

# AUTOIMMUNE DISEASE

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## DISEASE OUT OF NOWHERE!



BERTIE 2009  
(3 years old)

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### BERTIE'S STORY

- Presented 31/07/2014 with IMTP that had further progressed into IMHA with a platelet count of 33 (200 - 500), a red cell count of 3.61 (5.4 - 8.5) non regenerative
- He was on Prednisolone 20mg b.i.d. and Azathioprine 75mg s.i.d.
- Initial remission in March 2014 on Pred 25mg b.i.d. then as it was reduced he crashed and despite the Azathioprine he continued to deteriorate
- Multiple side effects from the drugs given

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### 'THIS IS A PUZZLING CASE AS THERE IS NO KNOWN UNDERLYING CAUSE FOR THIS DOGS CURRENT STATE'

The size of the issue we are up against

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## BERTIE'S CASE

- Breed - Golden Retriever
- Diagnosed with hypersensitivity to mould and soya in the first year of life - hot spots and pruritus after the first and most subsequent vaccinations (Vaccinated annually)
- TPLO repair 2 years of age - intolerance to NSAID's post operatively
- IBS - onset 3 years of age - multiple courses of antibiotic - fed common brand kibble and tinned food - MMD/high grain/open formula throughout life

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- Recurrent Haematoma with no obvious underlying ear disease
- Behaviour change at 4 years of age - marked noise sensitivity (No thyroid bloods done)
- Given NSAID and antibiotic 48 hours before he "was like death walking" in March 2014 (8 years) - the start of his final disease process

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## BERTIE AT JUST 8 YEARS OLD (31/07/2014)



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## HOW BIG IS THE PROBLEM?

- Finding prevalence rates in humans and animals is extremely difficult - there is very little published at all for animals
- In humans - the National Institute of Health (NIH) in the USA estimated up to 23.5 million Americans (in 2005) suffered from autoimmune disease and the prevalence is rising (equivalent to approx. 3.2%)
- These figures are based upon only 24 named diseases (Jacobson List) for which good epidemiological studies were available and may grossly underestimate the true figures
- Compare this figure to that published by the same body of 9 million for cancer and 22 million for heart disease

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**EXAMPLES OF AD'S IN ANIMALS**

120 PLUS known AD's in humans

Hypothyroidism, IMHA, IMTP, Pancreatitis, Addison's Disease, IBS, Myasthenia Gravis, Pemphigus complex, Demodicosis, GME, CDRM, Equine recurrent uveitis, BSE, Rodent ulcer, Bullous pemphigoid, arthritis, SLE, SLO

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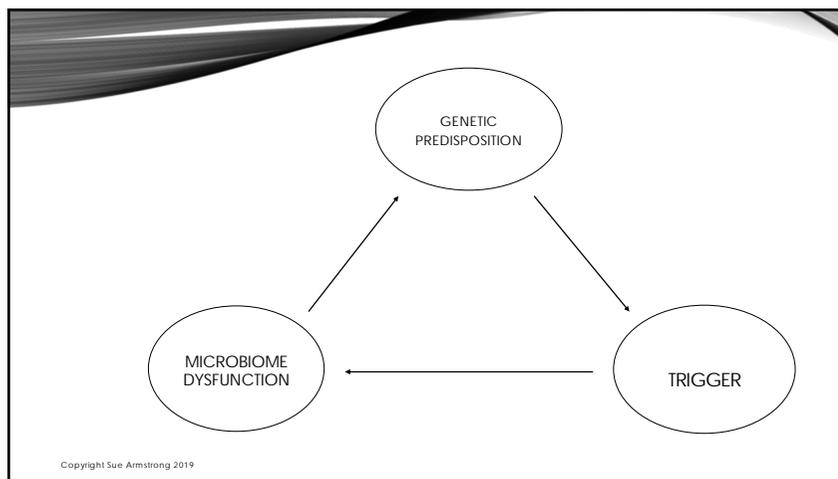
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**WHAT IS AUTOIMMUNE DISEASE?**

