The Epigenetic Management of Autoimmune Disorders

Shared molecular neuropathology across major psychiatric disorders parallels polygenic overlap

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Genes overlap across psychiatric disease
Many genome-wide studies have examined genes associated with a range of neuropsychiatric disorders. However, the degree to which the genetic underpinnings of these diseases differ or overlap is unknown. Gandal *et al.* performed meta-analyses of transcriptomic studies covering five major psychiatric disorders and compared cases and controls to identify co-expressed gene modules. From this, they found that some psychiatric disorders share global gene expression patterns. This overlap in polygenic traits in neuropsychiatric disorders may allow for better diagnosis and treatment.

The predisposition to neuropsychiatric disease involves a complex, polygenic, and pleiotropic genetic architecture. However, little is known about how genetic variants impart brain dysfunction or pathology. We used transcriptomic profiling as a quantitative readout of molecular brain-based phenotypes across five major psychiatric disorders—autism, schizophrenia, bipolar disorder, depression, and alcoholism—compared with matched controls. We identified patterns of shared and distinct gene-expression perturbations across these conditions. The degree of sharing of transcriptional dysregulation is related to polygenic (single-nucleotide polymorphism–based) overlap across disorders, suggesting a substantial causal genetic component. This comprehensive systems-level view of the neurobiological architecture of major neuropsychiatric illness demonstrates pathways of molecular convergence and specificity.

We identified 1099 genes whose differential gene expression is replicated in Autism, 890 genes for schizophrenia, and 112 genes for bipolar disorder,
The transcriptome may reflect the cause or the consequence of a disorder. To refine potential causal links, we compared single-nucleotide polymorphism (SNP)–based genetic correlations between disease pairs with their corresponding transcriptome overlap. SNP coheritability was significantly correlated with transcriptome overlap across the same disease pairs, suggesting that a major component of these gene-expression patterns reflects biological processes coupled to underlying genetic variation.

Cross-Disorder Group of the Psychiatric Genomics Consortium, International Inflammatory Bowel Disease Genetics Consortium (IIBDGC)
, Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. Nat. Genet. 45, 984–994 (2013).doi:10.1038/ng.2711pmid:23933821

When examining health issues there are two aspects to consider

1. **Phenotype- how genes express themselves to repair, regenerate and maintain health and wellness.**
2. **Genotype- What you were conceived with from your parents genome. Your constitution.**

An autoimmune disease is a condition arising from an abnormal immune response to a normal body part. There are at least 80 types of autoimmune diseases. Nearly any body part can be involved. Common symptoms include low grade fever and feeling tired.

"Autoimmune diseases fact sheet". *OWH*. 16 July 2012. Archived from the original on 5 October 2016. Retrieved 5 October 2016.

Some autoimmune diseases such as lupus run in families, and certain cases may be triggered by infections or other environmental factors.
Women are more commonly affected than men. Often they start during adulthood.

"Autoimmune diseases fact sheet". *OWH*. 16 July 2012. Archived from the original on 5 October 2016. Retrieved 5 October 2016.

For a disease to be regarded as an autoimmune disease it needs to answer to *Witebsky's postulates* -
1. Direct evidence from transfer of disease-causing antibody
2. or disease-causing T lymphocyte white blood cells i.e. TH cell imbalance.

Witebsky E, Rose NR, Terplan K, Paine JR, Egan RW (1957). "Chronic thyroiditis and autoimmunization". *J. Am. Med. Assoc.* 164(13): 1439–47.

Thus there are two challenges that need to be positive to confirm the presence of an Autoimmune Disease.

Firstly a positive challenge to the immunoglobulin markers:

IgA - parasites
IgE – short term half life – 2-3 days - allergen
IgG – longer response half life – 18-21 days – allergen
IgM – similar to IgG
(Strength to weakening)

Immunoglobulin A is an antibody that plays a crucial role in the immune function of mucous membranes. The amount of produced is greater than all other types of antibody combined. In absolute terms, between 3-5gm are secreted into the intestinal lumen each day.

Secretory IgA is the main immunoglobulin found in mucous secretions, including tears, saliva, sweat, colostrum and secretions from the genitourinary tract, gastrointestinal tract, prostate and respiratory epithelium. Prevents colonization by pathogens especially parasites

Immunoglobulin E
Binds to allergens and triggers histamine release from mast cells and basophils, and is involved in allergy. Also protects against parasitic worms.
Half life 2-3 days
Active on first exposure.

Immunoglobulin G
In its four forms, provides the majority of antibody-based immunity against invading pathogens. The only antibody capable of crossing the placenta to give passive immunity to the fetus.
Half life 18-21 days.
Active on second exposure..

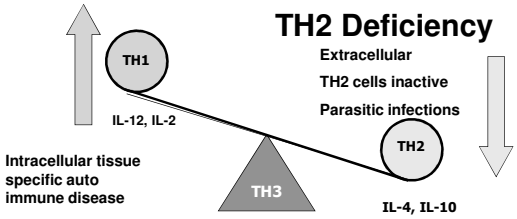
Immunoglobulin M
Expressed on the surface of B cells and in a secreted form with very high avidity (accumulated strength of *multiple* affinities). **Eliminates pathogens in the early stages of B cell-mediated (humoral) immunity before there is sufficient IgG.**
Half life 18-21 days.
Active on second exposure..

Second challenge with
TH1 and TH2 markers

TH1 Weakens – TH2 strengthens
or
TH2 weakens – TH1 strengthens

The Immune System
TH1 weakens – TH2 strengthens

TH1 Excess

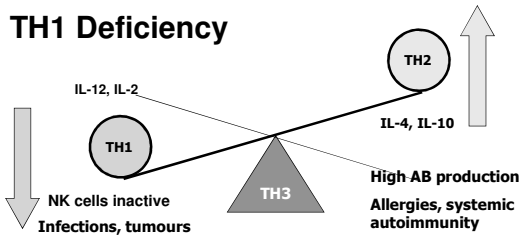


TH2 Deficiency
Extracellular
TH2 cells inactive
Parasitic infections

The Immune System
Thymus Gland
TH2 weakens – TH1 strengthens

TH2 Excess

TH1 Deficiency



Autoimmune diseases tend to have one of three characteristic pathological effects which characterize them as:

1. **Damage to or destruction of tissues**
2. **Altered organ growth**
3. **Altered organ function**

Autoimmune disorders: MedlinePlus Medical Encyclopedia". *www.nlm.nih.gov*. Archived from the original on 2016-01-12. Retrieved 2016-01-21.

All diseases have the following in common. Autoimmune diseases are typical examples

1. Oxidative stress

2. Inflammation

3. Immune system

4. Cell apoptosis

Normally the adaptive immune system produces T cells & B cells that are capable of being reactive with self-antigens. BUT these are usually killed prior to becoming active – placed into a state of anergy or removed by regulatory cells

Harrison's Principles of Internal Medicine: Volumes 1 and 2, 18th Edition (18 ed.). McGraw-Hill Professional. 2011-08-11. ISBN 9780071748896. Archived from the original on 2016-05-29

- **When these mechanisms fail leads to a reservoir of self-reactive cells that become active.**
- **Prevention of self reactive cells takes place in thymus as the T cell is developing into a mature immune cell.**

***Harrison's Principles of Internal Medicine: Volumes 1 and 2, 18th Edition** (18 ed.). McGraw-Hill Professional. 2011-08-11. ISBN 9780071748896. Archived from the original on 2016-05-29*

Autoimmunity is the presence of self-reactive immune response (e.g., auto-antibodies, self-reactive T-cells), with or without damage or pathology resulting from it.
Certain organs – thyroiditis

***Harrison's Principles of Internal Medicine: Volumes 1 and 2, 18th Edition** (18 ed.). McGraw-Hill Professional. 2011-08-11. ISBN 9780071748896. Archived from the original on 2016-05-29*

Or involve a particular tissue in different places, eg. Goodpasture's disease affects the basement membranes in lung & kidney.

***Harrison's Principles of Internal Medicine: Volumes 1 and 2, 18th Edition** (18 ed.). McGraw-Hill Professional. 2011-08-11. ISBN 9780071748896. Archived from the original on 2016-05-29*

In both autoimmune and inflammatory diseases, the condition arises through aberrant reactions of the human adaptive or innate immune systems. In autoimmunity, the patient's immune system is activated against the body's own proteins.

In chronic inflammatory diseases, neutrophils and other leukocytes are constitutively recruited by cytokines and chemokines, leading to tissue damage.

Mukundan L, Odegaard JI, Morel CR, Heredia JE, Mwangi JW, Ricardo-Gonzalez RR, Goh YP, Eagle AR, Dunn SE, et al. (Nov 2009). "PPAR-delta senses and orchestrates clearance of apoptotic cells to promote tolerance". *Nat Med.*

Theories as to how an autoimmune disease state arise.

- **Molecular mimicry**
- **Altered glycan theory**
- **Hygiene hypothesis**

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Molecular Mimicry describes a situation in which a foreign antigen can initiate an immune response in which a T or B cell component cross-recognises self.
The cross reactive immune response is responsible for the autoimmune disease state.

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Molecular Mimicry
Similarity between molecules found on some disease- causing microorganisms and on specific body cells or tissues.
Stimulates the immune system to set up a self reactive response where it attacks healthy body cells or tissues.

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Molecular Mimicry
The immune system acts in this way because the 2 molecules – the disease causing organism and the body's cells or tissues share a sequence in the protein molecule or structural similarities. e.g. in Type 1 Diabetes with pancreas beta cells.

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Altered Glycan theory
The effector function of the immune response is mediated by the glycans (polysaccharides) displayed by the cells & the humoral components (antibody responses) of the immune system.

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Individuals with autoimmunity have alterations in their glycosylation profile such that a pro-inflammatory immune response is favoured (Glycosylation is the addition of a saccharide unit to a protein). Glycosylated Hemoglobin marker HgA1c.

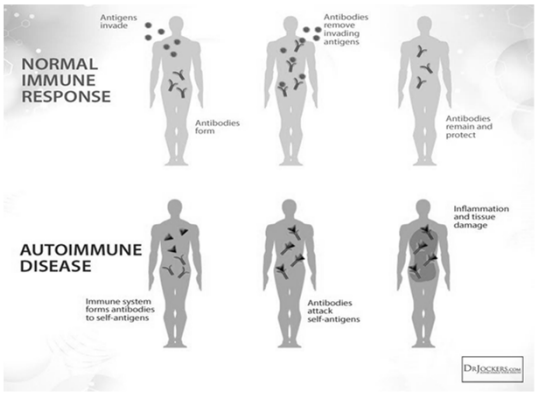
Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

Hygiene hypothesis
High levels of cleanliness expose children to fewer antigens than in the past, causing their immune system to become overactive & more likely to misidentify own tissues as foreign, resulting in autoimmune conditions.

Wucherpfennig KW, Strominger JL (1995). "Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein". *Cell.* 80 (5): 695–705. doi:10.1016/0092-8674(95)90348-8. PMID 7534214

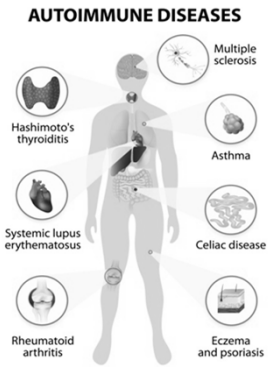
Query the long-term effects of vaccinations against childhood diseases.

What happens when artificial immunity runs out over time?



2 days

- **Crohn's**
- **Blepharitis**
- **Fibromyalgia**
- **Autoimmune indicators**



Secrets of your cells

The basic job of our immune system is to recognise "self" & "other", while collaborating with the brain, gut, thoughts, beliefs and hormones.

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

ID markers on cells are called Human Leukocytes histocompatibility antigens (HLAs). Their biological role is to provide the immune cells with self protection.
Since all cells reveal markings of the "self", immune cells are

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

Trained early on in utero not to react against the self. Those that do are eliminated. Some self destructive cells escape detection & later in life can lead to AI diseases. Also over a lifetime the ability of cells to discriminate self may decrease

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

- **In AI the recognition of "self" is compromised – our own cells are no longer identified as "ours" – become the enemy**
- **In addition to mistaken identity, this response fails to be suppressed**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

- **So AI can be an error in both recognition & regulation**
- **Mechanisms of failed recognition vary**
- **Some proteins change their ID markings so are seen as "not self" – their identity has been hijacked**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

- **In other situations – case of mistaken identity**
- **The immune cells make an error & misinterpret self markings as if they are those of a foreign invader**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

Emotional Reflection

"When have I lost the ability to discriminate between people, places or behaviours that are well matched to me and those that are not?"

