinetobacter* possesses a molecular sequence that is almost identical to one found in brain tissue. According to Dr. Ebringer's theory, this similarity causes antibodies produced by the body against this bacterium to attack the brain .
- This would make mad-cow disease -- and its human form, Creutzfeldt Jacob disease, or vCJD -- not some exotic protein-caused "prion" disease, but one of a known class of diseases called autoimmune diseases. In these diseases, such as rheumatic fever, the body's own immune system mistakes parts of the body for disease-causing agents and attacks them

Alzheimer's the next frontier

- Researchers from the Universities of Bonn, Munich, Frankfurt, Marburg and Indianapolis. Based on previous findings that Alzheimer's patients have significantly lower levels of anti β -amyloid antibodies than non-demented controls, and that antibodies against β -amyloid are available in commercial IVIG preparations:
- 6 patients with Alzheimer's Disease were treated with IVIG and followed in a prospective, controlled clinical study. Each of the patients received a dose of 0.4g/kg body weight on 3 consecutive days, every four weeks for 24 weeks.

Healthy brain

Brain affected by Alzheimer's

- Results:
- In all patients the concentration of total β -amyloid in cerebrospinal fluid decreased following 6 months of treatment (mean 23.5%). Reducing the β -amyloid concentration in CSF is thought to have a beneficial effect on neuropsychological sequelae of Alzheimer's disease.

Healthy neuron

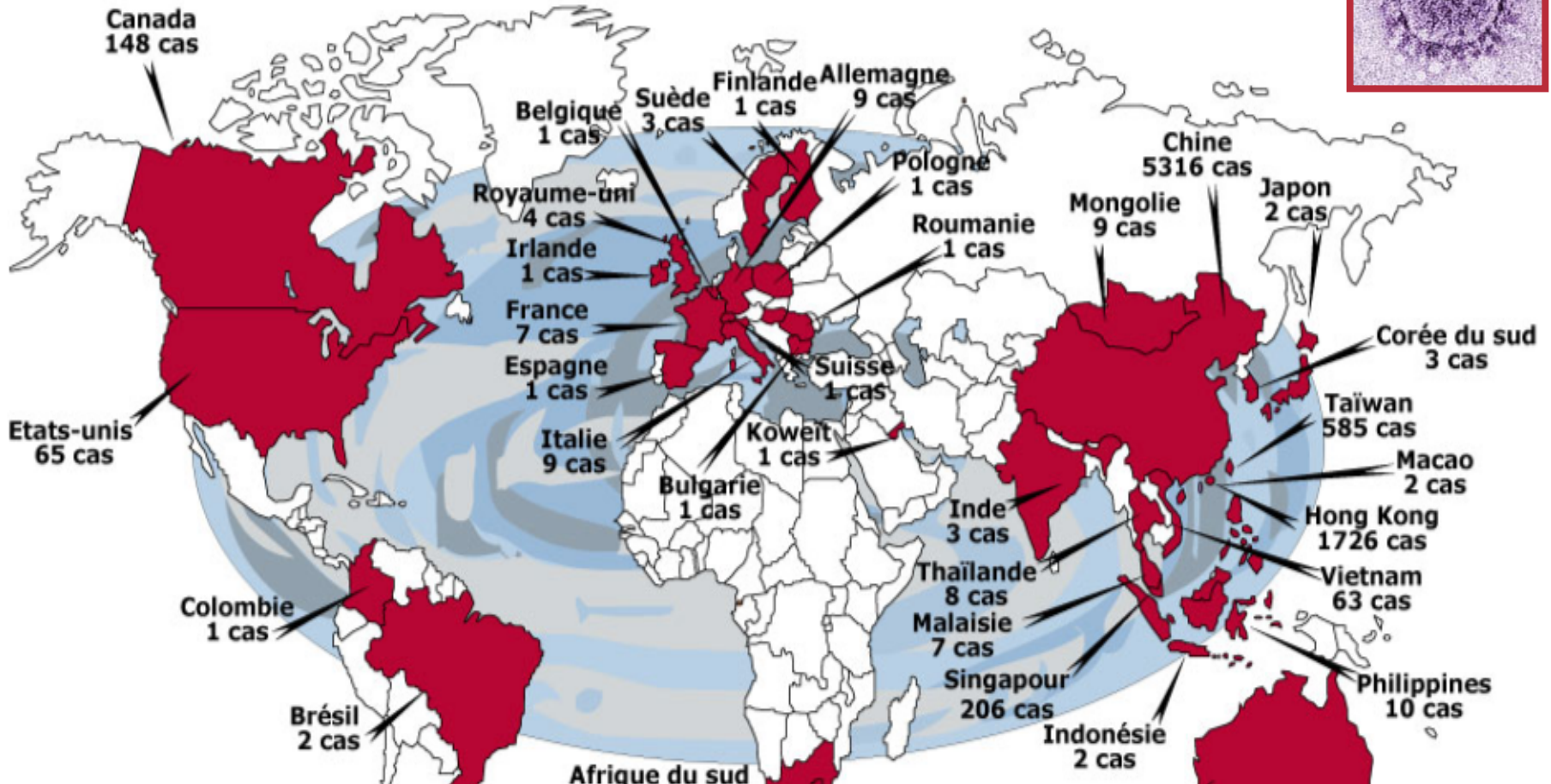
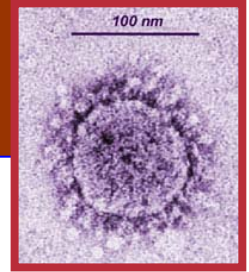
Diseased neuron

