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Food Intolerance, Allergy and Sensitivity: Rationale, Investigations and Treatment

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'Lifting the Veil' Part II – Chronic Disease: What's REALLY Going On?

Academy of Nutritional Medicine (AONM)

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Introduction

- Historically, one man's meat is another man's poison.
- From the way in which people have reacted over the years, it has been known that some particular groups have alactasia. Others have been intolerant of wheat, as in Ireland.
- Alactasia affects most Chinese people and many of the people from the Indian subcontinent, as well as many from Africa.
- People have been aware of coeliac disease since the Second World War.
- At that time, bananas were being imported for people with wheat intolerance as an alternative to wheat.
- It began to be realised that many people with coeliac disease or wheat intolerance were developing symptoms.

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Coeliac Disease and Schizophrenia

- Dr Dohan of the University of Pennsylvania surveyed the wartime changes in hospital admissions for schizophrenia from government data in Finland, Sweden and Canada and from more limited data from Norway, Switzerland and Denmark.[1]
- There was a drop in the incidence of schizophrenia in all these countries. Conversely, in the USA and Australia there was no drop in schizophrenia.
- The most outstanding common wartime experience of these people was a change in their diets.[2]

[1]*Dohan FC. Cereals and schizophrenia: data and hypothesis. Acta Psychiat Scand. 1966;42:1-23.*
[2]*Dohan FC. Cereals and schizophrenia: data and hypothesis. Acta Psychiat Scand. 1966;42:125-52.*

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Coeliac Disease and Schizophrenia (cont.)

- Dohan has also recorded reports that a history of childhood coeliac disease occurs more frequently than would be expected by chance in adults with schizophrenia.[1]
- He therefore undertook a study in which two groups of schizophrenics, allocated on admission at random, were put on either a high cereal diet or a cereal-free, milk-free diet. The rate of discharge of these patients from a locked ward was compared.[2]
- The cereal-free group was discharged at twice the rate of the other group. This difference did not occur when gliadin was secretly added to the diet. [2]

[1]*Dohan FC. Cereals and schizophrenia: data and hypothesis. Acta Psychiat Scand. 1966;42:125-52.*
[2]*Dohan FC, et al. Relapsed schizophrenics: more rapid improvement on a milk- and cereal-free diet. Brit J Psychiat. 1969;115:596-6.*

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Coeliac Disease and Autism

- Gastrointestinal disorders observed in autistic children prompted a series of related investigations of biological abnormalities.
- TCDC [Transcephalic Direct Current] electrophysiologic recordings, histamine wheal response tests, eosinophile counts, blood cortisol determinations, and behavioural observations involving 15 autistic children were conducted.
- Abnormal response of their TCDC system to gliadin and cortisol postulated an underlying cerebral defect affected by stress, diet, or other chemical change.

Goodwin MS, Cowen MA, Goodwin TC. Malabsorption and cerebral dysfunction: a multivariate and comparative study of autistic children. J Autism Child Schizophr. 1971;1:48-62.

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Coeliac Disease and Autism (cont.)

- Coincidence of autism with celiac disease was first noted in a 6-year old boy who was among the first of 65 autistic children observed in a research project on communication disorders … in the mid-1960's (Goodwin, M. S., & Goodwin, T. C., 1969).

Goodwin MS, Cowen MA, Goodwin TC. Malabsorption and cerebral dysfunction: a multivariate and comparative study of autistic children. J Autism Child Schizophr. 1971;1:48-62.

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Food Allergy Books in the Breakspear Library

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- Rowe AH. Elimination diets and the patient's allergies. 1941.
- Pulay E. Allergic man: susceptibility and hypersensitivity. 1942.
- Coca AF. Familial nonreaginic food-allergy. 2nd ed. 1945.
- Feinberg SM. Allergy in practice. 1946.
- Taub SJ. Clinical allergy. 2nd ed. 1951.
- Randolph TG. Human ecology and susceptibility to the chemical environment. 1962.
- Miller JB. Food allergy: provocative testing and injection therapy. 1972.
- Rowe AH, Rowe A. Food allergy, its manifestations and control and the elimination diet. 1972.
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- Hills HC. Good food, gluten-free. 1976.
- Hills HC. Good food, grain-free, milk-free. 1977.
- Eagle R. Eating and allergy. 1979.
- Golos N, Golbitz FG. Coping with your allergies. 1979.
- Rapp DJ. Allergies and the hyperactive child. 1979.
- Mandell M, Scanlon L. Dr. Mandell's five day allergy relief system. 1980.