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

Emotional Crisis of Self Identity

Emotional Reflection

- **Emotionally lost self identity**
- **Can't differentiate between yourself & others**
- **Have become like others**
- **Influenced by others, taken on the behaviour of others**
- **Not true to yourself**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

Meridian VEP Perfume

- **Essential oils for the specific meridian as a perfume**
- **Blended to complement the 6 essential oils. Maintains the full efficacy in terms of treating the emotional state**
- **Roll on 50 ml miron bottle**

- **Draws parallels between our own sense of self & the self identity of the cell**
- **"Who Am I" – answered by our cells & our psyche, which together engage in an ongoing conversation to keep us safe**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

- **Body & mind share a common responsibility to self identity, safeguarding us from danger & knowing what to trust**
- **Both detect & protect our boundaries**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

- **Body's immune system determines cellular boundaries & identities, while the emotional response navigates our psychological ones**

Sondra Barrett PhD "Secrets of Your Cells – Discovering Your Body's Inner Intelligence". 2013 ISBN 978-1-60407-819-0

Autoimmune diseases
Addison's disease
Celiac
Crohn's
Endometriosis
Inflammatory bowel disorder
Multiple sclerosis
Myasthenia gravis
Polymyalgia rheumatica
Polymyositis
Psoriasis
Rheumatoid arthritis
Scleroderma
Sjogren's syndrome
System Lupus Erythematosus
Temporal arteritis
Thyroiditis / Hashimoto's / Graves
Type 1 Diabetes
Vasculitis
Vitiligo

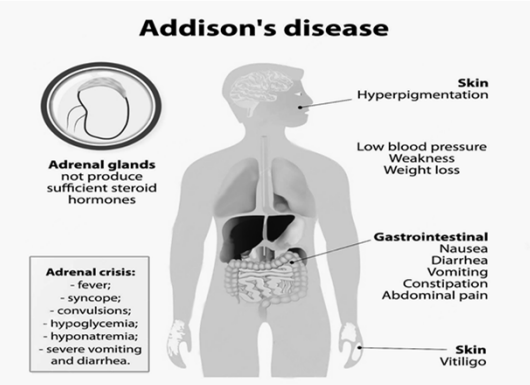
Addison's Disease
Adrenal Gland

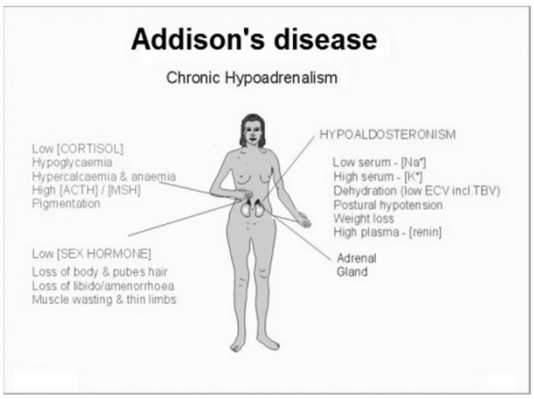
- **Body produces insufficient amounts of adrenal gland hormones – cortisol and aldosterone**
- **Result of body attacking the adrenal cortex**
- **Cortisol converts food fuels into energy**

"Adrenal Insufficiency & Addison's Disease" NIDDK. May 2016. Archived from the original on 13 March 2016. Retrieved 13 March 2016

- **Plays a role in immune system inflammatory process**
- **Helps the body respond to stress**
- **Aldosterone maintains the balance of Na & K to keep blood pressure normal**

"Adrenal Insufficiency & Addison's Disease" NIDDK. May 2014. Archived from the original on 13 March 2016. Retrieved 13 March 2016





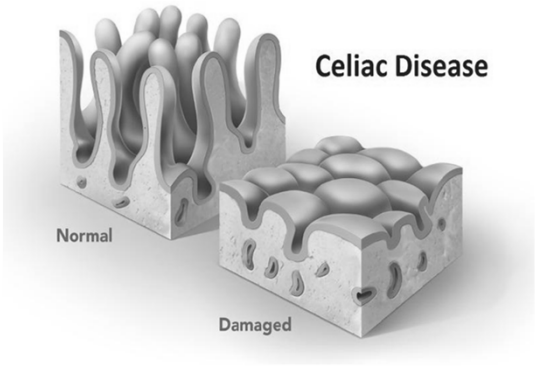
Addison's disease Symptoms

Extreme fatigue
Weight loss and decreased appetite
Darkening of skin (hyperpigmentation)
Low blood pressure and fainting
Salt craving
Low blood sugar (hypoglycaemia)
Nausea, diarrhoea, vomiting
Abdominal pain
Muscle/joint pains
Irritability
Depression
Body hair loss
Sexual dysfunction in women

Celiac Disease
Small Intestine

- **Occurs in genetically predisposed people where the ingestion of gluten leads to damage to SI**
- **Estimated to affect 1 in 100 people worldwide**
- **On eating gluten the body mounts an immune response that attacks the SI**

"Celiac Disease" NIDDKD. June 2015. Archived from the original on 13 March 2016. Retrieved 17 March 2016



- **Leading to damage on the villi which promote nutrient absorption**
- **Hereditary – first degree relative have a 1 in 10 risk**
- **At any age**
- **Can lead to additional Autoimmune diseases & serious health issues**

"Celiac Disease" NIDDKD. June 2015. Archived from the original on 13 March 2016. Retrieved 17 March 2016

- **Type 1 diabetes, MS, dermatitis herpetiformis, anemia, osteoporosis, infertility, miscarriage**
- **Neurological conditions like epilepsy & migraine**
- **Intestinal cancer**

"Celiac Disease" NIDDKD. June 2015. Archived from the original on 13 March 2016. Retrieved 17 March 2016

Inflammatory Bowel Disorders (IBD)

- **Irritable bowel disease (IBS) is not an Autoimmune disorder, it is a functional bowel disorder**
- **However some Autoimmune diseases mimic or overlap with IBS, eg Celiac disease & Inflammatory Bowel disease, cause similar symptoms**

https: irritablebowelsyndrome.net

Crohn's Disease and Ulcerative Colitis are 2 main forms of IBD

Crohn's Disease

- **Inflammation of the gut, can affect any part of the gut, most commonly affected is the end of the ileum (last part of the SI) or colon**
- **Areas of inflammation often patchy with sections of normal gut in between**
- **May be small or extensive**

www.crohnsandcolitis.org.uk

- As well as affecting the lining, damage may penetrate deeper into the bowel wall
- Can start at any age, usually between 10 and 40
- Surveys suggest that cases are being diagnosed more often, particularly teenagers and children

www.crohnsandcolitis.org.uk

Symptoms

Abdominal pain & diarrhoea
Tiredness & fatigue
Feeling unwell & feverish
Mouth ulcers
Loss of appetite & weight loss

www.crohnsandcolitis.org.uk

Other health issues:

Inflammation of the eyes
Thin & weak bones
Liver inflammation
Blood clots (including deep vein thrombosis)
Anaemia (reduced red blood cells)

www.crohnsandcolitis.org.uk

- **1 in 3 people experience inflammation of the joints, usually the elbows, wrists, knees, ankles**
- **More rarely the joints in the spine and pelvis become inflamed – ankylosing spondylitis**

www.crohnsandcolitis.org.uk

Causes

Genetic

Abnormal reaction of the Immune system to certain bacteria in the intestines

Unknown triggers that could include viruses, bacteria, diet, smoking, stress or something environmental

www.crohnsandcolitis.org.uk

Ulcerative Colitis

- **Causes inflammation & ulceration of the inner lining of the rectum & colon**
- **Ulcers develop on the surface on the lining, these may bleed and produce mucus**
- **Inflammation usually begins in the rectum & lower colon, but may affect entire colon**

www.crohnsandcolitis.org.uk

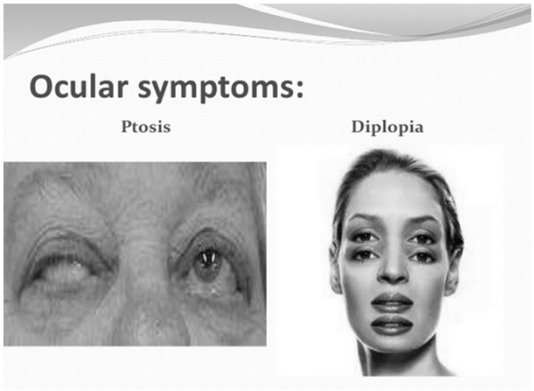
- **If it is only in the rectum it is called proctitis**
- **If the whole colon is affected it is called total colitis or pancolitis**
- **Similar to Crohn's – causes, symptoms, can develop joint inflammation & ankylosing spondylitis**

www.crohnsandcolitis.org.uk

Myasthenia Gravis
Muscles

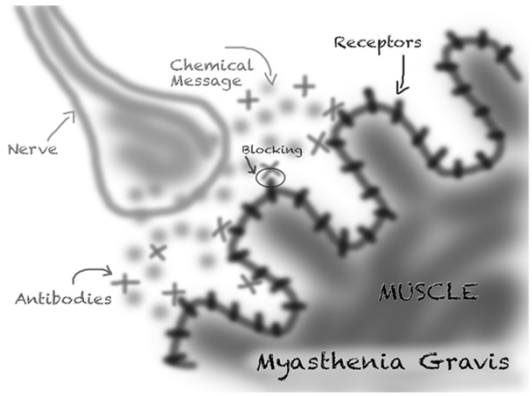
- **Abnormal weakness of certain muscles**
- **Caused by a defect in the action of Acetylcholine at neuromuscular junctions**
- **Most commonly affected, muscles of the eyes, face, swallowing, double vision**

"Myasthenia Gravis Fact Sheet" NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016



- **Drooping eyelids, trouble talking & walking**
- **Results from antibodies destroying the nicotinic acetylcholine receptors at the junction of nerve & muscle**

"Myasthenia Gravis Fact Sheet" NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016



- **Thus preventing nerve impulses from triggering muscle contractions**
- **In a myasthenia crisis a paralysis of the respiratory muscle occurs. Crisis triggered by infection, fever, adverse reaction, emotional stress**

"Myasthenia Gravis Fact Sheet" NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016

- **Thymus gland cells form part of the body's immune system. With MG the thymus gland is large & abnormal. It sometimes contains clusters of immune cells indicating lymphoid hyperplasia**

"Myasthenia Gravis Fact Sheet" NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016

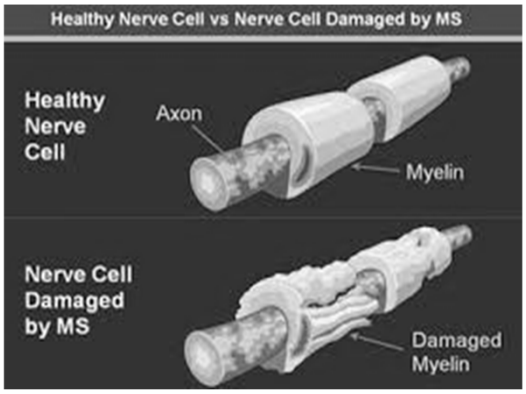
- **Lymphoid hyperplasia is the rapid growth of normal cells that resemble lymph tissue**
- **Gives wrong instructions to immune cells**

"Myasthenia Gravis Fact Sheet" NINDS. 10 May 2016. Archived from the original on 27 July 2016. Retrieved 8 August 2016

Multiple Sclerosis
CNS

- **Immune-mediated disease in which the immune system mistakenly attacks myelin in the CNS**
- **T cells pass from the bloodstream into CNS to attack the myelin coating around the nerve fibres**

Compston A, Coles A (Oct 2008) "Multiple Sclerosis" Lancet 372 (9648) : 1502-17



- **When any part of the myelin sheath is damaged or destroyed, nerve impulses travelling to & from the brain & spinal cord are distorted or interrupted**
- **The damaged myelin forms scar tissue – disease name**

Compston A, Coles A (Oct 2008) "Multiple Sclerosis" Lancet 372 (9648) : 1502-17

- **Proposed causes – genetics and environmental factors, triggered by a viral infection**
- **Symptoms – physical, mental & psychiatric problems**
- **Double vision, blindness, muscle weakness, sensation & coordination**

Compston A, Coles A (Oct 2008) "Multiple Sclerosis" Lancet 372 (9648) : 1502-17

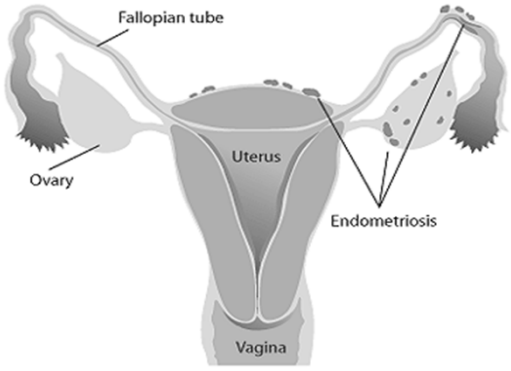
- **MS takes several forms. New symptoms occurring in isolated attacks or building up over time**
- **Between attacks symptoms may disappear, however permanent neurological damage remains**

NINDS Multiple Sclerosis Information. National Institute of Neurological Disorders & Stroke. 19 November 2015. Archived from the original on 13 February 2016. Retrieved 6 March 2016

Endometriosis
uterus

- **Layer of tissue normally covers the inside of the uterus grows outside of it**
- **Ovaries, fallopian tubes, tissues around uterus & ovaries**
- **Main symptoms – pain in pelvis, during menstruation, sexual intercourse**

Endometriosis: Overview" www.nichd.nih.gov. Archived from the original on 18 May 2017. Retrieved 20 May 2017.



- **Urinary urgency & frequency, infertility. 25% women have no symptoms**
- **The areas of endometriosis bleed each month resulting in inflammation & scarring**
- **Pain caused by organ dislocation from adhesion binding internal organs**

Endometriosis: Overview" www.nichd.nih.gov. Archived from the original on 18 May 2017. Retrieved 20 May 2017.

- **Ovaries, uterus, oviducts, peritoneum & bladder can all be bound together, pain all the time**
- **Cause – theory of retrograde menstruation**
- **During menstrual flow some of the endometrial debris flows backwards**

Endometriosis: Overview" www.nichd.nih.gov. Archived from the original on 18 May 2017. Retrieved 20 May 2017.