- An adaptive immune response that develops against self antigens
  - Causes inflammation
  - Leads to tissue damage
- As infectious disease rates have declined, AD rates have increased
- Can be organ specific expressions e.g. Type 1 Diabetes mellitus against the pancreatic islets or systemic as in systemic lupus erythematosus (SLE)
- Autoimmune disease can be permanent or temporary e.g. localized demodicosis of the young dog

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**GENETIC PREDISPOSITION**

- Major histocompatibility complex – MHC
  - The region involves genes associated with both the innate and adaptive immune response
  - Genes code for molecules that recognise, bind and transport antigens to the surfaces of APCs (antigen presenting cells), where they are presented to T-cells
- Most autoimmune diseases are polygenic
- Genes involved in increased susceptibility are often involved in autoantigen availability and clearance, apoptosis, signalling, cytokine gene expression and expression of co-stimulatory molecules

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### BREEDS WITH KNOWN PREDISPOSITION TO AUTOIMMUNE DISEASE

Many breeds of dog show genetic predisposition to autoimmune disease. Some show predisposition to multiple AD's.

- Nova Scotia Duck Tolling Retriever
  - IMRD (Immune mediated rheumatic disease)
  - SRMA (steroid responsive meningitis arteritis)
  - AD (Addison's Disease)
- German Shepherd Dog
  - congenital focal alopecia areata
  - SLE (Systemic lupus erythematosus)
  - EPI (Exocrine pancreatic insufficiency)
  - AF (Anal furunculosis)
  - CSK (Chronic superficial keratitis)
  - MG (Myasthenia gravis)
- Bearded Collie
  - AD
  - SLO (Symmetrical lupoid onychodystrophy)

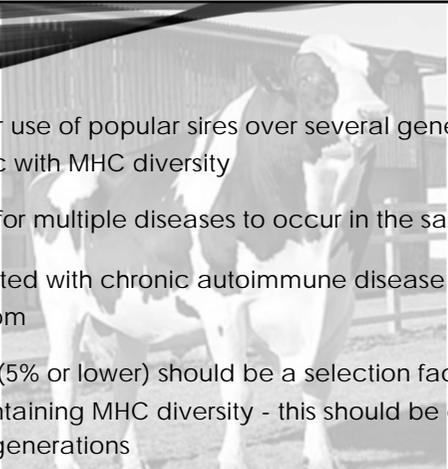
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- Modes of inheritance are not fully known
- Multiple genes are likely to be involved
- The immune system is governed by a group of genes called the Major Histocompatibility Complex (MHC)
  - located on a single chromosome
  - highly polymorphic - as many as 100 different alleles
  - higher mutation rate than normal
  - Each individual inherits 2 copies of the MHC - haplotypes - greater opportunity for diversity and ability to create appropriate immune responses in different situations
- DIVERSITY

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- The regular use of popular sires over several generations can play havoc with MHC diversity
- Tendency for multiple diseases to occur in the same family
- Dogs affected with chronic autoimmune disease should not be bred from
- Low COI's (5% or lower) should be a selection factor and can aid in maintaining MHC diversity - this should be calculated over 8-10 generations

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## TRIGGERS



- Hormones
  - Sex hormones
  - Stress hormones
- Infections
  - Viral
  - Bacterial
  - Parasites
  - Mycoplasma
  - Nanobacteria
- Vaccinations
- Environmental
  - Chemicals
  - Drugs

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## HORMONES

- Oestrogens can stimulate both innate and adaptive responses
- Progesterone prevents the bitch from rejecting the foetuses as foreign - also dampens the general immune response
- Testosterone may suppress the immune system
- Prolactin and GH - complex interaction
- Complex feedback regulation - thyroid and general immune system

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## STRESS

- In human medicine retrospective studies found a high proportion (up to 80%) of patients reported uncommon emotional stress before disease onset
- Vicious cycle of stress
- Stress triggered neuroendocrine hormones lead to immune dysregulation which ultimately results in autoimmune disease, by altering or amplifying cytokine production
- The treatment of all autoimmune disease must include stress management

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## INFECTIONS

- Many organisms are implicated as triggers in both humans and animals e.g. *Borrelia burgdorferi*, *Streptococcus pyogenes*
- Mechanisms of action:
  - Molecular mimicry
  - Epitope spreading
  - Bystander activation
  - Cryptic antigens