Tangles

Plaque

- At the end of 6 months treatment with Octagam, improvement was noted in the Alzheimer's Disease Assessment scale. Mean improvement was 4.2 points. (7 points is equivalent to reversal of a years cognitive deterioration).

SARS Virus

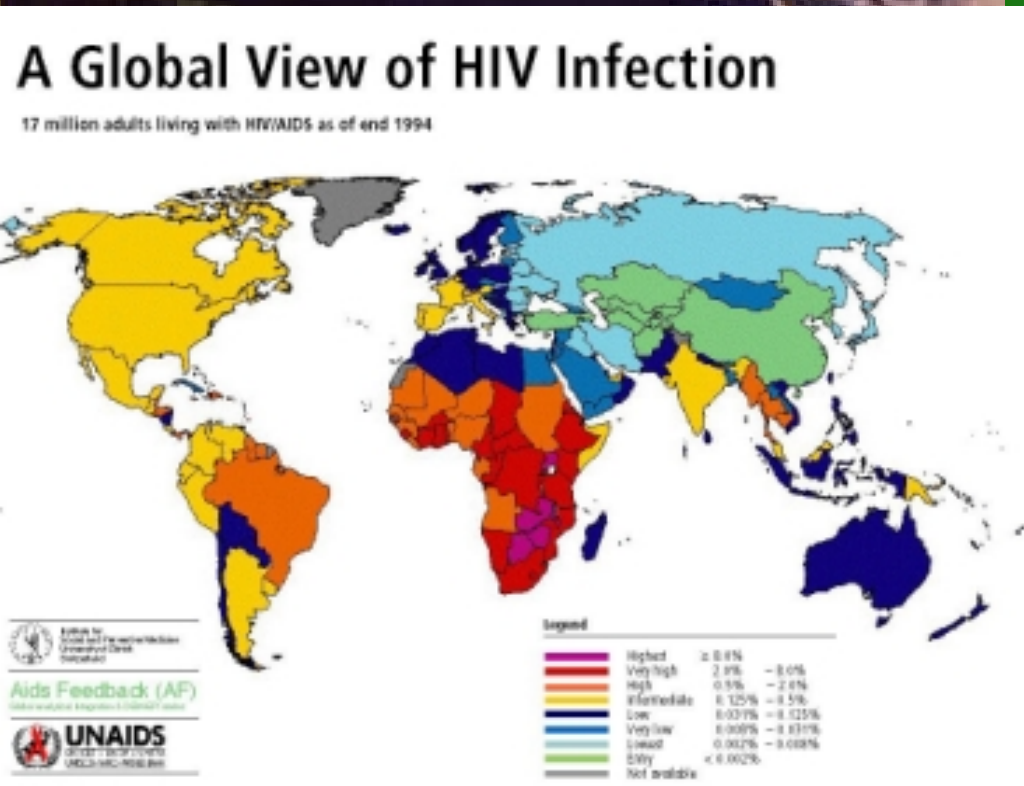


- Management of hospital-acquired severe acute respiratory syndrome with different disease spectrum. All patients received standard treatment: ribavirin 1000 mg orally daily for 10 days, Levofloxacin 500 mg orally daily for 7 days, and intravenous immunoglobulin (IVIG) 1 g/kg/day for 2 day after the onset of symptoms. If severe hypoxia ($PaO_2/FiO_2 < 200$) occurred, protective strategy of mechanical ventilation and methylprednisolone 2 mg/kg/day were given.)

• J Chin Med Assoc. 2003 Jun;66(6):328-38. Chiang CH, Chen HM, Shih JF, Su WJ, Perng RP.