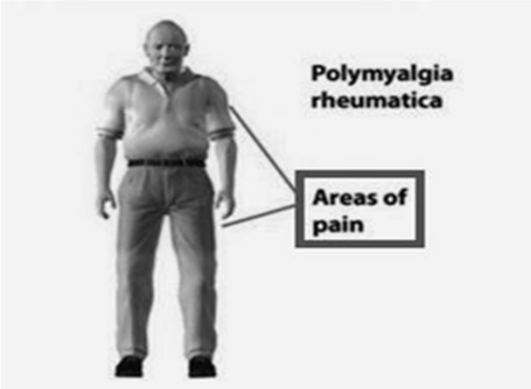
- **Through the fallopian tubes & into the peritoneal cavity attaching to the peritoneal surface (lining of the abdominal cavity) where it can proceed to invade the tissue as endometriosis**

Gleicher N, el-Roeiy A, Confino E, Friberg J (July 1987). "Is endometriosis an autoimmune disease?". Obstetrics and Gynecology. 70 (1): 115–22. PMID3110710

- **Researchers are investigating the possibility that the immune system may not be able to cope with the cyclic onslaught of retrograde menstrual fluid, leading to autoimmune responses**

Gleicher N, el-Roeiy A, Confino E, Friberg J (July 1987). "Is endometriosis an autoimmune disease?". Obstetrics and Gynecology. 70 (1): 115–22. PMID 3110710

Polymyalgia Rheumatica
"Pain in many muscles"



- **Pain or stiffness usually in the neck, shoulders, upper arms, hips, groin, buttocks which inhibits activity**
- **Disease of the "girdles"**
- **"pain in many muscles" Greek**
- **Results from the activity of inflammatory cells & proteins**

"Polymyalgia Rheumatica & Temporal Arteritis" WebMD. Retrieved 2008-06-10

- That are normally a part of the body's disease fighting immune system and the inflammatory activity is concentrated in tissues around the joints
- The white blood cells attack the lining of the joints causing inflammation

"Polymyalgia Rheumatica & causes" Mayoclinic. . Dec 4, 2010. Retreived 2012-01-19

- Inherited factors play a role. Viral stimulation of immune system in genetically susceptible individuals
- Some studies – particular virus, adenovirus, human parvovirus (children), human parainfluenza virus

"Polymyalgia Rheumatica & causes" Mayoclinic. . Dec 4, 2010. Retreived 2012-01-19

- Usually have high levels of CRP, produced in the liver in response to injury or infection. Although this is not a specific test.

"Polymyalgia Rheumatica & causes" Mayoclinic. . Dec 4, 2010. Retreived 2012-01-19

Polymyositis
Systemic muscle disease

- **Rare, autoimmune systemic muscle disease**
- **Mediated by cytotoxic T cells with as yet unknown autoantigen**
- **Chronic inflammation of the muscles, inflammatory myopathy**

Kenneth W. Stauss, Hermann Gonzalez-Burrita, Munther A Khamashta, Graham R.V. Hughes (1989). "Polymyositis-dermatomyositis: a clinical review". Postgraduate Medical Journal 65:437-443 doi 10. 1136/pgmj. 65. 765. 437

- **Weakness and/or loss of muscle mass in the proximal musculature (body's midline), flexion of neck & torso, hip extensors**
- **Skin involvement - dermatomyositis**

Kenneth W. Stauss, Hermann Gonzalez-Burrita, Munther A Khamashta, Graham R.V. Hughes (1989). "Polymyositis-dermatomyositis: a clinical review". Postgraduate Medical Journal 65:437-443 doi 10. 1136/pgmj. 65. 765. 437

- **Can have dysphagia – difficulty in swallowing**
- **Foot drop – damage to common fibular nerve & muscles in lower leg**
- **Can involve Interstitial lung disease & cardiac problems – heart failure, conduction abnormalities**

Kenneth W. Stauss, Hermann Gonzalez-Burrita, Munther A Khamashta, Graham R.V. Hughes (1989). "Polymyositis-dermatomyositis: a clinical review". Postgraduate Medical Journal 65:437-443 doi 10. 1136/pgmj. 65. 765. 437

Psoriasis
Skin

- **Long lasting autoimmune disease characterised by patches of abnormal skin – red, itchy & scaly**
- **Varies in severity – small patches to complete body**
- **Several different types – vulgaris. Red patches with white scales on top**

Palfreeman AC, McNamee KE, McCann FE (March 2013). "New developments in the management of Psoriasis & Psoriatic Arthritis: a focus on apremilast" Drug Des Devel Ther. 7: 201-210 doi: 10.2147/DDDT. S32713. PMC 3615921 PMID 23569359

- **Some types can be pus-filled blisters or in skin folds**
- **Genetic disease triggered by environmental factors. Can worsen in winter, with certain medications, infections & psychological stress**
- **Immune system reacting to the skin cells**

Palfreeman AC, McNamee KE, McCann FE (March 2013). "New developments in the management of Psoriasis & Psoriatic Arthritis: a focus on apremilast" Drug Des Devel Ther. 7: 201-210 doi: 10.2147/DDDT. S32713. PMC 3615921 PMID 23569359

- **Study suggested that Vitamin D3 cream can help**
- **Napkin psoriasis – subtype in infants. Red papules with silver scale in nappy area, may extend to torso & limbs. Often misdiagnosed as napkin dermatitis (nappy rash)**

"Questions & Answers about Psoriasis" National Institute of Arthritis & Musculoskeletal & Skin Diseases. October 2013. Archived from the original on 8 July 2015. Retrieved 1 July 2015

- **Strong hereditary genetic component & many genes can be associated with it. Most of the genes identified relate to immune system, particularly the Major Histocompatibility (MHC) & T cells**

Nestle FO, Kaplan DH, Barker J (2009). "Psoriasis". N Engl J Med 361 (5): 496-509. doi: 10.1056/NEJMra 0804595. PMID 19641206

- **Major determinant is PSORS1 located on chromosome 6**
- **2 major immune system genes can be involved on chromosome 5q & chromosome 1p**

Nestle FO, Kaplan DH, Barker J (2009). "Psoriasis". N Engl J Med 361 (5): 496-509. doi: 10.1056/NEJMra 0804595. PMID 19641206

- **Mechanism of the disorder**
- **Abnormally excessive & rapid growth of epidermal layer of the skin**
- **Skin cells replaced 3-5 days, normally 28-30 days**
- **Believed to stem from premature maturation of keratinocytes induced by**

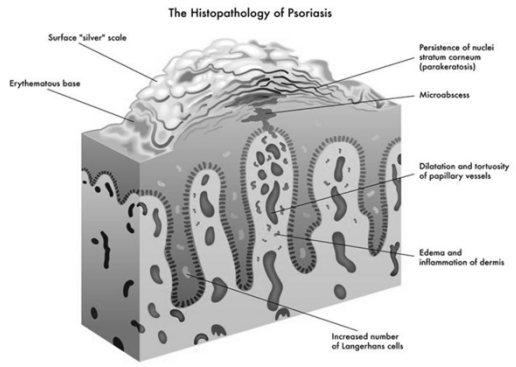
Nestle FO, Kaplan DH, Barker J (2009). "Psoriasis". N Engl J Med 361 (5): 496-509. doi: 10.1056/NEJMra 0804595. PMID 19641206

- **Inflammatory cascade in the dermis involving dendritic cells, macrophages & T cells (3 subtypes of white blood cells)**
- **One hypothesis – defect in regulatory T cells & in regulatory cytokine interleukin 10**

Nestle FO, Kaplan DH, Barker J (2009). "Psoriasis". N Engl J Med 361 (5): 496-509. doi: 10.1056/NEJMra 0804595. PMID 19641206

- **Gene mutations of proteins involved in the skin's ability to function as a barrier have been identified as markers of susceptibility for the development of psoriasis**

Nestle FO, Kaplan DH, Barker J (2009). "Psoriasis". N Engl J Med 361 (5): 496-509. doi: 10.1056/NEJMra 0804595. PMID 19641206



Autoimmune Dermatitis
Skin

- **Skin irritation associated with immune dysfunction**
- **Rashes, blisters, papules, patches of dryness**
- **The immune system mistakenly identifies something in the skin as harmful & starts attacking it**

www.wisegeek.com/what -is-autoimmune-dermatitis.htm

- **Can onset at any age**
- **People with other Autoimmune diseases can develop dermatitis. Sign that the condition is getting worse**
- **It can start anywhere on the body and spread over time**
- **Itching & pain around the site of an outbreak, hot & dry**

www.wisegeek.com/what -is-autoimmune-dermatitis.htm

- **May develop in response to allergies, with the body reacting to allergens found in & around the skin**
- **Autoimmune progesterone dermatitis or oestrogen, where flare ups occur at various phases of the menstrual cycle**

www.wisegeek.com/what -is-autoimmune-dermatitis.htm

- **Skin can crack & peel , creating an open sore which may allow infectious organisms to enter the body & cause infection**

www.wisegeek.com/what -is-autoimmune-dermatitis.htm

Eczema is not directly caused by an Autoimmune disorder, but some forms have been associated with skin disorders.

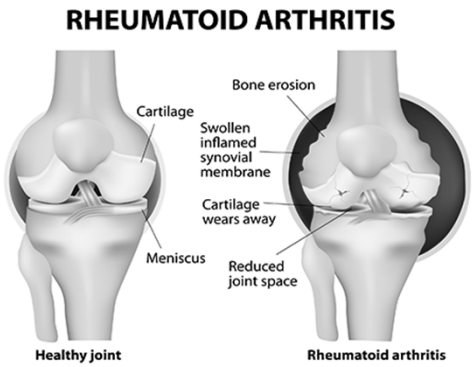
Atopic dermatitis, the most common type of eczema, stems from an immune system imbalance.

www.sharecare.com/health/eczema

Rheumatoid Arthritis
Joints

- **Primarily affects joints, warm, swollen, painful, stiff. Most commonly wrists & hands**
- **Low red blood cell count can lead to inflammation around lungs and heart**
- **Underlying mechanism – immune system attacking joints**

"Handout on health: Rheumatoid Arthritis". National Institute of Arthritis & Musculoskeletal & Skin Diseases. August 2014. Archived from the original on June 30, 2015. Retrieved July 2, 2015



- **This results in inflammation & thickening of the joint capsule. Affects the underlying bone & cartilage**
- **Pain associated with RA as opposed to Osteo Arthritis is at the site of inflammation, classified as nociceptive rather than neuropathic**

"Handout on health: Rheumatoid Arthritis". National Institute of Arthritis & Musculoskeletal & Skin Diseases. August 2014. Archived from the original on June 30, 2015. Retrieved July 2, 2015

- In OA movement induces pain
- As RA progresses, inflammatory activity leads to tendon tethering, erosion & destruction of joint surface, impairs movement, leads to deformity
- More prone to stroke, atherosclerosis, heart attack

"Gaffo A, Saag KG, Curtis JR (2006) "Treatment of Rheumatoid Arthritis" AM J Health Syst Pharm. 63(24): 2451-2465. doi: 10.2146/ajhp050514. PMC 2038957. PMID 17158693

- Risk factors. Strong association with genes of inherited tissue type Major histocompatibility complex (MHC) antigen
- Genome-wide association studies examining SNIPs found 100 genes associated with RA risk

"Gaffo A, Saag KG, Curtis JR (2006) "Treatment of Rheumatoid Arthritis" AM J Health Syst Pharm. 63(24): 2451-2465. doi: 10.2146/ajhp050514. PMC 2038957. PMID 17158693

- Most of these genes involving the HLA system which controls recognition of self versus non-self molecules

"Gaffo A, Saag KG, Curtis JR (2006) "Treatment of Rheumatoid Arthritis" AM J Health Syst Pharm. 63(24): 2451-2465. doi: 10.2146/ajhp050514. PMC 2038957. PMID 17158693

Scleroderma
Connective tissue

- **Group of AI diseases resulting in changes to the skin, blood vessels, muscles and internal organs**
- **Symptoms include areas of thickened skin, stiffness, tiredness, poor blood flow to fingers and toes in the cold**

"Scleroderma" NORD (National Organisation for Rare Disorders). 2007. Archived from the original on 8 September 2016. Retrieved on 14 July 2017.

- **Underlying mechanism – abnormal growth of connective tissue occurring as a result of body immune system attacking healthy tissue**
- **Systemic – shortened life expectancy. Death from lung, GI or heart complications**

"Scleroderma" NORD (National Organisation for Rare Disorders). 2007. Archived from the original on 8 September 2016. Retrieved on 14 July 2017.

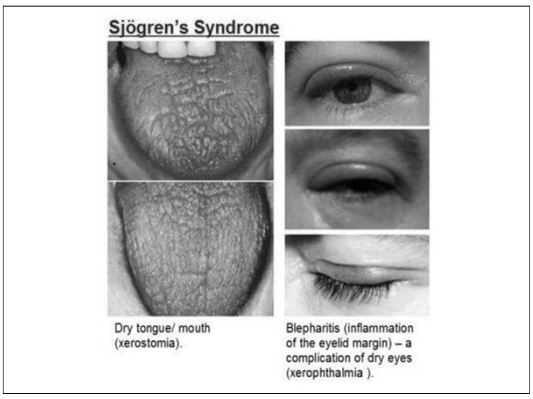
- **Cause is genetic & environmental factors. Mutations in HLA genes.**
- **Exposure to chemicals – aromatic & chlorinated solvents, ketones, trichloroethylene, welding fumes and white spirit**

"Scleroderma" NORD (National Organisation for Rare Disorders). 2007. Archived from the original on 8 September 2016. Retrieved on 14 July 2017.