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## MASTICATORY MUSCLE MYOSITIS

- Portugese Water Dog X - 05/2014 - Female entire
- Nov 2014 Jaw pain - Rx steroids
- Prior multiple cystitis episodes treated with antibiotics
- 05/2015 lethargic, pain in the jaw, ice cubes - Prednisolone 20mg - non regenerative anaemia
- Presented 06/2015- a urinary tract infection preceded the issue and this can lead to 2M antibody formation as similar antigenicity to UTI bacteria



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6 Point Thyroid test – non-regenerative anaemia may be secondary to hypothyroidism  
Bladder infection was the likely primary trigger

Treated:  
Urinalid  
Spatone  
Thuja and Picric acid

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## MYCOPLASMA THEORY

- Hypothesis that mycoplasma's can remain in the cells of a tissue or organ and only express when the immune system is under pressure
- 'Chameleon like' microbes inc. L-form bacteria
- Major contaminant in cell culture laboratories

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## VACCINATION

- Host identical and host similar tissue is injected along with every vaccine
- Stimulation of Type I and IV hypersensitivity reactions in some
- Some can be immunosuppressant with induction of autoimmunity e.g. parvo, rabies and distemper vaccines
- Viral Disease and Vaccination with single or combined modified live viruses may trigger immune mediated blood disease, bone marrow failure and organ dysfunction
- Killed rabies vaccine and leptospirosis vaccine can trigger immediate or delayed vaccinosis reactions

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## MODIFIED LIVE VACCINES

- It is known that MLV's can induce autoimmune disease e.g. autoimmune haemolytic anaemia
- Stated in the Merck Manual
- The Merck Manual also states that patients with or from families with B and/or T cell immunodeficiencies should not receive live vaccines

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## SELF ORGANISED CRITICALITY THEORY

- Repeated immunisation with antigen causes systemic autoimmunity in mice otherwise not prone to spontaneous autoimmune diseases
- Development of autoantibody inducing CD4<sup>+</sup>T cell which has undergone T cell receptor revision
- This was not as a result of cross reaction with the antigen but by revision

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## PURDUE UNIVERSITY SCHOOL OF VETERINARY MEDICINE STUDIES (1999 HAYWARD STUDY ON VACCINES)

- Vaccinated dogs developed autoantibodies to fibronectin, laminin, DNA, albumin, cytochrome C, cardiolipin and collagen
- Laminin is involved in cell adhesion, spread, differentiation, proliferation and movement
- Cardiolipin autoantibodies associated with thrombus formation, bleeding into the skin, foetal loss, neurological conditions

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**Table 1.** Autoimmune diseases reported after vaccination

Disease	Type of vaccine	Ref
Systemic lupus erythematosus	HBV, tetanus, anthrax	30
Rheumatoid arthritis	HBV, tetanus, typhoid/paratyphoid, MMR	29
Multiple sclerosis	HBV	18, 23, 24
Reactive arthritis	BCG, typhoid, DPT, MMR, HBV, influenza	15, 29, 31
Polymyositis/dermatomyositis	BCG, smallpox, diphtheria, DPT	14, 15
Polyarteritis nodosa	Influenza, pertussis, HBV	14, 15
Guillain-Barré syndrome	Influenza, polio, tetanus	16, 21, 22
Diabetes mellitus – type I	HiB	19, 26, 27
Idiopathic thrombocytopenia	MMR, HBV	14, 15

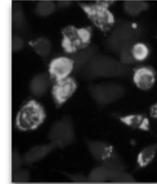
HBV = hepatitis B virus, BCG = Bacillus Calmette-Guerin, DPT = diphtheria-tetanus, MMR = measles-

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## THE HYGIENE HYPOTHESIS

- **The decreasing incidence of infections in western countries is at the origin of the increasing incidence of both autoimmune and allergic diseases**
- **Some infectious agents especially those that co-evolved with us are able to protect against a large spectrum of immune mediated disorders**
- **Microbiota changes could contribute to the modulation of immune disorders**



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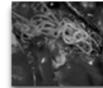
## ANIMAL MODEL