Division of Pulmonary Immunology and Infectious Diseases, University Taipei, Taiwan,

HIV travelers to tropical areas



For HIV-infected individuals from the industrial world, travel to the tropics leads to an increased risk of exposure to a variety of cosmopolitans as well as geographically focal pathogens. The unavoidable risks of tropical travel can probably be reduced by careful employment of the standard techniques of emporiatic medicine

For those who are severely immunosuppressed, preexposure prophylaxis with monthly IVIG is recommended prior to travel to endemic areas

By Christopher L. Karp, M.D., Associate Professor of Medicine, and Molecular Microbiology & Immunology, Johns Hopkins University

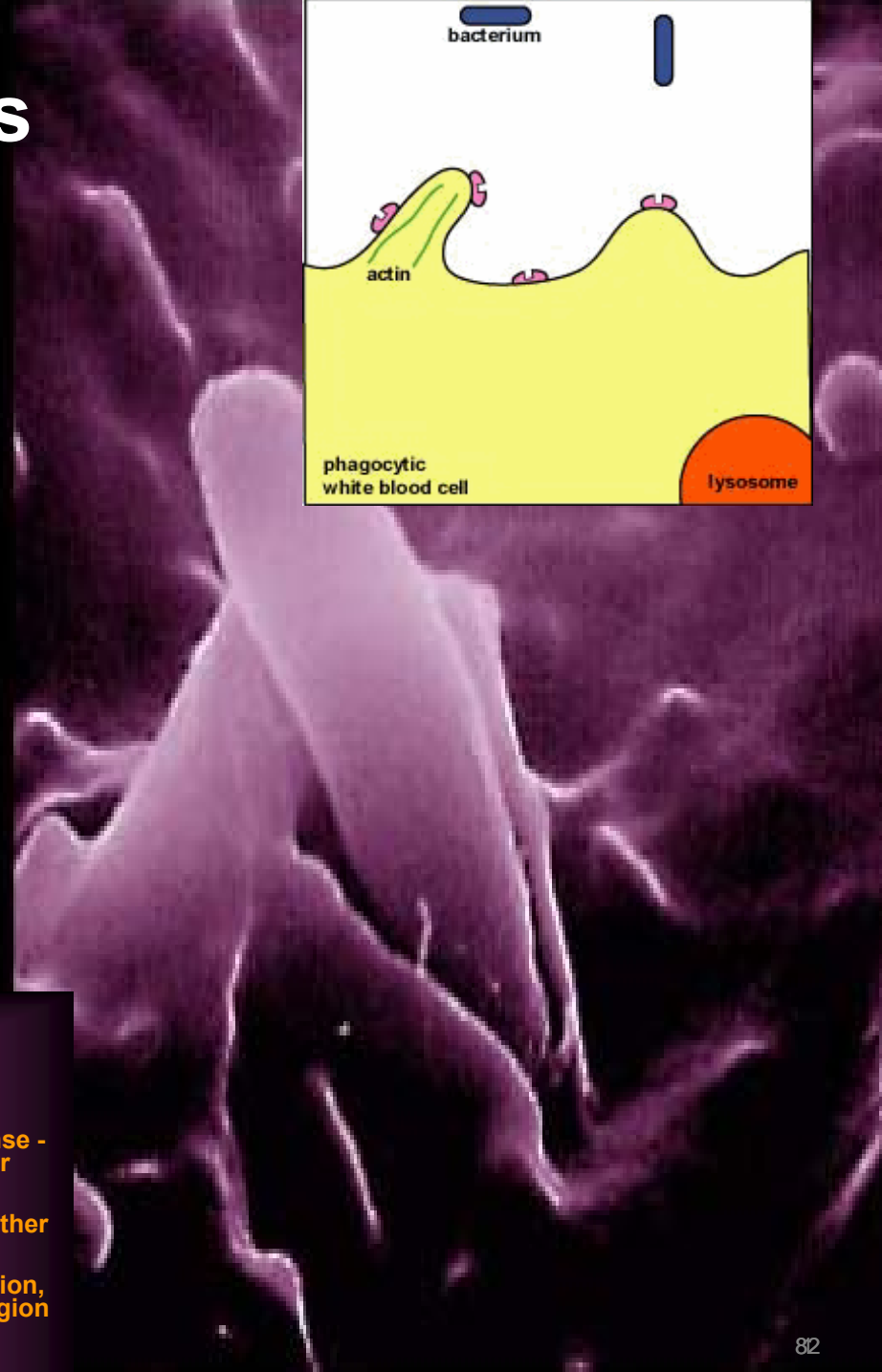
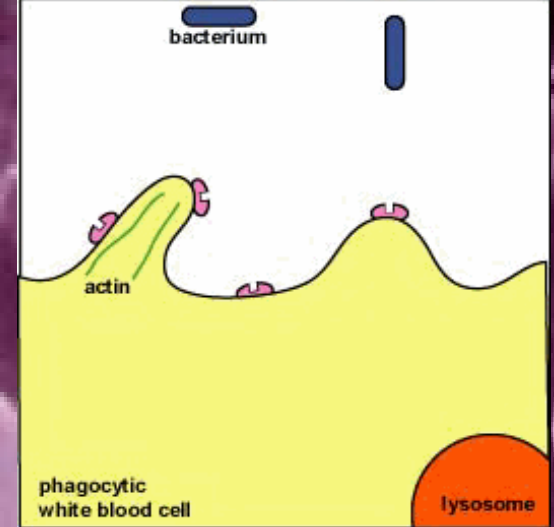
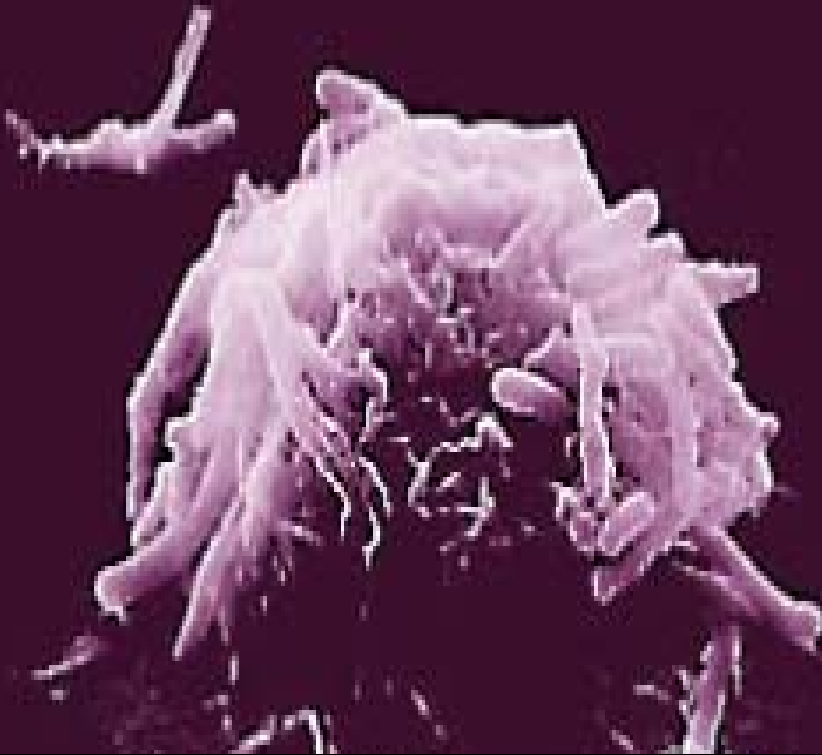
What about cost of IVIG