- **Characterised by increased synthesis of collagen leading to the sclerosis**
- **Damage to small blood vessels, activation of T lymphocytes and production of altered connective tissue**

Valanciene G, Jasaitiene D, Valnkeviciene S (2010) "Pathogenesis & Treatment Modalities of localised Scleroderma". Medicina. 46 (10): 649-56. PMID 21393982. Archived from the original on 2014-03-06

Sjogren's Syndrome
(Show-grins)
Moisture producing glands



- **Long term AI disease affecting the moisture producing glands of the body**
- **Dry mouth and dry eyes**
- **Other symptoms – dry skin, chronic bronchitis, vaginal dryness, numbness in arms & legs, tired, muscle & joint pains, thyroid, lymphoma**

Elsevier, Dorlands, Illustrated Medial Dictionary, elsevier

- **Genetic and environmental – virus, bacteria**
- **The inflammation that results progressively damages the glands**
- **Skin dryness is caused by lymphocyte infiltration into the skin glands**

Elsevier, Dorlands, Illustrated Medial Dictionary, elsevier

- **Viral proteins, engulfed molecules or degraded self structures may initiate autoimmunity by molecular mimicry & increase risk SS**
- **Epstein Barr, Hepatitis C, human T cell leukaemia virus most studied**

Elsevier, Dorlands, Illustrated Medial Dictionary, elsevier

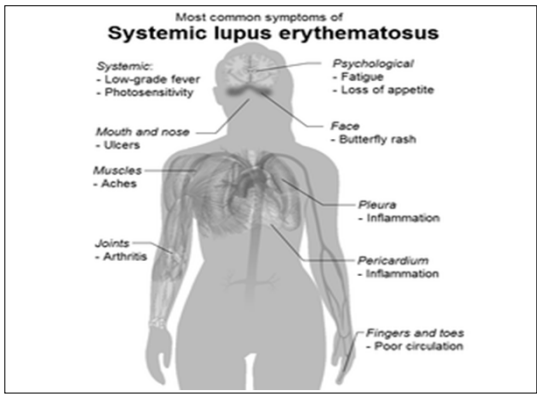
- **Damaged self structures targeted for apoptosis may be mistakenly exposed to immune system, triggering autoimmunity in the exocrine glands**
- **Cause – genetic background, environmental & hormonal factors – estrogen deficiency**

Elsevier, Dorlands, Illustrated Medial Dictionary, elsevier

- **Lead to triggering of infiltration of lymphocytes – T cells, B cells, plasma cells, causing glandular dysfunction in the salivary & lacrimal glands**

Voulgarelis M, Tzionfas A.G (2010) "Pathogenic mechanisms in the initiation & perpetuation of Sjogren's Syndrome". Nature Reviews Rheumatology. 6: 529-537. doi: 10.1038/nrrheum. 2010.118

Systemic Lupus Erythematosus
Skin & body parts



- **Immune system attacks healthy tissues in many parts of the body**
- **Symptoms: painful & swollen joints, fever, chest pain, hair loss, mouth ulcers, swollen lymph nodes, tired, red rash on the face**
- **Periods of flares & remission**

Handout on Health: Systemic Lupus Erythematosus" www.niams.nih.gov February 2015. Archived from the original on 17 June 22016. Retrieved 12 June 2016

- **Factors to increase risk: genetics, environment, female sex hormones, sunlight, smoking, Vitamin D deficiency, infections**
- **70% have skin symptoms – classic molar rash (butterfly)**

Handout on Health: Systemic Lupus Erythematosus" www.niams.nih.gov. February 2015. Archived from the original on 17 June 22016. Retrieved 12 June 2016

- **SLE is associated with many genetic regions – oligogenic trait, means that there are several genes that control susceptibility to the disease**
- **One aspect is abnormalities in apoptosis. Increased in monocytes & keratinocytes**

Kelly, J.A; Moser, K.L; Harley, J.B (2002-10-01). "The genetics of Systemic Lupus Erythematosus: putting the pieces together". Genes & Immunity. 3 Suppl 1:S71-85. doi:10.1038/sj.gene.6363885. ISSN 1466-4879 PMID 12215907

- **Necrosis is increased in T lymphocytes**
- **Defects in apoptotic clearance, damaging effects caused by apoptotic debris**
- **When apoptotic material is not removed by phagocytes, it is captured by antigen-presenting cells**

Kelly, J.A; Moser, K.L; Harley, J.B (2002-10-01). "The genetics of Systemic Lupus Erythematosus: putting the pieces together". Genes & Immunity. 3 Suppl 1:S71-85. doi:10.1038/sj.gene.6363885. ISSN 1466-4879 PMID 12215907

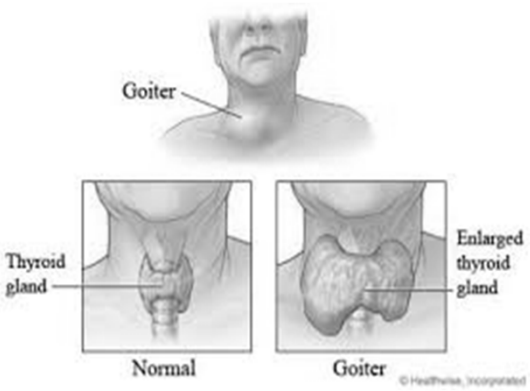
- **This leads to the development of anti-nuclear antibodies**

Kelly, J.A; Moser, K.L; Harley, J.B (2002-10-01). "The genetics of Systemic Lupus Erythematosus: putting the pieces together". Genes & Immunity. 3 Suppl 1:S71-85. doi:10.1038/sj.gene.6363885. ISSN 1466-4879 PMID 12215907

Thyroiditis / Hashimoto's / Graves' Disease

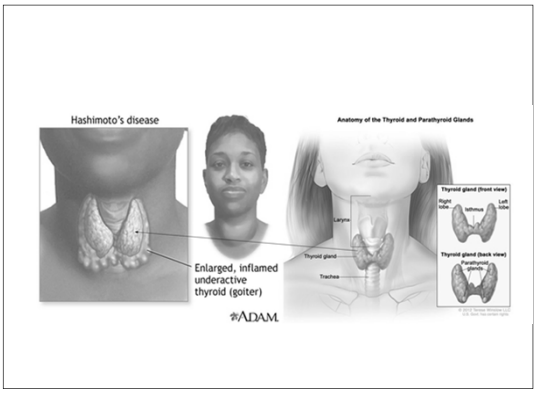
- **Thyroiditis is a group of disorders that cause thyroidal inflammation**
- **Caused by antibodies that attack the thyroid**

"Thyroiditis" www.thyroid.org 2005. American thyroid Association. 13 March 2008. 8 December 2015



- **Hashimoto's – hypothyroidism condition**
- **Can initially present with excessive thyroid hormone**

"Thyroiditis" www.thyroid.org 2005. American thyroid Association. 13 March 2008. 8 December 2015



- **Thyroid gland is gradually destroyed, the thyroid may enlarge forming a goiter but not always**
- **Enlargement is due to lymphocytic infiltration & fibrosis**
- **After many years the thyroid shrinks in size**

"Thyroiditis" www.thyroid.org2005. American thyroid Association. 13 March 2008. 8 December 2015

- **Antibodies against thyroid peroxidase, thyroglobulin & TSH receptors cause gradual destruction of follicles in the thyroid gland**
- **Thyroid peroxidase oxidises iodide ions to form iodine atoms for addition to tyrosine residues on thyroglobulin, T4**

"Hashimoto's Disease" NIDDK. May 2014. Archived from the original on 22 August 2016. Retrieved 9 August 2016

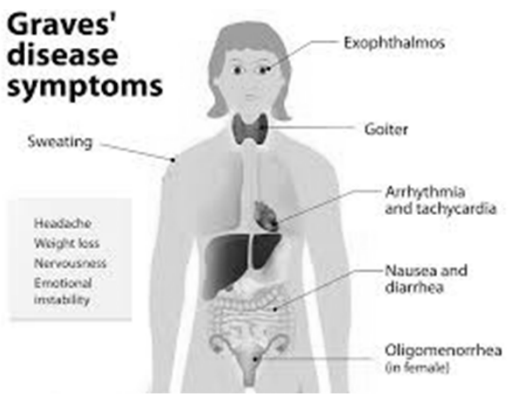
Graves' Disease
Hyperthyroid

- **Body produces antibodies to the receptor for thyroid-stimulating hormone**
- **Hyperthyroidism since they bind to the TSHr & chronically stimulate it, leading to an abnormally high levels of T3 & T4**

"Graves' Disease" www.niddk.nih.gov August 10 2012. Archived from the original on April 2 2015. Retrieved 2015-04-02

- **Leads to clinical symptoms of hyperthyroidism & the enlargement of thyroid gland visible as a goiter**
- **Hyperthyroidism leads to bone loss from osteoporosis, caused by an increased excretion of Ca & Phosphorus in urine & stools**

"Graves' Disease" www.niddk.nih.gov. August 10 2012. Archived from the original on April 2 2015. Retrieved 2015-04-02



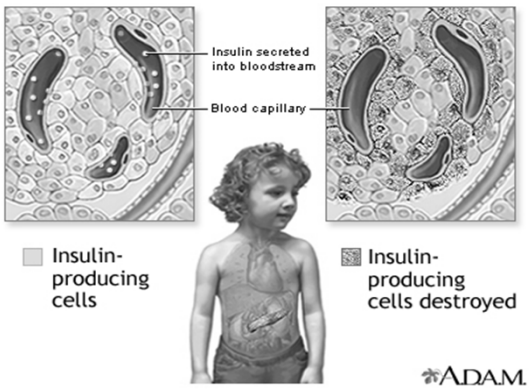
- **2 signs are truly diagnostic of Graves' disease:**
- **Non pitting edema**
- **Thyroid associated ophthalmopathy**
- **Form of lymphocytic orbital inflammation, autoimmune activation of orbital fibroblasts**

"Graves' Disease" www.niddk.nih.gov August 10 2012. Archived from the original on April 2 2015. Retrieved 2015-04-02

- **Hypertrophy of the extraocular muscles causes expansion of orbital fat & muscle components**
- **Leads to increased intraocular pressure, venous congestion, periorbital edema, lid retraction & exposure keratopathy**

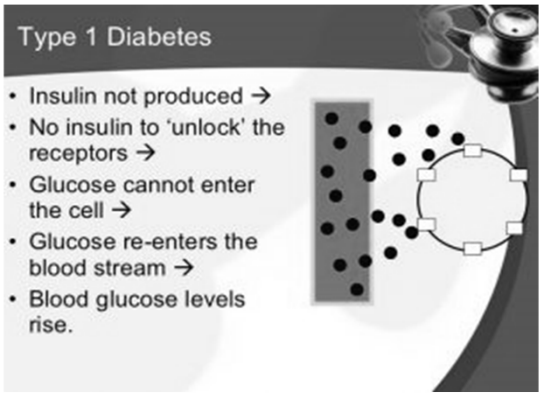
"Graves' Disease" www.niddk.nih.gov August 10 2012. Archived from the original on April 2 2015. Retrieved 2015-04-02

Type 1 Diabetes
Pancreas



- **Diabetes mellitus type 1 is a disease where not enough insulin is produced**
- **This results in high blood sugar in the body**
- **Underlying mechanism involves an autoimmune destruction of the insulin-produce beta cells pancreas**

"Types of Diabetes" NIDDK. February 2014. Archived from the original 16 August 2016. Retrieved 31 July 2016.



- More than 50 genes are associated with it. The strongest gene IDDM1 is on chromosome 6
- An increased rate of urinary infection due to diabetic nephropathy which causes a decrease in bladder sensation, which in turn can

"Types of Diabetes" NIDDK. February 2014. Archived from the original 16 August 2016. Retrieved 31 July 2016.

- Cause increased residual urine, a risk factor for urinary tract infections
- High level of reactive oxygen species created as a result of the disease – a supply of antioxidants can combat this
- Some studies suggest that gliadin (protein in gluten)

"Types of Diabetes" NIDDK. February 2014. Archived from the original 16 August 2016. Retrieved 31 July 2016.

- May play a role in development of the disease
- Increased intestinal permeability & subsequent loss of barrier function allows pro-inflammatory substances into the blood, may induce the autoimmune response if genetically predisposed

"Types of Diabetes" NIDDK. February 2014. Archived from the original 16 August 2016. Retrieved 31 July 2016.

