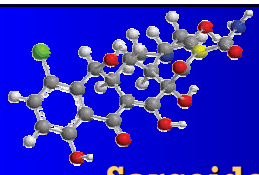
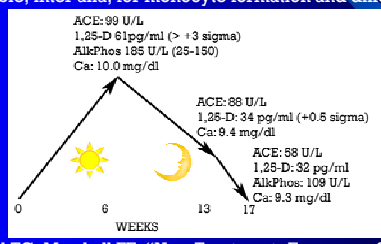


Sarcoidosis Succumbs to Antibiotics – Implications for Autoimmune Disease

Presented By:
Trevor G. Marshall, PhD
Autoimmunity Research Foundation

SARCOIDOSIS- "NEW treatments EMERGE…"

Sarcoidosis is a Th1 disease, customarily thought to be caused by inhaled allergens, but where a strong link with Mycobacteria had been demonstrated over several decades. Autoantibodies are typically not found, although they are often present during disease progression. There are high levels of 1,25-dihydroxyvitamin-D, a key Th1 hormone, responsible, inter alia, for monocyte formation and differentiation.



Marshall TG, Marshall FE: "New Treatments Emerge as Sarcoidosis Yields up its Secrets" Clinmed 2003 Jan 27;2003010001

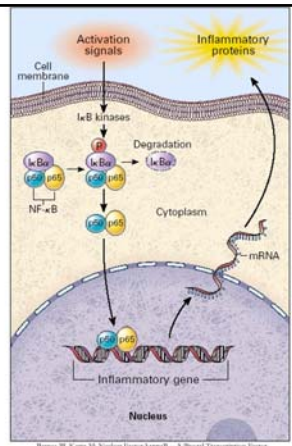
SARCOIDOSIS- "ARB dosing Regimes.."

2001 Case Study: Two sarcoidosis patients being treated for hypertension with the Angiotensin-II Receptor Blocker, Valsartan (Diovan), reported that the drug caused psychedelic dreams and significantly increased feelings of fatigue, anxiety, irritability and paresthetic pain

It was decided to administer the ARB more frequently. Not only did the hallucinogenic side effects disappear, but the patients reported that the Valsartan was beneficially suppressing symptoms of fatigue, anxiety, irritability and paresthetic pain which they had suffered since their sarcoid diagnoses, symptoms which had not previously responded to treatment

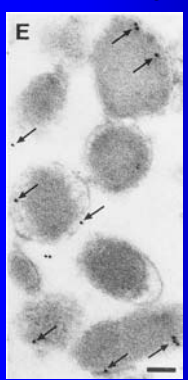
So Angiotensin II is somehow related to Th1 disease…

Marshall TG, Marshall FE: "Valsartan Dosing Regime Modulates Psychotic Events in Two Sarcoidosis Patients" Clinmed 2003 Jan 27;2003010001



Macrophage immune response

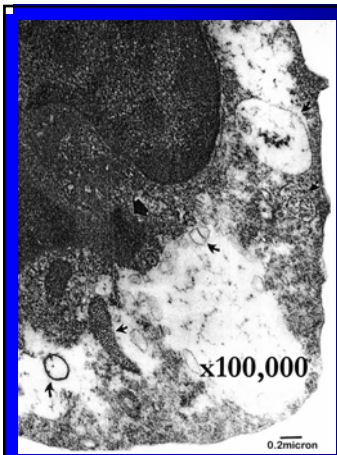
Bacterial Pathogens in the Phagocyte Cytoplasm - a new ballgame altogether…



Nilsson, et al,

"Presence of Rickettsia Helvetica in granulomatous tissue from Patients with Sarcoidosis"

Journal of Infectious Diseases, 2002: 185: 1128



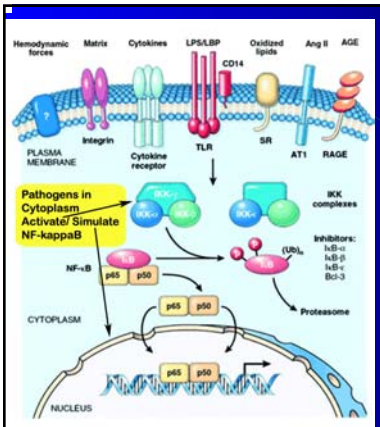
The Wirostko Study

TEM photograph taken of a monocyte from the vitreous of the eye of a sarcoidosis patient showing hundreds of tiny coccoids (in colonies) have parasitized this phagocyte

The very phagocytes which are supposed to kill bacterial pathogens are providing safe harbor for them

Bacteria are not being killed – therefore there are no antibodies being formed.