- Cost to the patient (Immune suppression, weight gain, Gastric Ulcers, Cataracts, Skin atrophy, Hypertension, Osteoporosis, arthritis, Depression, Glaucoma, Heart disease, Myopathy, Coronary artery disease & Cushing's Syndrome,).
- Cost to Insurance: In treating all the above side effects the cost to the insurance carrier will be 5 -10 times more than with IVIG.
- Cost to Physician: Increased risk.
- Cost in dollars of IVIG only appears high but at the end of the day it's the only long term safe treatment. (Do No Harm).
- Eur J Neurol. 2003 Nov;10(6):687-94.

Cost-utility analysis of intravenous immunoglobulin and prednisolone for chronic inflammatory demyelinating polyradiculoneuropathy.

- **A cost-benefit analysis of intravenous immunoglobulin treatment in children with Kawasaki disease.**
- **J Med Assoc Thai. 2003 Jun;86 Suppl 2:S179-88.**
- **Estimation of total costs for follow-up and treatment for healthy life (until 60 years old) was more expensive in the non-IVIG treatment than the IVIG treated group (75,482,803 baht vs 29,883,833 baht). The authors conclude that treatment of all KD cases in Thailand with IVIG is likely to result in lower cost and better outcome when compared to no treatment with the IVIG policy.**

Phagocytosis



- **Opsonins are freely circulating serum molecules which are produced to attach to the surface of microbes, so rendering them more attractive to phagocytes. The process of coating a particle with opsonins is called opsonization.**
- **Examples of opsonins include IgG antibody - part of the immune response - and the C3b molecule of the complement system. Each has receptors for both foreign particle and host phagocyte.**
- **Opsonisation can itself stimulate the local activation of complement, further enhancing the local production of C3b opsonin and phagocytosis.**
- **Organisms have produced a myriad of ways of circumventing opsonization, for example, Staphylococcal alpha toxin, an exotoxin, binds to the Fc region of antibody, so preventing binding of phagocyte with the opsonin.**