Vasculitis
Blood vessels

- **Group of disorders that destroy blood vessels by inflammation**
- **The immune system attacks the blood vessels instead of defending them against infection**
- **Both arteries & veins are affected. Phlebitis, arteritis**

"Glossary of dermatopathological terms. DermNet NZ". Archived from the original on 2008-12-20. Retrieved 2009-01-08

- **Different types affect one size of blood vessel**
- **Takayasu's arteritis & Giant cell or Temporal arteritis is large vessel vasculitis since they mainly affect the aorta & the largest arteries as they branch off**

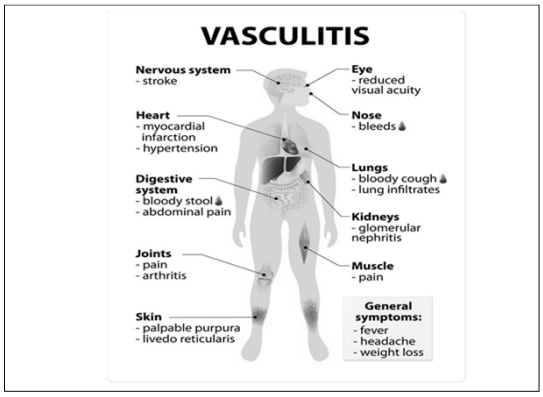
www. Vasculitis.org.uk

- **Polyarteritis nodosa & Kawasaki disease are called medium vessel vasculitis since they affect middle sized arteries as they go into the organs**
- **Wegener's granulomatosis & microscopic polyangiits cause inflammation in small**

www. Vasculitis.org.uk

- **Vessels, the capillaries that supply the insides of the organs**

www. Vasculitis.org.uk



Vitiligo
Skin

- **Patches of skin losing their pigment. The patches of skin become white & usually have sharp margins. The hair on the skin may also become white**
- **Often the patches begin on areas of skin that are exposed to the sun**

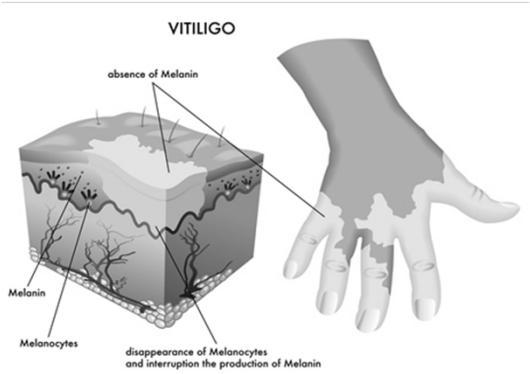
Ezzedine,K; eleftheriadon, V; Whitton,M; Van Geel, N (4 July 2015) "Vitiligo" Lancet 386 (9988): 74-84 doi: 10.1016/s0140-6736(14) 60763-7. PMID 25596811

- **Depigmented skin tends to occur on extremities. The loss of skin pigmentation is particularly noticeable around body orifices – mouth, eyes, nostrils, genitalia, umbilicus**
- **Michael Jackson**

Ezzedine,K; eleftheriadon, V; Whitton,M; Van Geel, N (4 July 2015) "Vitiligo" Lancet 386 (9988): 74-84 doi: 10.1016/s0140-6736(14) 60763-7. PMID 25596811

- **Autoimmune disease that results in destruction of skin pigment cells. The immune system attacks & destroys the melanocytes**

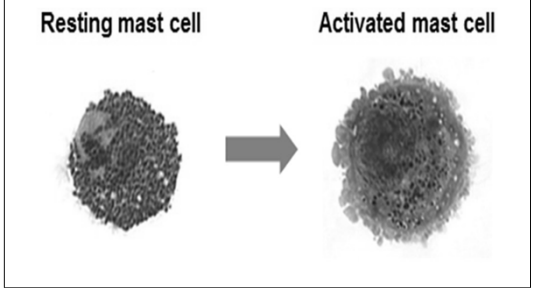
Ezzedine,K; eleftheriadon, V; Whitton,M; Van Geel, N (4 July 2015) "Vitiligo" Lancet 386 (9988): 74-84 doi: 10.1016/s0140-6736(14) 60763-7. PMID 25596811



- **Classified into 2 main types: segmental & non-segmental**
- **Most cases are non-segmental, both sides body**
- **The affected areas of skin expand over time**
- **10% cases are segmental, the affected areas do not expand over time**

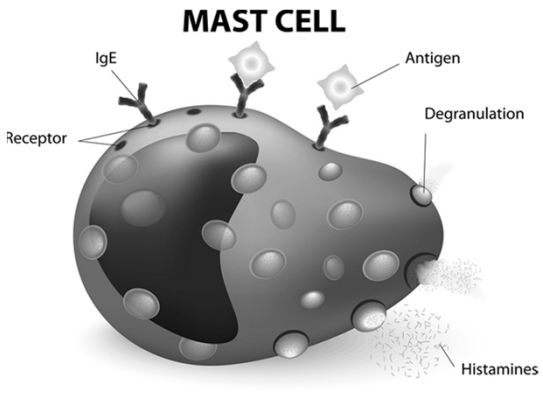
Ezzedine,K; eleftheriadon, V; Whitton,M; Van Geel, N (4 July 2015) "Vitiligo" Lancet 386 (9988): 74-84 doi: 10.1016/s0140-6736(14) 60763-7. PMID 25596811

Mast Cell Activation Disease



- **Mast cells are "guards" able to sense a wide range of threats to the body (ie infections or toxins)**
- **When a mast cell senses a threat it "activates", producing & releasing chemical signals "mediators" appropriate for the threat**

Valent P (2013). "Mast Cell Activation Syndromes: Definition and Classification". Allergy. 68 (4): 417–24. doi:10.1111/all.12126. PMID 23409940



- In Mast cell activation diseases, mast cells activate in abnormal ways in response to threats & even when there is no threat
- General term for diseases of inappropriate mast cell activation
- Releases too much histamine

Valent P (2013). "Mast Cell Activation Syndromes: Definition and Classification". Allergy. 68 (4): 417–24. i:10.1111/all.12126. PMID 23409940

- It is linked to some cancers, CV disease, connective tissue disorders, inflammation including the brain, allergy & asthma, IBS, skin diseases & other Autoimmune diseases like RA & Lupus

www.mastcellresearch.com

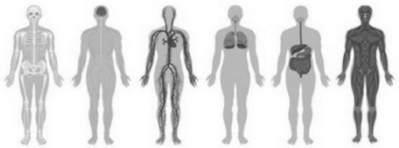
- Mast Cell Activation Syndrome (MCAS) features inappropriate mast cell activation with little or no inappropriate mast cell proliferation
- Mastocytosis features both activation & prolieration

www.mastcellresearch.com

- **2 principal types of mastocytosis**
  - **Cutaneous - limited to skin**
  - **Systemic - throughout body**
- **Most common cutaneous is urticarial pigmentosa**
- **Mast cell disease can drive auto-immune conditions**
- **Genetic & environmental**

www.mastcellresearch.com

Mast Cell Activation Disorders



- Mast Cell (MC) Disorders can affect any organ system, particularly
  - Gastrointestinal tract, Skin, Respiratory Tract
  - MC also have been found in joints, uterus
- Disorders can results from
  - Increased proliferation (mastocytosis, monoclonal MCAS)
  - Increased Activity (nonclonal, overactive Mast Cells)

The Immune System
Innate and Adaptive

In both autoimmune and inflammatory diseases, the condition arises through aberrant reactions of the human innate immune system or the adaptive immune system.
In autoimmunity, the patient's immune system is activated against the body's own proteins.

In chronic inflammatory diseases, neutrophils and other leukocytes are constitutively recruited by cytokines and chemokines, leading to tissue damage.

Mukundan L, Odegaard JI, Morel CR, Heredia JE, Mwangi JW, Ricardo-Gonzalez RR, Goh YP, Eagle AR, Dunn SE, et al. (Nov 2009). "PPAR-delta senses and orchestrates clearance of apoptotic cells to promote tolerance". *Nat Med.*

The Immune Connection

When there is lowered immune system function we need to increase immune system activity.

When there is an increased system function we need to decrease immune system activity as in autoimmune disorders.

Classification of White Blood Cells

Non-specific innate immune system (Phagocytes*)

Granulocytes:	70%	Neutrophils*	65%	(HOCl) NA
		Eosinophils	4%	(H2O2) GABA, Glycine, Taurine
		Basophils	1%	(Histamine)
		(Mast cells)		Histamine
Agranulocytes	30%	Monocytes* (Macrophages)	(NO*)	Dopamine
		Natural Killer Cells	15%	Excitatory

Adaptive Specific

Lymphocytes	25%	B-Lymphocytes S	
		T-Lymphocytes:	ACh
		Helper T-Cells	
		Memory T-Cells	
		Killer T-Cells	
		Suppresser T-Cells	

It is generally recognized that there are two parts of the human immune system

1. The innate immune system

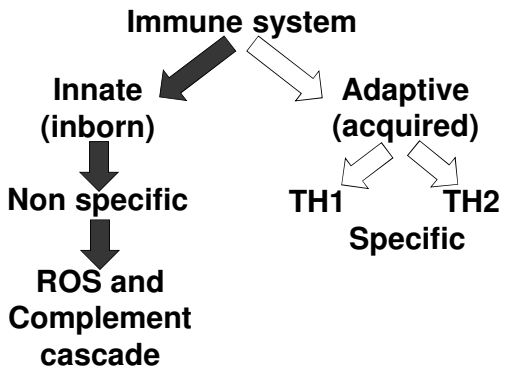
2. The adaptive immune system

The question is:
what part(s) of the immune system should we increase or decrease?

Innate immune system?

Adaptive immune system?
(TH1 or TH2)

The solution in some patients (mainly acute) is to optimize innate immune function rather than focus only on adaptive immune response.



In the innate immune system the body's initial response is to eliminate microbes & infections immediately or within hours.

Innate Immune System

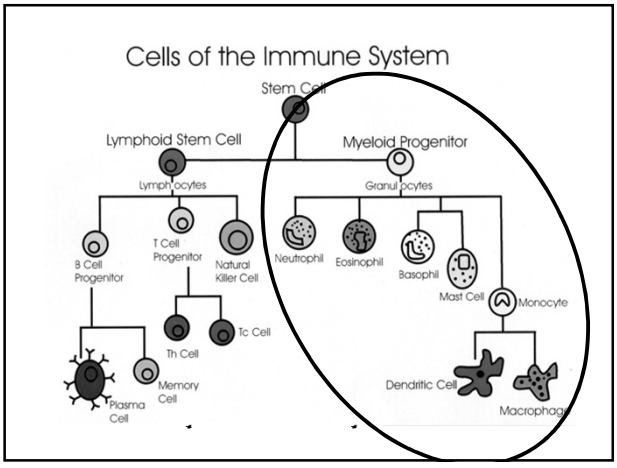
The innate immune responses do not improve with repeated exposure to a given infection and involve the following:

1. Phagocytes (neutrophils, monocytes, & macrophages)

2. Cells that release inflammatory mediators (basophils, mast cells, & eosinophils)

3. Natural killer cells (NK cells)?

4. Molecules such as complement proteins, acute phase proteins & cytokines.



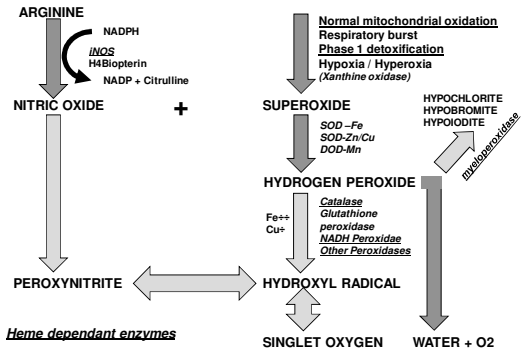
Innate immune system
Non-specific defence against pathogens.
Activates complement system.
No long-lasting or protective immunity for the host.

The adaptive immune system does this.

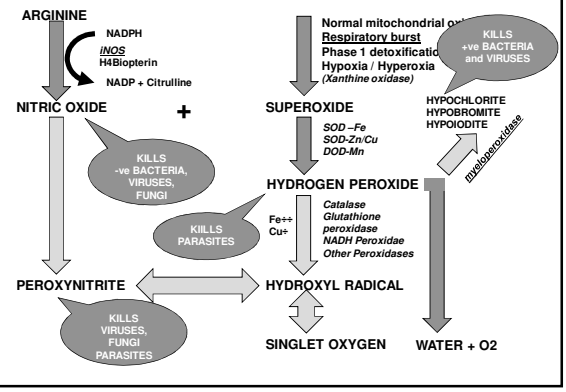
Innate immune system
Complement cascade
Triggers inflammation
Identifies & removes foreign substances
Attracts phagocytes
Activates adaptive immune system

Innate immune system
Evolutionarily older defence strategy.
Found in all classes of plant and animal life.
Deals with immune challenges that have been around for centuries e.g. TB, syphilis, etc.
Depends on adequate Ca & Mg.
Triggers inflammation.