The more advanced the infection, the fewer the antibodies…



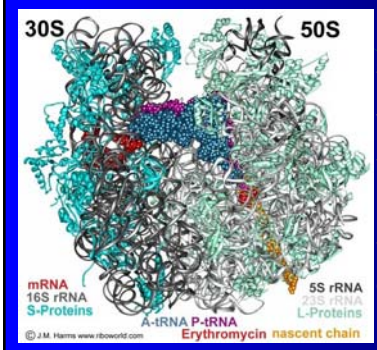
Intra-cellular bacteria *directly* drive the Th1 immune response

How do we kill the Th1 bacteria?

THE PATHOGENS ARE LARGELY RESISTANT TO ANTIBIOTICS, WE WEAKEN THEM - THE IMMUNE SYSTEM WILL KILL THEM

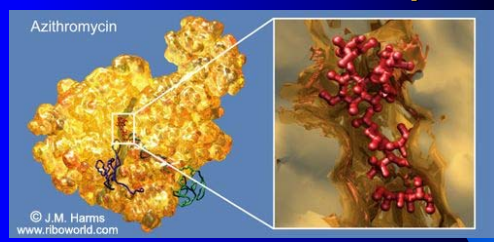
1. Reduce the level of 1,25-dihydroxyvitamin-D, by
   a. Controlling the ingestion of Vitamin D
   b. Controlling exposure to the Outdoors
   c. Fastidiously Protecting eyes from light
2. Apply an Angiotensin Blockade
3. Use low-dose, pulsed, bacteriostatic antibiotics to help the immune system to kill the intra-cellular pathogens
4. Continue low dose abx therapy for 12-36 months, until all herxheimer has disappeared - indicating disappearance of the pathogens – HERXHEIMER controlled by DOSAGE

Bacterial Protein Synthesis - 70S Ribosome



1) Charged tRNA carries amino acid
2) Binds to acceptor site on 50S subunit
3) Peptidyl tRNA already on donor site on 50S subunit
4) Peptidyl transferase catalyzes donation of growing peptide chain to aminoacyl tRNA
5) tRNA at donor site released (uncharged)
6) Growing chain at acceptor site moves to donor site and process starts again

Low Dose abx block Protein Synthesis



1) When Th1 intra-phagocytic bacteria die, there is a cytokine release
2) The cytokine release can be life-threatening if too many bacteria are killed at once
2) Bacterial death is therefore controlled by inhibiting protein synthesis, and only using low-doses of bacteriostatic antibiotics
3) One bacterium weakened if just one abx molecule is bound in one 50S – low doses proportionally control the rate of bacterial death

Th1 Diagnoses Responding

Sarcoidosis	Lupus Pernio
Hashimoto's Thyroiditis	Psoriasis
Rheumatoid Arthritis	Polymiositis
Psoriatic Arthritis	Tinnitus
ADD	CFS/ME
Cerebellitis	Chronic Lyme
Fibromyalgia	Pericarditis
Reiters Syndrome	Uveitis
Scleroderma	Early MS
Early Parkinson's	Ménière's Disease

THESE ARE EARLY DAYS - DATA IN WHITE IS STILL AT LEVEL OF 'ANECDOTAL'

What about the Autoantibodies?

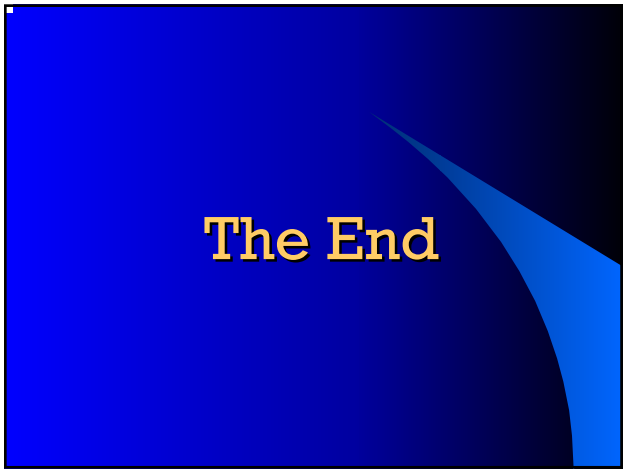
We are familiar with how a virus mutates genes, but bacterial infections also change human genes

463 human genes are changed during an infection with Mycobacterium Tuberculosis, for example[1]

These mutated genes function in various cellular processes including intracellular signalling, cytoskeletal rearrangement, apoptosis, transcriptional regulation, cell surface receptors, cell-mediated immunity and cellular metabolic pathways

Do these altered genes make the proteins against which the 'autoantibodies' are produced?

1. XU Yongzhong et al: Using a cDNA microarray to study cellular gene expression altered by Mycobacterium tuberculosis. Chin Med J 2003;116(7):1070-1073


The End