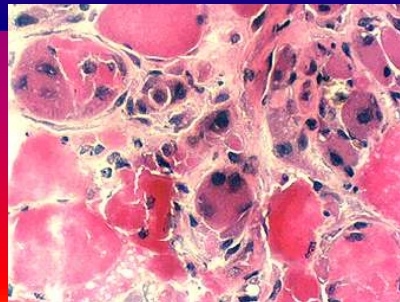
Super bugs

M.R.S.A



Paraneoplastic Syndromes

- **Autonomic dysfunction** *Abnormal pupil response, Constipation, Impotence, Orthostatic hypotension, Sweating abnormalities*
- **Brainstem encephalitis** *Dizziness/vertigo, Dysphagia, Ophthalmoplegia, Oscillopsia, Dysarthria*
- **Cerebellar degeneration** *Dysarthria, Gait ataxia, Nystagmus*
- **Focal cortical encephalitis**
- **Lambert Eaton Myasthenic Syndrome (LEMS)** *Muscle weakness/fatigue, Reduced or absent muscle reflexes*
- **Limbic encephalitis** *Anxiety, Confusion, Dementia, Depression, Hallucinations, Memory loss, Seizures*
- **Myelitis**
- **Opsoclonus/myoclonus**
- **Retinopathy** *Night vision problems, Photosensitivity, Visual loss, Visual obscurations*
- **Sensory neuropathy**



Cryoglobulinemia

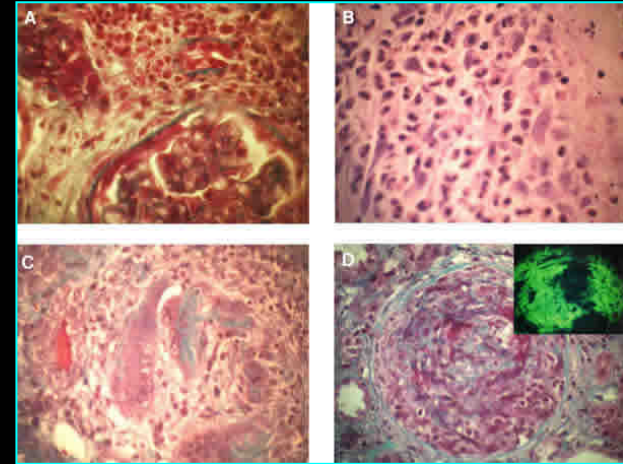
- **Proteins which precipitate with cold temperature.**
- **Bind to Gammaglobulin.**
- **Cause arthritis**
- **Cause vascular occlusion.**

- The term cryoglobulinemia indicates the presence of cryoglobulins in the blood. These are abnormal forms of protein molecules that precipitate at cold temperatures and redissolve at normal body temperature. Hence, when a person with cryoglobulinemia is exposed to cold, he or she may experience impaired circulation in the small blood vessels. This may lead to color changes in the skin, hives, damage to the extremities, bleeding into the skin (purpura), and other problems. The underlying cause of this very rare condition may include diseases of the immune system [e.g. Waldstrom's macroglobulinemia], of certain cells in the bone marrow [e.g. monoclonal gammopathy of undetermined significance (MGUS) or its malignant form, multiple myeloma], and some infectious diseases [e.g. hepatitis C virus]. The diagnosis depends on demonstrating the presence of cryoglobulins in the blood and searching for a possible underlying cause."



Churg-Strauss Syndrome (Allergic Granulomatosis)

- Cause vascular occlusion. IgE elevated
- (1) asthma, (2) eosinophilia greater than 10% on a differential white blood cell count, (3) mono- or polyneuropathy, (4) nonfixed pulmonary infiltrates, (5) paranasal sinus abnormalities, and (6) biopsy containing a blood vessel with extravascular granulomas.