Reactive Oxygen Species



Reactive Oxygen Species



INNATE IMMUNE CYTOKINES

IL-1 – Monocytes
IL-6 – Monocytes, Macrophages
IL-8 – Macrophages
IL-12 – Macrophages
INF-γ – Macrophages, NK cells
TNF- – Macrophages, Mast cells

Innate Immune Challenge

1. Superoxide = Superoxide + NADPH
2. H2O2 = H2O2
3. Hypochlorite = H2O2 + Hypochlorite
4. Nitric oxide = Nitric oxide
5. Peroxynitrite = Superoxide + NADPH + ` Nitric oxide

EMOTION	MERIDIAN	NEURO TRANSMITTER	NUTRITION	MUSCLE	COLOUR	IMMUNE	IMMUNE NUTRITION
Shame & Humiliation	Bl 1	↓ Serotonin	Tryptophan, B3, B6, Folic, Fe, Zn, Mg	Tibialis post Peroneals		↓ B cells	Vit C, Vit E, Astragalus, Echinacea, Ginseng, Immune WHY 600,
Anxiety & Fear	Kid 27	↑ Serotonin	Cu, B2, SAM (Mg, Zn), AcetylCo, Glutathione, Glucuronic, Sulfur	Kidney Iliacus Upper trap		↑ B cells	Omega 3, Flax oil, DHA, Astragalus, Chilli, Moly, Ginseng, Vit D, E, K, Sugar
Guilt & Blame	GB 1	↓ Acetylcholine	Acetyl CoA, Choline B1, Mn	Popliteus		↓ T cells	Sel, Astragalus, Horseradish, Cats claw, Echinacea, Glutamine
Pride & Scorn	Liv 14	↑ Acetylcholine	B, B3, Mn, Mg, Zn	PMS Rhomboids		↑ T cells	Sugar, Cortisol, Gamma & Xrays, Hg, Statins
Apathy & Despair	LI 20	↓ GABA	Glutamate, B6, Mg, Zn	TFL Hamstrings Quadratus lum		↓ Eosinophils	Zn, Cu, mn, Fe, Ginger, Turmeric, Mustard, Horseradish
Anger & Hate	Lung 1	↑ GABA	B6, Mg, Zn	Deltoid Coracobrach Serratus Ant		↑ Eosinophils	Catalase, Ginkgo biloba
Grief & Regret	CV 24	↓ Dopamine	Tyrosine, B3, B6, Folic, Fe, Zn, Mg	Supraspinatus Infraspinatus		↓ Monocytes	Mag mal
Craving & Desire	GV 27	↑ Dopamine	Cu, B2, SAM (Mg, Zn), AcetylCo, Glutathione, Glucuronic, Sulfur	Teres major		↑ Monocytes	Tobacco
Acceptance	St 1	↓ Histamine	Histidine, B6, Mg, Zn	PMC Neck flexors		↓ Basophils	Allergens
Willingness	Sp 21	↑ Histamine	Cu, B2, SAM (Mg, Zn),	Latissimus d Triceps		↑ Basophils	Mg, Vit E, Zn, Lutein / Zeaxanthine, Quercitin, Hesperadin
Reason	SI 19	↓ Noradrenalin	Tyrosine, B3, B6, Folic, Fe, Zn, Mg, B12, Cu, Vit C	Quadriceps Abdominals		↓ Neutrophils	I, Br, Cl, Sel, Zn, Ionic silver, Ginger, Turmeric, Mustard
Love	Ht 1	↑ Noradrenalin	Cu, B2, SAM (Mg, Zn), AcetylCo, Glutathione, Glucuronic, Sulfur	Subscapularis		↑ Neutrophils	Catalase, Sugars
Trust	TW 23	↓ Excitatory	Aspartate, B6, Zn, Glutamate, Mg	Teres min		↓ NK	Sel, Rhodiola, Vit A, B5, B12, C, D, E, Shark liver oil, Germanium
Courage	CX 1	↑ Excitatory	B2, Fe, Mg, B6, Vit C.	Gluteals Sartorius Gracilis		↑ NK	Glucocorticoids, Excess dietary fats

Screening remedies for innate immune response

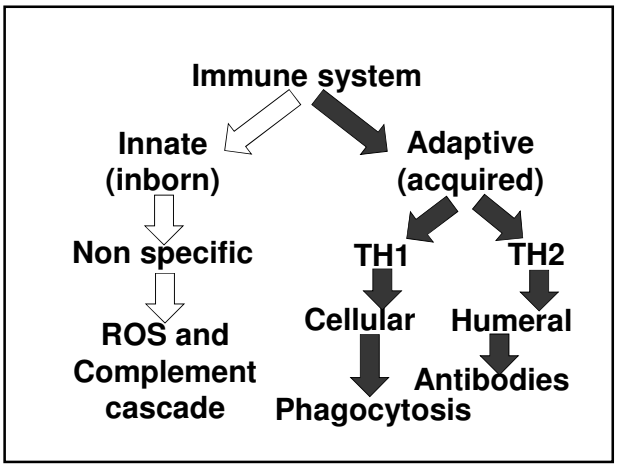
1. Ginger to boost the respiratory burst to produce Superoxide.
2. Zinc / Copper for SOD to convert Superoxide to H2O2.
3. Silver to block catalase / stimulate myeloperoxidase.
4. Maybe Iodine / Bromine / Chlorine

Screening remedies for innate immune response
5. Arginine to stimulate Nitric oxide
6. Maybe Vitamin C and Zinc as iNOS cofactors.
7. Selenium to inhibit viral replication

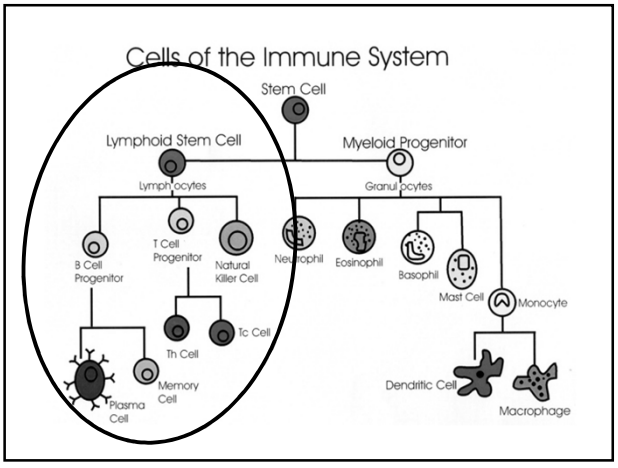
Screening remedies for innate immune response

Vitamin D	**Glucosamine**
Astragalus	**Echinacea**
Golden seal	**Garlic**
Cayenne	**Ginger**
Olive leaf	**Lemon balm**
Black walnut	**Elderberry**

The Adaptive Immune System



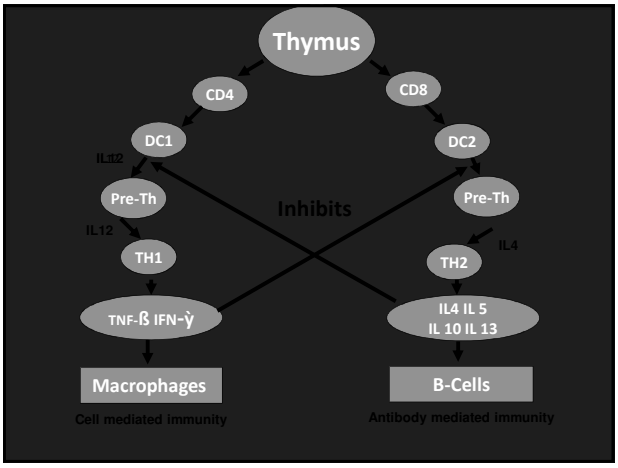
It takes 5-7 days after encountering a new antigen for the adaptive immune system to reach full activity…
…why a "cold" lasts about a week.



Adaptive immune system -
T-cells & B-cells

T Lymphocytes mature in thymus
T Helper cells
T Regulatory (T suppressors)

B Lymphocytes mature in bone marrow. Make antibodies
Spleen



Helper T- Cells are a type of T-Lymphocyte white blood cell. Helper T-Cells stimulate B-Lymphocytes and other types of T-Lymphocytes to activate an immune response to Antigens. Helper T-Cells stimulate the conversion of B-Lymphocytes to Plasma Cells.

Helper T-Cells stimulate the growth of NK Lymphocytes. Interleukin 2 is manufactured by Helper T-Cells (in response to instructions from Interleukin 1). Helper T-Cells counterbalance the function of Suppressor T-Cells: The normal ratio of Helper T-Cells to Suppressor T-Cells is between 1.02:1 and 2.46:1.

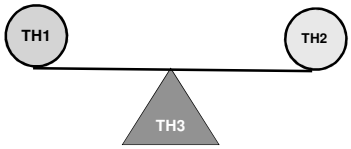
Ideally, TH1 Helper T-Cells should be in equal balance with TH2 Helper T-Cells.

When either subset of Helper T-Cells dominate, illness results.

Plasma Cells are responsible for the production and transport of Antibodies (Immunoglobulins) in response to Antigens.

The Immune System

BALANCE = HEALTH



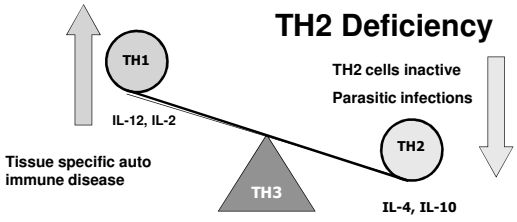
A shift to a dominance in one pathway over another has been linked with tissue specific autoimmunity and hyper-inflammatory conditions.

An excess of one pathway is at the expense of the other pathway.

The Immune System

TH1 Excess

TH2 Deficiency



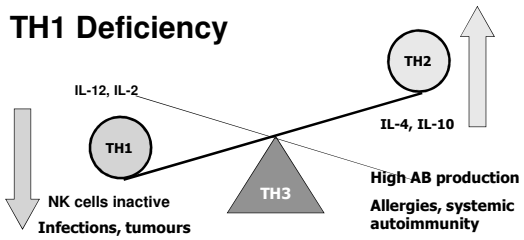
Some of the conditions that have been found to be characterised by TH1 Excess
Hashimoto's Thyroiditis, Multiple Sclerosis, Type-1 diabetes, Rheumatoid arthritis, Vitiligo, Crohn's disease, Ulcerative colitis, Psoriasis, Unexplained recurrent abortions, Coeliac disease, Alzheimer's disease, Dementia.

Thymus Gland

The Immune System

TH2 Excess

TH1 Deficiency



Some of the conditions that have been found to be characterised by TH2 Excess
Allergies, Hay fever, Rhinitis, Asthma, Eczema, Dermatitis, Irritable Bowel Syndrome, Chronic Fatigue Syndrome, Graves disease, Endometriosis

TH3

Various researchers have identified regulatory T cells that were all associated with mucosal immune response.

***Werner et al* coined the term TH3 cells for those cells activated in Peyer's patches after exposure to antigens.**

These TH3 cells produced a powerful cytokine, Transforming Growth Factor (TGF-β).

This group suggested that TH3 cells are responsible for *oral tolerance*.

This is the activation of an antigen-specific non-response to an antigen given via the oral route.

Animal studies show that inflammatory bowel disease is due to an imbalance between the pro-inflammatory cytokines INF-γ, TNF-β and TGF-β.

Monteleone et al **have found markedly reduced levels of TGF-β in the serum of patients with Ulcerative colitis and Crohn's disease.**

Approximately 70% of the immune system is localised in the gastrointestinal tract (TH3) with the mucosa having around 200 times the surface area of the skin.

Any compromise of the mucosa-associated lymphoid tissue (MALT) results in increased entry sites for environmental toxins and antigens (leaky gut due to high levels of Lipopolysaccharide) with resultant compromise of general immunity.

THelper 17 cells are a subset of pro-inflammatory T helper cells defined by their production of interleukin 17 (IL-17).

TH17s are developmentally distinct.from TH1 and TH2 lineages.

TH17 cells play an important role in maintaining mucosal barriers and contributing to pathogen clearance at mucosal surfaces, but they have also been implicated in autoimmune and inflammatory disorders. The loss of TH17 cell populations at mucosal surfaces is linked to chronic inflammation and microbial translocation.

Testing for TH17
The TH1 and TH2 put on together gives the IL17 response which is almost always a maker for food sensitivities.

Common TH1 and TH2 Cytokines

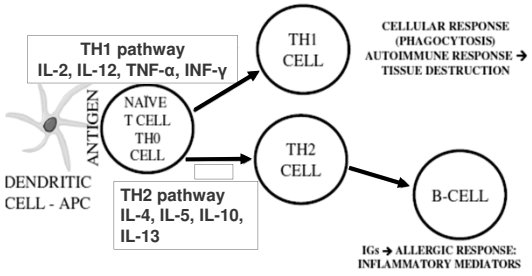
TH1	TH2
IL-2	IL-4
IL-12	IL-5
TNF-α	IL-10
INF-γ	IL-13

Cytokines direct the immune response

IL-12 directs TH1 responses to living pathogens –Bacteria, Viruses, Fungi

IL- 4 and IL-5 directs TH2 responses to non living things such as Foods, Pollens, Bad fats, Toxic metals and Parasites

TH1 & TH2 RESPONSE PATHWAYS



Stimulate TH1 cells

		NTs
Zinc	Melatonin	Acetyl CoA
Omega 3	Chlorella	Choline
L. Acidophilus	Licorice	Thiamine tri
L. Casei	Lemon balm	Manganese
L. Rhamnosus	Panax Ginseng	NAC
L. Paracasei	Grape Seed	Glutathione
L. Salivarius	Extract	
B. Longum	Echinacea	Dairy
L. Brevis	Reishi	Thyroxin
S. Boulardei	mushroom	BCAAs
Cumin	Olive leaf &Oil	
Astragalus	Almonds	Vitamin D

Inhibit TH1 cells

		NTs
UVB light	Omega 3	Vitamin B2
White pepper	Black cumin oil	Vitamin B3
Cinnamon	Ginkgo	Manganese
Rice	Milk thistle	
Bilberry	SAMe	
Turmeric	Vit A	
Bromelain		

TH2 IMMUNE REACTIONS
Antibody-Mediated Immunity
Help B-cells produce antibodies (e.g. IgE, IgG)
Non-living: foods, pollens (some parasites)
Extracellular Immunity (includes traditional allergic reactions)

TH2 Helper T-Cells are primarily responsible for the Humoral Immunity arm of the Immune System which involves the differentiation of B-Lymphocytes which leads to Antibodies responding to and limiting the damage induced by extracellular detrimental micro-organisms.