- **Comparison of animals in a natural environment with those in a sterile laboratory environment**
- **Both groups have identical antibodies**
- **Wild animals - their antibodies are not aggressive towards self and can fight off parasites**
- **Lab animals - not able to fight off parasites and develop high levels of allergies and autoimmune disease**

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## DRUGS AS TRIGGERS

- **Newer combinations of monthly heart worm preventatives**
- **Potentiated sulphonamides, anticonvulsant drugs**
- **ANY DRUG CAN HAVE THE POTENTIAL TO TRIGGER IMMUNE RELATED SIDE EFFECTS IN SUSCEPTIBLE INDIVIDUALS**
- **Drugs may exacerbate existing autoimmune disease**



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## WARNING!

- As with repeat use of drugs it has been reported that autoimmune disease has been linked to the long term use of some herbs:

■ **Echinacea and Spirulina platensis implicated in 2 human patients flaring with pemphigus vulgaris**  
**Spirulina and Aphanizomenon flos-aquae - associated with a severe flare up of dermatomyositis**

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## OTHER TRIGGERS

- Electromagnetic waves
- Ultraviolet radiation
- Friend or Foe?
- Ultrasound
- Triggers and/or maintaining causes

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## ENVIRONMENTAL

- Heavy metals: Mercury, lead and cadmium
- Electrosmog:
  - Microwave frequencies
  - (VDR) Vitamin D receptor dysfunction
  - 5G
  - Microwave shielding fabric

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## TREATMENT

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## CONVENTIONAL

- **Lack specificity or subtlety**
- **Non targeted Immunosuppression**



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## MEDICATIONS USED

- **Glucocorticoids**
- **Azathioprine**
  - **Cytotoxic - indiscriminately kills rapidly dividing cells e.g. activated T cells**
- **Cyclosporine**
  - **Inhibits the signals that activate T cell response**
- **Antibiotics**
  - **Enhance immune response**
- **Chrysotherapy**
  - **Use of gold salts - Myochrysine®**

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## REDUCE STRESS & TOXIC SUBSTANCES

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## HERBS

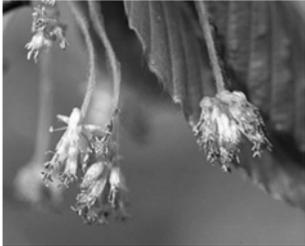
- **Yellow Dock**
- **Ginkgo biloba**
- **Astragalus**
- **Wisteria**
- **Bilberry**
- **Cordyceps/Maitake**
- **Cats claw**



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## FLOWER ESSENCES

- **Holly**
  - Intense illnesses, severe immune responses
- **Crab apple**
  - Uncleanliness, infection, toxicity
- **Beech**
  - Restores tolerance and flexibility - tolerance to substances in the environment



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## SUPPLEMENTS

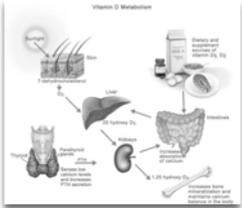
- **Vitamin E**
- **Selenium**
- **Zinc**
- **Vitamin C, D**
- **Vitamin B6 (Pyridoxine)**
- **Probiotic**
- **Liver Support**
- **Transfer Factor**



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## VITAMIN D

- **Important regulator of the immune system**
- **Invariant natural killer T cells (iNKT) are important suppressors of autoimmune diseases**
- **Vit D deficiency can lead to low levels of iNKT (also if maternal levels are low it can affect the offspring)**



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## VITAMIN D DEFICIENCY

**CAUSES**

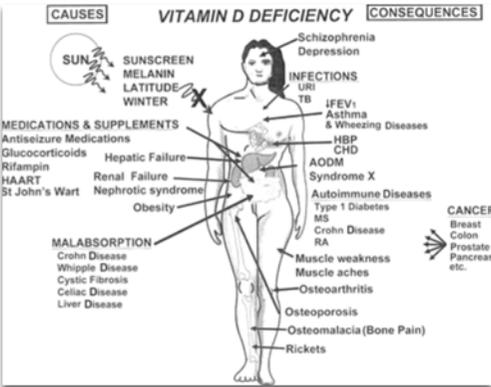
- SUN
- SUNSCREEN
- MELANIN
- LATITUDE
- WINTER