•Ann Rheum Dis. 2004 Dec;63(12):1649-54. Complete clinical and functional recovery with a long term stable remission and a low incidence of side effects can be achieved by intravenous immunoglobulin associated with plasmapheresis



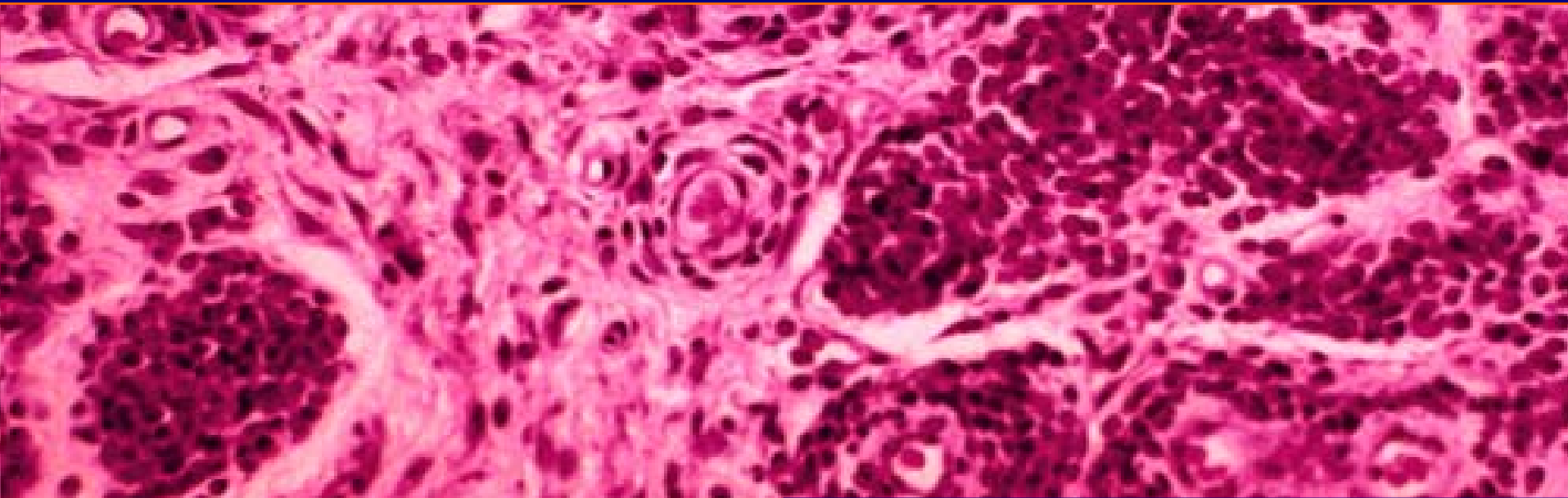
• Clin Exp Rheumatol. 1990 Nov-Dec;8(6):603-8.

High dose immunoglobulin therapy in severe juvenile chronic arthritis: long-term follow-up in 16 patients.
Priour AM, Adleff A, Debre M, Boulate P, Griscelli C.

Immunologie et Rhumatologie Pediatriques, INSERM U 132, Hopital des Enfants-Malades, Paris, France.

Sixteen children with severe juvenile chronic arthritis received high dose intravenous immunoglobulin (IVGG). Extra-articular symptoms improved to some degree in 6 of ten patients. A decrease in the number of active joints occurred in 7 patients of the 11 who received more than ten months of IVGG. Hemoglobin levels increased, the ESR and platelet counts decreased and the IgG levels diminished in most of the patients who received long term treatment. The treatment was totally ineffective in three children who had very severe disease. Two children had respectively a vasculitic rash and urticaria thought to be side effects of the treatment. One had proteinuria. This last might have been due to other therapeutic agents given. Although clinical and biological benefits occurred in some, the state of the patients who had short term (m = 2-3 months) or long term (m = 2-7 years) therapy was not different at the last visit.

PMID: 2289332 [PubMed - indexed for MEDLINE]



Dysautonomia

• Clin Exp Rheumatol. 1999 Nov-Dec;17(6):733-6.

Acute dysautonomia secondary to autoimmune diseases: efficacy of intravenous immunoglobulin and correlation with a stimulation of plasma norepinephrine levels.

**Dupond JL, Gil H, Bouhaddi M, Magy N, Berthier S, Regnard J.
Department of Internal Medicine, University Hospital, Besancon, France. jean-louis.dupond@ufc-chu.univ-fcomte.fr**

Acute dysautonomia is a disorder characterized by severe sympathetic and parasympathetic failure with relative preservation of motor and sensory function. The disease is considered to be idiopathic in most cases, but there is now a trend towards considering the disorder as an uncommon variant of Guillain Barre syndrome. We report two cases of acute dysautonomia which did not fulfill the criteria of the idiopathic form. The first case was associated with Sjogren's syndrome and the second with thyroiditis and antiganglioside antibodies which were correlated with the severity of the disease. Intravenous gammaglobulin (IVGG) was effective in both cases, as has been reported for the idiopathic form,. PMID: 10609075 [PubMed - indexed for MEDLINE]