Stimulate TH2

1000's	Others	NTs
Carotenoids	Lycopene	Acetyl CoA
Nettle leaf / root	Resveratrol	Choline
Caffeine	Pycnogenol	Thiamine tri
Green Tea Extract	Curcumin	Manganese
Pine Bark Extract	Quercitin	UVB light
White Willow Bark	Echinacea	Dairy
	Almonds	Thyroxin
	Asparagus	BCAAs
		Vitamin A

Inhibit TH2 cells

1000's	Others	NTs
Turmeric	Olive leaf and Oli	Vitamin B2
Star anise	Astragalus	Vitamin B3
Ginger	Devil's claw	Manganese
Cinnamon	Licorice	Zinc
L. Reuteri	Glutathione	Magnesium
L. Plantarum	Bilberry	
L Salivarius	Black cumin oil	SAMe
L. Lactic	Bromelain	UVA light
NAC	Omega 3	Vit D
Glutathione	Ginkgo	
Rice	Milk thistle	

Probiotics and fish oil during pregnancy could cut children's allergy risk

By Tim Cutcliffe

02-Mar-2018 - Last updated on 02-Mar-2018 at 08:35 GMT

The systematic review and meta-analysis, published in *PLOS Medicine*, was commissioned by the UK's Food Standards Agency (FSA) and pooled data from more than 400 studies involving around 1.5 million people. It is one of the largest ever investigations into the impact of maternal diet on their children's allergy and eczema risk.

"A daily probiotic supplement such as L. rhamnosus, taken from around 36 to 38 weeks gestation through the first 3 to 6 months of lactation, may reduce risk of eczema in the child," recommended the researchers. However, use of this species should be avoided earlier in pregnancy, the researchers cautioned.

TH1 and TH2 modulating compounds:
Probiotics
Vitamin A
Vitamin E

T-regulatory supporting compounds:
Vitamin D
EPA and DHA

Autoimmune diseases

<u>Causes</u>

Chemical
- **Allergy**
- **Infection Local, Systemic, GUT**
- **Toxicity**
- **Nutritional deficiencies**
  - **Essential fatty acid deficiency –**
    - **Prostaglandins**
    - **Leukotriens**
- **Minerals – Ca, Mg, Se, Zn**
- **Vitamins – A, D**
- **Hypoxia leading to ROS and Antioxidants**
- **Hormones – Hypoadrenia - Low Cortisol**

Emotional

Common Allergens

Gluten –	**Wheat, Rye, Barley, Oats**
Cow's milk-	**Casein**
	Lactose
Cheese	**Especially mature**
	Cooked
Egg-	**White**
	Yolk
Fish	

Common Allergens

Tree nuts -	**Brazil, Hazelnuts, Almonds, Walnuts**
Ground nuts -	**Peanuts**

Shell fish
Soya products
Citrus fruits
Chocolate
Tea
Coffee

Common Allergens

Maize (Corn)
Lupin
Yeast
Rice
Mustard
Celery and Celeriac
Yeast
Onion / Garlic

Common Allergens
Tyramine foods
- **Chocolate, Old avocado, Old banana, Old cheese, Fermented foods**

Solanene foods
- **Potatoes, Tomatoes, Aubergines, Peppers, Chilli**

Infections Bacteria
Zinc
Vitamin C, Vitamin D, Vitamin A
Arginine Olive leaf
Ginger Echinacea
Golden seal Colloidal silver
Immune WHY600
Mannose, Other Saccharides
Black walnut tincture

Infections Virus
Ionic Iron, Calcium, Zinc
Vitamin C, Vitamin A, Vitamin D
Echinacea Astragalus
Olive leaf Garlic
Colloidal silver
Black walnut tincture
Immune WHY 600
Glucosamine
NAC for Post virus

Probiotic may help beat the common cold, suggests study

By Tim Cuteliffe

A proprietary mixture of two probiotic strains developed by Swedish company Probi AB may help people catch fewer winter colds. Details of the study will be revealed in a webinar on March 1st.

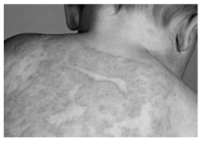
Probi Defendum (a combination of the patented strains *Lactobacillus plantarum* HEAL9 and *Lactobacillus paracasei* 8700:2), significantly reduced recurrent common colds in study participants given the supplement, compared with placebo.

Infections Parasites
Protease
Iodine
Artemesia Annua
Black walnut tincture and caps
Wormwood
Wormwood combination
AP Formula
Saccharides
Probiotics

Infections Fungi
Amylase
Saccharides – Arabinogalactin
Zinc SA
Oregano
Probiotics
Coconut oil
Pau D'arco tincture or caps
AF Cream locally
Always check for EFAs

Infections GUT -Lipopolysaccharides
Digestive enzymes
Saccharides – Arabinogalactin
Prebiotics - Inulin
Probiotics
Fibre – Psyllium
Chlorella
Water
Check for Folates, Zinc, Glutamine.

Toxins – Toxic metals
Black walnut
Coriander herb **Coriander spice**
Lemon balm **Lipoic acid**
Yarrow **Glutathione**
Vitamin C for nickel
Potassium ascorbate
NAC
CBS
Allclear



Toxins – Chemicals
Black walnut
Coriander spice **NAC**
Lemon balm **Rosemary**
Yarrow **Other spices**
Chlorella **Allclear**
CBS
Zinc **Potassium ascorb**
Nutrient Phase 1&2
Taurine SA **Ornithine SA**

Isothiocyanate foods

Isothiocyanates are derived from the hydrolysis (breakdown) of glucosinolates—sulfur-containing compounds found in cruciferous vegetables.
Brussels sprouts, Broccoli, Cabbage, Kale, Watercress, Garden cress, Mustard greens, Turnip, Kohlrabi, Horseradish, Cauliflower, Pak choi, Spinach.

Solanine foods

Potatoes especially if green (also chaconine)
Tomatoes
Green peppers (also capsaicin)
Aubergines (egg plants)
Tobacco
Paprika
Goji berries
Ashwagandha

The following foods contain solanine, but are not a part of the nightshade family, including:
Blueberries
Apples
Cherries
Sugar beets
Huckleberries
Okra
Artichokes
Ascorbyl Palmitate (it's potatoes)
Yeast (Most yeast contains potato)

Tyramine foods

Tyramine is an indirect acting catcholaminergic amine found in aging Bananas and Avocados, Barley grass, Mandarin, Tangerine, Orange, Lemon, Grapefruit, Tomato, Pea, Plum, Aubergine, Cacao, Potato, older mature Cheese, Sour cream, Pizzas, Chocolate.

Pickled Herrings, Caviar, Liver, Salamis, Broad Beans pods.

Fermented dairy products such as Yoghurt, Sauerkraut

Yeast extracts including Beer and Wine, Bovril, Oxo, Marmite, MSG and all fermented Soya Bean products.

Soy sauce, Thai and Vietnamese fish sauce contain high levels of tyramine and should be avoided. Do not drink tap beer, unpasteurized beer or ale, and check with your practitioner before you consume red or white wine, since tyramine content can vary among different types.

Purine high foods (Uric acid)

Red meats which come from cows or sheep and include steak, chops, corned beef and larger pieces of meat usually roasted in the oven. Game. Meat extracts (e.g Oxo, Bovril). Gravy.
Brains, kidneys, liver & heart (offal), sweetbreads.
Shellfish such as , mussels, oysters and sea eggs.
Anchovies, herrings, mackerel, sardines.
Peas and beans.
Alcohol. especially beer and wine.

Salicylate foods

Cold & flu remedies
Medicines used for pain from headache, periods, sinus
Some antacids
Drugs used for inflammatory bowel disease
Many complementary and alternative medicines, especially those used for Pain and joint problems
Teething gels.
Foods containing high levels of salicylate include tea (except fruit and camomile tea), coffee, dried herbs and spices, black pepper, sharp green apples, cherries, strawberries, dried fruit, tomatoes (fresh, puree and ketchup), fruit juices, cider, wine, peppermints and liquorice.

Monosodium glutamate (MSG) 3 pages

Autolyzed yeast - which contains free glutamate
Other menu items that contain soy sauce, natural flavors, autolyzed yeast or hydrolyzed protein which can contain up to 20% free glutamic acid - the active part of MSG.
Hamburger Helper Microwave Singles® (targeted towards children)
Doritos®
Campbell's® soups - all of them - based on their commitment to add "umami" (read - MSG)
Pringles® (the flavored varieties)
Lipton® Noodles and Sauce
Lipton® Instant soup mix
Unilever or Knorr® products - often used in homemade Veggie dips.
Kraft® products nearly all contain some free glutamate
Cup-a-soup® or Cup-o-Noodles®
Planters® salted nuts - most of them
Accent® -this is nearly pure MSG
Braggs® Liquid Aminos - sold at Whole Foods
Tangle extract (seaweed extract) - found in sushi rolls (even at Whole Foods)
Fish extract - made from decomposed fish protein - used now in Japanese sushi dishes.

Monosodium glutamate cont

Sausages - most supermarkets add MSG to theirs
Processed cheese spread
Marmite®
Supermarket poultry or turkeys that are injected or "self-basting"
Restaurant gravy from food service cans
Boullion - any kind
Instant soup mixes
Many salad dressings
Most salty, powdered dry food mixes - read labels
Flavoured potato crisps
Monopotassium glutamate
Glutamic acid
Gelatin
Hydrolyzed vegetable protein, like canned tuna and even hot dogs)
Hydrolyzed plant protein, like canned tuna and even hot dogs)
Sodium caseinate
Textured protein
Beet juice - it is used as a coloring, but MSG is manufactured from beets and the extract may contain free glutamic acid - Yo Baby - organic baby yogurt has just changed the formula to include beet extract
Yeast extract

Monosodium glutamate cont

Yeast food or nutrient
Soy protein isolate
Soy sauce
Worcestershire sauce
Kombu extract
Dry milk and whey powder
"Natural flavours" - may contain up to 20% MSG
Carageenan
Dough conditioners
Malted barley
Malted barley flour - found in many supermarket breads and all-purpose flours
Body builder drink powders containing protein
Parmesan cheese - naturally high in free glutamate
Over-ripe tomatoes - naturally high in free glutamate
Mushrooms - naturally high in free glutamate
Medications in gelcaps - contain free glutamic acid in the gelatin
Cosmetics and shampoos - some now contain glutamic acid
Fresh produce sprayed with Auxigro in the field. (Yes the EPA approved this. It appalled us too.)

Histamine foods

Prickly pear **Stinging nettle**

Cabbage **Milk thistle**

Shepherds purse

Celendine **Melon**

Sunflower
Bass, Beer, Chicken, Cocoa, Chocolate, Cod, Crab, Haddock, Ham, Lobster, Milk (cow and goat), Mutton, Oyster, Salmon, Scallop, Shrimp, Trout, Tuna, Turkey, Yeast.

Oxalates 2 pages
Very high -
Avocados, Dates, Grapefruit, Kiwi, Oranges, Raspberries, Canned and dried pineapple, Dried figs, Bamboo shoots, Beets, Fava beans, Okra, Olives, Parsip, Kidney beans, Rhubarb, Spinach, Tomato sauce, Raw carrots, Soy beans, Brussel sprouts, Potatoes, Brown rice,

Oxalates
Very high -
Avocados, Dates, Grapefruit, Kiwi, Oranges, Raspberries, Canned and dried pineapple, Dried figs, Bamboo shoots, Beets, Fava beans, Okra, Olives, Parsnip, Kidney beans, Rhubarb, Spinach, Tomato sauce, Raw carrots, Soy beans, Brussel sprouts, Potatoes, Brown rice, Couscous, Tahini, Pasta, Veggie burgers, All nuts,
Carrot juice, Hot chocolate, Lemonade, Rice milk, Soy milk, Tea, Clam chowder, Miso soup, Lentil soup.
High – Tangerines, Figs, Dried prunes, Celery, Collards, Whole wheat, White rice.

Caffeine
Coffee (also avoid decaf – is only 97% caffeine free) and Tea
Soda, energy drinks other beverages
Chocolate
Hot Chocolate, mocha- and coffee-flavoured ice cream and frozen yogurt.
Caffeine-Fortified Foods such as sunflower seeds, nuts, frozen waffles, snack chips, beef jerky -- even marshmallows, jelly beans and gummy bears.
Protein bars and candy bars
Fancy flavoured water
Alcohol flavoured energy drinks
Weight loss pills, Pain relievers
Breath fresheners, Caffeinated mints
Some instant oatmeal

Extras

Globe artichoke Grapes, lupine seeds, black mulberry and artichoke resulted positive in the patients under study.

Onions produce sulfenic acids.

Toxins – Radiation
Chlorella
Coriander spice
Smart Vitamin C (Rutin)
Turmeric
Allclear
CBS
Ornithine SA
Taurine SA
Yarrow

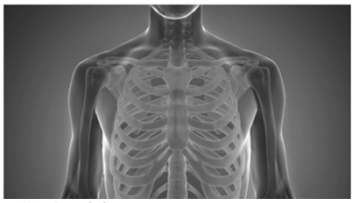
Essential Fatty Acid Deficiency
Borage seed oil GLA
Evening primrose oil GLA
Omega 3 EPA+DHA
DHA
Omega 3,6 and 9
Flax seed oil Hempseed oil
Wheat germ oil
Black cumin seed oil
Smart Thinking oil, Rapeseed oil

GLA is obtained from vegetable oils such as evening primrose (*Oenothera biennis*) oil (EPO), blackcurrant seed oil, borage seed oil, and hemp seed oil. GLA is also found in varying amounts in edible hemp seeds, oats, barley, and spirulina.