**MEDICATIONS & SUPPLEMENTS**

- Antiepileptic Medications
- Glucocorticoids
- Rifampin
- HAART
- St John's Wort

**MALABSORPTION**

- Crohn Disease
- Whipple Disease
- Cystic Fibrosis
- Celiac Disease
- Liver Disease



**CONSEQUENCES**

- Schizophrenia
- Depression
- INFECTIONS
- URI
- TB
- IFEV, Asthma & Wheezing Diseases
- HBP
- CHD
- AODM
- Syndrome X
- Autoimmune Diseases
- Type 1 Diabetes
- MS
- Crohn Disease
- RA
- Muscle weakness
- Muscle aches
- Osteoarthritis
- Osteoporosis
- Osteomalacia (Bone Pain)
- Rickets
- CANCER
- Breast
- Colon
- Prostate
- Pancreatic etc.

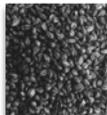
Vitamin D Receptor Dysfunction or Primary Deficiency

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## SUPPLEMENTS CONT...

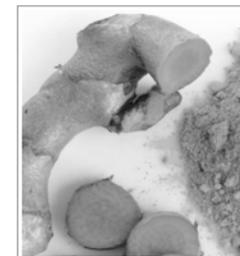
- **Quercetin** - stabilises collagen in blood vessels, -protects cells from free radical damage
- **Bromelain**
- **Taurine**
- **Proanthocyanidins** - Grape Seed - Pine Bark
- **Inhibit cyclooxygenase** which converts arachidonic acid to chemicals that contribute to inflammation and allergy reactions
- **Decrease histamine release**
- **Amino acids:** L-Arginine, L-Ornithine, L-Cysteine, L-Methionine, L-Lysine



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## TCM HERBAL FORMULA

- **Blood-Heat Formula**
- From the ancient formula **Liang Xue Jie Du Tang**
- Chi Shao - **Paeonia** - cool blood and clear heat
- Dan Shen - **Salvia** - cool blood and activate blood
- Di Fu Zi - **Kochia** - clear heat and detoxify
- Mai Men Dong - **Ophiopogon** - nourish yin
- Huang Bai - **Phellodendron** - clear heat and detoxify
- Shen Di Huang - **Rehmannia** - cool blood and nourish yin
- Yu Jin - **Curcuma** - cool blood, clear heat and detoxify
- Mu Dan Pi - **Moutan** - cool blood, move blood and eliminate stagnation
- Xuan Shen - **Scrophularia** - cool blood, clear heat and resolve nodules



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## PREVENTION OF AUTO-IMMUNE DISEASE

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## WHAT DOES AUTOIMMUNE DISEASE LOOK LIKE?

- Because any tissue in the body can be attacked and with a wide range from a mild to a severe attack, autoimmune diseases can look like many other things
- Autoimmune thyroid disease e.g. **lethargy**, mental **lassitude**, **weight gain**, dull coat, skin infections, **constipation**, **diarrhoea**, cold intolerance, skin odour, **hair loss**, greasy skin, **dry skin**, reproductive problems, **aggression**, and more.
- Ulcers and blisters particularly on the margins of mucous membranes
- Sores that do not heal, low grade symptoms that persist or flare up with stress or come on within a few weeks of vaccination or a course of drug treatment

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## BECOME WELL INFORMED

- Know your breed - know your dogs ancestors - get to know your dogs weak spots
- Vaccination decisions
- Chemical decisions e.g. wormers
- Neutering decisions - stress management
- Treatment options in sickness
- **NEVER IGNORE A REACTION THAT YOUR DOG HAS TO AN INTERVENTION and assume it was a one off**

None of this is simple!

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## IN CONCLUSION

- **Cases may present at a stage where they are already highly compromised and deeply suppressed both in the period prior to onset of autoimmunity (causal suppression) and as part of the conventional treatment (palliative suppression)**
- **Reduce stress**
- **Remove toxins from the food and local environment**
- **Support the immune system**
- **Support the liver**

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