- Thank you
- Imran Khan



IVIg reimbursable Diagnosis

- **Primary immunodeficiency diseases** (such as congenital agammaglobulinemia (X-linked agammaglobulinemia), hypogammaglobulinemia, common variable immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency, and Wiskott-Aldrich syndrome)
- **Immune or idiopathic thrombocytopenic purpura (ITP)**
- **B-cell chronic lymphocytic leukemia (CLL):** for patients with hypogammaglobulinemia associated with CLL and recurrent infections or specific antibody deficiency
- **Allogeneic bone marrow transplantation:** IVIG is indicated to prevent the risk of acute graft-versus-host disease, associated pneumonia (infectious or idiopathic), and infections (e.g., cytomegalovirus infections, varicella-zoster virus infection, and recurrent bacterial infection) in the first 100 days after bone marrow transplantation
- **Secondary immunosuppression** associated with major surgery (such as cardiac transplants) and certain diseases (hematologic malignancies, extensive burns, or collagen-vascular diseases)
- **Polymyositis Dermatomyositis**
- **Multifocal motor neuropathy**
- **Guillain-Barré syndrome**
- **Myasthenia gravis**
- **Lambert-Eaton myasthenic syndrome**
- **Moersch-Woltmann (Stiff-Person syndrome)**
- **C.I.D.P.**
- **Relapsing-remitting multiple sclerosis**
- **Systemic lupus erythematosus**
- **Selective IgG subclass deficiencies with severe infection**
- **Parvovirus B19 infection**
- **Pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid**
- **Multiple myeloma**

Off label & Labeled indications for IVIg

Anti Neutrophil Cytoplasmic Antibody ANCA

- Nippon Jinzo Gakkai Shi. 2004 Feb;46(2):79-83.
[Successful treatment of severe ANCA-associated RPGN with high-dose IVIg therapy]

Gomada M, Akamatsu A.

Division of Nephrology, Ehime Prefectural Central Hospital, Ehime, Japan.

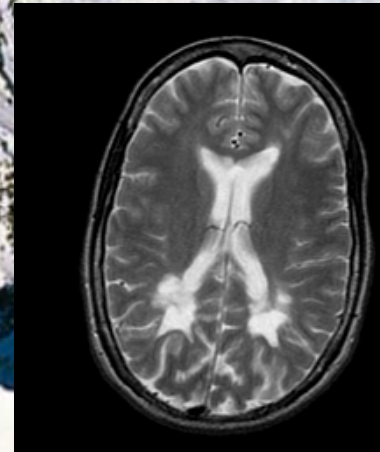
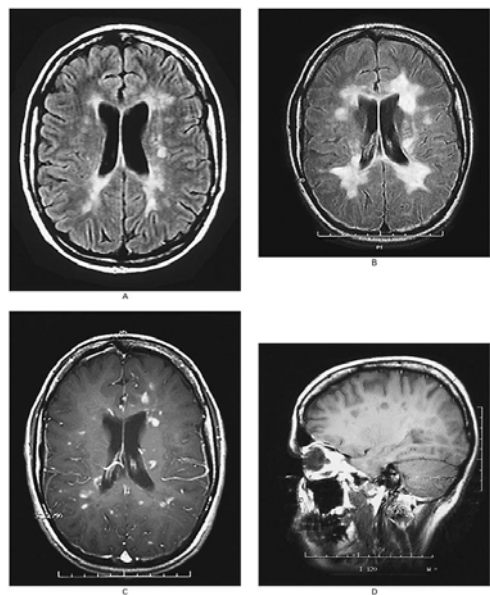
We report a case of anti-neutrophil cytoplasmic antibody(ANCA)-associated rapid progressive glomerulonephritis (RPGN) that was treated with intravenous immunoglobulin (IVIg) therapy. A 37-year-old woman was admitted to our hospital because of a low-grade fever, general malaise, and a poor appetite. At the time of admission, her renal function had severely deteriorated (serum creatinine level 9.5 mg/dl; mean Ccr 3.3 ml/min) and she had severe anemia (Hb 6.6 g/dl). An immunological examination revealed the presence of ANCA-associated RPGN. A biopsy confirmed a diagnosis of pauci-immune-type necrotizing crescentic glomerulonephritis. After initial treatment with steroid pulse therapy (methylprednisolone, 1,000 mg/day x 3 days), her general condition deteriorated and two sessions of hemodialysis were required. On the 10th hospital day, a high dose of immunoglobulin was administered intravenously (IVIg 400 mg/kg/day x 5 days). This therapy immediately improved her general condition and lowered her serum titer of MPO-ANCA and her serum creatinine level. After two IVIg treatments, her MPO-ANCA titer returned to a normal level and her serum creatinine level improved from 9.5 mg/dl to 3.3 mg/dl. A second biopsy confirmed clinical improvement. These findings suggest that IVIg therapy is effective for cases of ANCA-associated glomerulonephritis that are difficult to treat using conventional immunosuppressive therapy.