α-Linolenic acid (ALA), is a polyunsaturated n–3 (omega-3) fatty acid, found in rapeseed canola oil, soybeans,pumpkin, walnuts, flax seed (linseed oil), chia, and hempseed.

Microbiome manipulation: Could fibre-rich muesli help fight arthritis and other autoimmune conditions?

By Nathan Gray



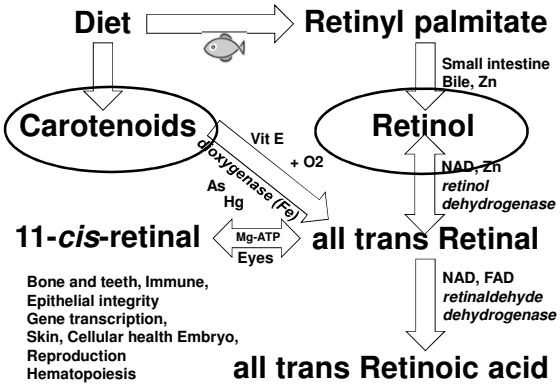
Source: *Nature Communications*
Volume 9, Article number: 55, doi: 10.1038/s41467-017-02490-4
"Short-chain fatty acids regulate systemic bone mass and protect from pathological bone loss"
Authors: Sébastien Lucas, *et al*

A diet rich in fibre could aid chronic inflammatory joint diseases, leading to stronger bones through the increased production of short-chain fatty acids in the microbiome, say researchers.

Mineral Deficiency
Calcium SA
Magnesium SA
Selenium phosphate
Zinc SA

Vitamin Deficiency
Vitamin A
Vitamin D

Vitamin A



Vitamin A, in the retinoic acid form, plays an important role in gene transcription. Once retinol has been taken up by a cell, it can be oxidized to retinal (retinaldehyde) by retinol dehydrogenases and then retinaldehyde can be oxidized to retinoic acid by retinaldehyde dehydrogenases which is tightly regulated, due to its activity as a ligand for nuclear receptors.

Nat Rev Immunol. Author manuscript; available in PMC 2010 Jul 20.
Published in final edited form as:
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doi: 10.1038/nri2378
PMCID: PMC2906676
NIHMSID: NIHMS185109

Vitamin effects on the immune system: vitamins A and D take centre stage

J. Rodrigo Mora,* Makoto Iwata,‡ and Ulrich H. von Andrian§

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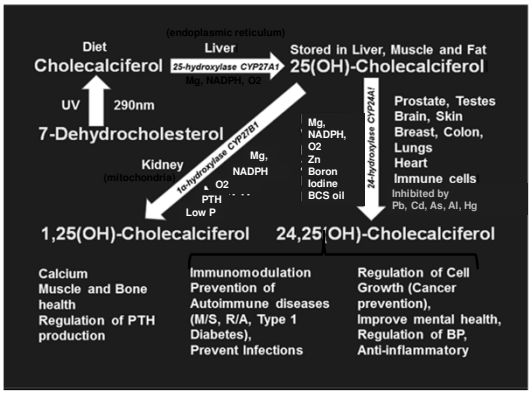
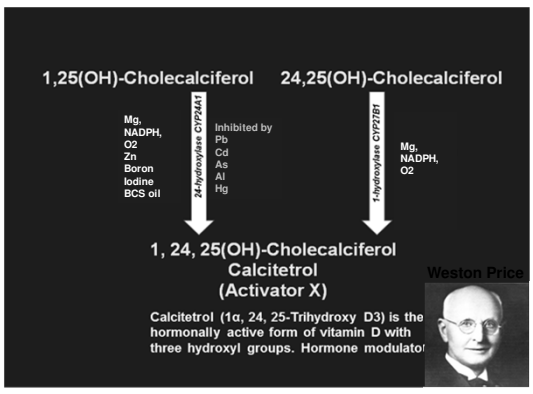
The publisher's final edited version of this article is available at Nat Rev Immunol
See other articles in PMC that cite the published article.

Abstract Go to:

Vitamins are essential constituents of our diet that have long been known to influence the immune system. Vitamins A and D have received particular attention in recent years as these vitamins have been shown to have an unexpected and crucial effect on the immune response. We present and discuss our current understanding of the essential roles of vitamins in modulating a broad range of immune processes, such as lymphocyte activation and proliferation, T-helper-cell differentiation, tissue-specific lymphocyte homing, the production of specific antibody isotypes and regulation of the immune response. Finally, we discuss the clinical potential of vitamin A and D metabolites for modulating tissue-specific immune responses and for preventing and/or treating inflammation and autoimmunity.

Vitamin D


(endoplasmic reticulum)
Diet
Liver
Stored in Liver, Muscle and Fat
Cholecalciferol
25-hydroxylase CYP27A1
25(OH)-Cholecalciferol
Mg, NADPH, O2
UV
290nm
7-Dehydrocholesterol
Mg, NADPH, O2 Zn Boron Iodine BCS oil
24-hydroxylase CYP24A1
Prostate, Testes Brain, Skin Breast, Colon, Lungs Heart Immune cells
Inhibited by Pb, Cd, As, Al, Hg
Kidney
1α-hydroxylase CYP27B1
Mg, NADPH
O2
PTH
Low P
1,25(OH)-Cholecalciferol
24,25(OH)-Cholecalciferol
Calcium Muscle and Bone health Regulation of PTH production
Immunomodulation Prevention of Autoimmune diseases (M/S, R/A, Type 1 Diabetes), Prevent Infections
Regulation of Cell Growth (Cancer prevention), Improve mental health, Regulation of BP, Anti-inflammatory


1,25(OH)-Cholecalciferol
24,25(OH)-Cholecalciferol
Mg, NADPH, O2 Zn Boron Iodine BCS oil
24-hydroxylase CYP24A1
Inhibited by Pb Cd As Al Hg
1-hydroxylase CYP27B1
Mg, NADPH, O2
1, 24, 25(OH)-Cholecalciferol
Calcitetrol
(Activator X)
Weston Price
Calcitetrol (1α, 24, 25-Trihydroxy D3) is the hormonally active form of vitamin D with three hydroxyl groups. Hormone modulato

The VDR may be involved in cell proliferation and differentiation. Vitamin D affects the immune system, and VDRs are expressed in several white blood cells, including monocytes and activated T and B cells.

Watkins RR, Lemonovich TL, Salata RA (May 2015). "An update on the association of vitamin D deficiency with common infectious diseases". *Canadian Journal of Physiology and Pharmacology*.

In vitro, vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells, and affects the synthesis of neurotrophic factors, nitric oxide synthase, and glutathione.

Puchacz E, Stumpf WE, Stachowiak EK, Stachowiak MK (February 1996). "Vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells". Brain Research. Molecular Brain Research.

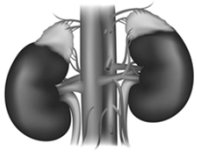
Sun tan vending machines 1950's

Oxygen Deficiency - Hypoxia
Iron
Adenosylcobalamin
Magnesium SA
Zinc SA
Pyridoxal-5-phosphate
Riboflavin-5-phosphate / FADH2
Folinic / CH2H4Folate, 5MTHF

Cortisol Deficiency

Magnesium SA
Zinc SA, Molybdenum
Pyridoxal-5-phosphate
Riboflavin-5-phosphate / FADH2
Vitamin C

Smart Adrenal
Adrenal Support



High success rates

Seventy-six percent of chronic fatigue patients in a clinical trial experienced health improvement after removing dental restorations containing allergenic metals, as identified by the MELISA test (2). An additional study of patients with autoimmune diseases showed that 71% of those with positive responses in MELISA improved after having their fillings removed (3). In a further study, patients with fibromyalgia were tested for allergy to metals with MELISA. By reducing their exposure to metals identified as problematic, significant health benefits were seen. 50% of patients no longer fulfilled the criteria for fibromyalgia diagnosis; the remaining 50% all reported an improvement in their symptoms (4).

Metal allergy testing. Exposure to metals in dental fillings and implants, joint prostheses, pacemakers, environmental pollutants and jewellery can lead to health problems in susceptible individuals. **http://www.melisa.org**

Autoimmune diseases and Applied Kinesiology

Preliminary Test
Strong Indicator Muscle

Before proceeding check indicator muscle for hypertonicity by testing with the corresponding meridian acetate on.
If the muscle weakens then it is hypertonic and do not use as an indicator.
e.g. Quadriceps and Small Intestine acetate.

Muscles and their meridian relationship.

Meridian	Muscles
Bladder	Tibialis ant, Tibialis post, Peroneus long/ brevis, Peroneus tertius
Kidney	Psoas, Iliacus, Upper trap
Gall bladder	Popliteus
Liver	PMS, Rhomoids
Large Intestine	TFL, Hamstrings, QL
Lung	Deltoid, Serratus ant, Coracobrachialis
CV	Supraspinatus, Diaphragm
GV	Teres major
Triple warmer	Teres minor, Infraspinatus
Circulation / sex	Glut max, Glut med/min, Piriformis, Adductors, Sartorius, Gracilis
Stomach	PMC, Neck flexors, Biceps, Brachialis, Pronator teres, Pronator quadratus
Spleen	Lat dorsi, Mid trap, Lower trap, Triceps
Small intestine	Quads, Abdominals
Heart	Subscapularis

Specific muscle to organ association have identified the Infraspinatus muscle as being specific to the Thymus gland and generally indicative of immune function. Other authors *(Portelli, Marcellino)* have cited the mid deltoid as also diagnostic of thymus gland problems.

In my experience (Pierotti) in almost all cases tested (over 100) neither the infraspinatus nor the mid deltoid have ever shown to be inhibited in "the clear" as we would expect with obvious immune dysfunction.

Any reactive hypertonicity rather than a hypotonic state was eliminated by using normotonic modulating methods.

However,
A challenge to the area of the thymus gland by a firm but gentle striking of the mid body of the sternum with a lateral edge of a closed fist over 4-5 repetitions elicited and unusual and consistently reproducible response on patients with T- cell dysfunction.

Bilateral inhibition of the Infraspinatus

OR

Bilateral inhibition of the Mid Deltoid

Cross checking with specific cytokine biomarkers found the following pattern;
Bilateral Infraspinatus inhibition correlated with;
TH2 excess

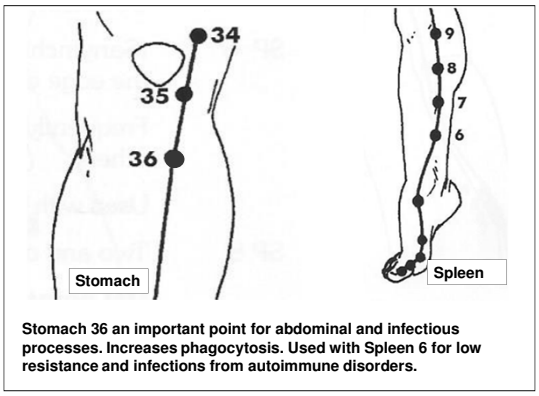
Bilateral Mid deltoid inhibition correlated with;
TH1 excess

The resultant inhibition once initiated persists for quite some time and allows the benefit of challenging for specific nutrients, botanicals or other therapeutic aids necessary for successful treatment of the dysfunction.

Correcting Immune Dysfunction

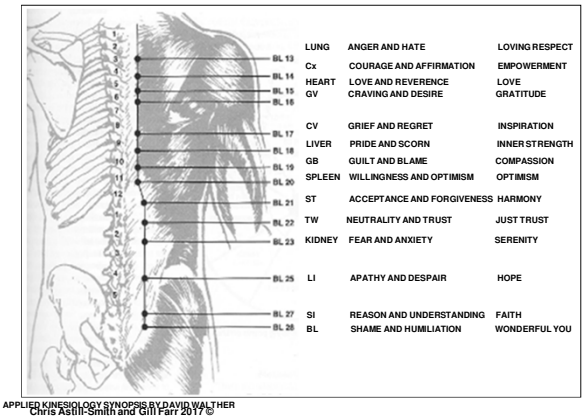
Thymus gland stimulation by the method as described by Portelli and Marcellino in their visceral procedures manuals seems to be the best and most effective method on all patients.

Patient supine with the head hanging off the end of the table, apply a steady A-P pressure over the manubrium as the patient inhales. As patient exhales apply repeated short amplitude thrusts over 4-5 cycles.
On the last deep inhalation suddenly release the A-P hold.



Stomach 36 an important point for abdominal and infectious processes. Increases phagocytosis. Used with Spleen 6 for low resistance and infections from autoimmune disorders.

Therapy Localisation Technique
With all positive nutrients on identify spinal level by therapy localisation.
Perform spiral field force prior to pulsing together. Practitioner puts one finger on spinal level and the other on the symphysis menti. Pulse together for about one minute.



APPLIED KINESIOLOGY SYNOPSIS BY DAVID WALTHER
Chris Astill-Smith and Gill Farr 2017 ©

If you cannot get a positive TL from the spinal level you are probably using a hyper muscle (e.g. a deltoid lung related muscle).

Must only be done at the end of a therapeutic session as all diagnostic markers will be negated.