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- ok

"Is it easy to diagnose MS?"

MRI Scan is the Golden Test



- **History of worsening after heat, hot water bath or exercise.**

Qualities of a winning team

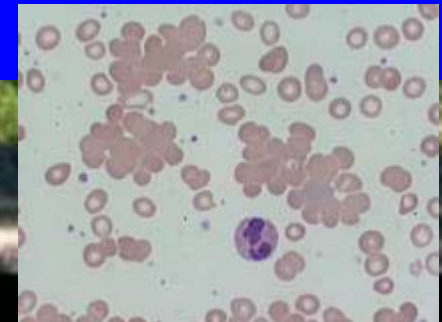
- Visionary, inspirational leadership
- A willingness to provide and share information
- Employee **empowerment** and accountability
- **Teamwork** - A collaborative, team-based work environment
- **Open Communication** - An emphasis on open, honest communication
- **Take Risk** - A readiness to innovate and take chances on new ideas
- Offer **Solutions**
- **Trust**

Treatment of MS

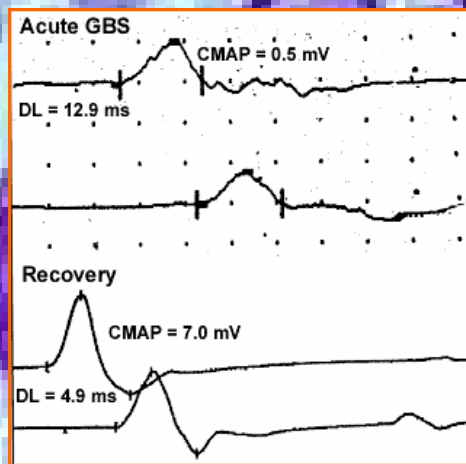
- **Brand Name Avonex, Betaseron, Copaxone, and Rebif.**
- **Glatiramer Acetate**
- **Mitoxantrone and chemotherapy**
- **Treating Exacerbations**
A true **exacerbation** of MS is caused by an area of inflammation in the central nervous system (CNS). It is also known as a relapse, an attack, or a flareup.
- **The treatment most commonly used to control exacerbations is intravenous, high-dose corticosteroids. IVIG**
- **Solu-Medrol (methylprednisolone)**
Methylprednisolone is one of the most commonly used corticosteroids in MS.
- **Plasmapheresis (Plasma Exchange)**
Only considered for the 10% or so who do not respond well to the standard steroid treatment.

Antibody Mediated Hemolysis

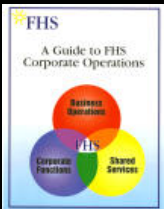
- **Antibody Mediated Hemolysis**
- In autoimmune hemolytic anemia (AIHA) RBCs are destroyed by antibodies made by a person against their own RBCs. AIHA is divided into two types: an IgG or "warm" type (optimally active at 37°C) and an IgM or "cold" type (optimally active at 4°C). In AIHA the antibody coated RBC membrane is removed bit by bit, usually in the spleen. As this happens the cell becomes increasingly spherical maintaining essentially the same volume. AIHA varies in severity and often waxes and wanes. Splenomegaly is usually present.
- Infections may initiate a hemolytic crisis in G-6-PD deficiency or in cases of meningococcal or pneumococcal septicemia cause a microangiopathic hemolytic anemia. Intravascular and extravascular hemolysis of infected RBCs may occur in malaria.
- Hemolysis after transplants).
- The DAT detects antibodies attached to the patient's RBCs. This is important for classifying and understanding the immune hemolytic anemias.
- The DAT is also known as the direct Coombs test.



Miller Fisher Syndrome



IVIG.



"So what causes Multiple Sclerosis?"

- **Injury Hypothesis (Mycoplasma)**

Autoimmunity

That MS is an autoimmune disease is the leading theory in the scientific-medical world.

Pathogen mediated

This is the other leading scientific theory of the mechanism for how multiple sclerosis operates. "Pathogen" is a generic word for the nasty little bacteria, virus, fungi and other microbes that cause so many other diseases. Some tantalizing work has found statistically significant links to a number of virus and bacteria including Epstein-Barr virus, Human Herpes Virus 6, Chlamydia Pneumonia and other pathogens

Genetic components

Diet and vitamin deficiencies