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Food Allergy Books in the Breakspear Library (cont.)

- Mandell FG. Dr Mandell's allergy-free cookbook. 1981.
- Randolph TG, Moss RW. Allergies, your hidden enemy. 1981.
- Yoder ER. A guide for an allergen-free elimination diet. 1982.
- Beall GN. Allergy and clinical immunology. 1983.
- Rippere V. The allergy problem: why people suffer and what should be done. 1983.
- Golos N, Golbitz FG. If this is Tuesday, it must be chicken: or how to rotate your food for better health. 1983.
- Mumby K. The food allergy plan: eat your way to recovery. 1985.
- Paterson B. The allergy connection. 1985.
- Katahn M. The rotation diet. 1986.
- Rapp DJ. The impossible child, in school – at home. 1986.
- Breneman JC, ed. Handbook of food allergies. 1987.
- Brostoff J, Challacombe SJ, eds. Food allergy and intolerance. 1987.
- Chu BD. How you too can outsmart your food allergies using the diversified rotation diet. 1987.
- Faelten S. The allergy self-help book. 1987.
- Katahn M, Katahn T. The rotation diet cookbook. 1987.
- McKenzie J. Living with allergies. 1987.

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Food Allergy Books in the Breakspear Library (cont.)

- Miller JB. Relief at last: neutralization for food allergy and other illnesses. 1987.
- Rapp DJ. Recognize and manage your allergies. 1987.
- Rockwell S. Allergy recipes. Revised ed. 1987.
- Crook WG. Detecting your hidden allergies. 1988.
- Rogers SA. You are what you eat. 1988.
- Davies R, Ollier S. Allergy: the facts. 1989.
- Rochlitz S. Allergies and Candida. Vol. 1. 2nd ed. 1989.
- Gershwin ME, Klingelhofer EL. Conquering your child's allergies. 1990.
- Rapp DJ. Is this your child? Discovering and treating unrecognized allergies. 1991.
- Somogyi JC, Muller HR, Ockhuizen T, eds. Food allergy and food intolerance. 1991.
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- Pall ML. Explaining "unexplained illnesses". 2007.

Dr Richard Mackarness
1916 – 1996

Richard Mackarness was a physician of great vision, a man of original mind who, though much frustrated by the sceptics in his own profession, fought with some success for the recognition in Britain of "Clinical Ecology". By his own example and as a doctor bringing relief to many people, he established that food allergies can be the cause of a variety of illnesses.

Independent 23 October 2011

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History of Allergy

- The recognition of allergy, or abnormal reactivity to foods, has been debated and its definition been controversial.
- In 1894, Emil von Behring introduced the term ‘hypersensitivity’ … to describe the exaggerated response of guinea pigs to repeated doses of diphtheria toxin.[1]
- Charles Richet described anaphylaxis in 1901/1902.[2]

[1]*Jackson M. Allergy: the history of a modern malady. London: Reaktion Books; 2006. p.31.*
[2]*Ibid. p.32.*

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History of Allergy (cont.)

- Clemens von Pirquet, in 1906, defined allergy as “altered reactivity”.[1]
- Subsequently the effect of histamine and antibodies was shown by Henry Dale, with immunological understanding of the pathogenesis of allergic disease.[2] (Dale won the Nobel Prize for his work on the chemical transmission of nerve impulses.)

[1]*von Pirquet C. Allergie. Münchener Medizinische Wochenschrift 1906;30:1457-8.*
[2]*Dale HH, Laidlaw PP. J Physiol. 1911;43:182-95.*

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Problems with Different Foods

- Different ethnic groups may be intolerant of milk due to alactasia.
- Favism is due to glucose-6-phosphate dehydrogenase deficiency (G6PD). Favism is a Mediterranean disease: broad beans cause collapse due to red cell disintegration.
- Coeliac disease – hypersensitivity to gluten (allergy to wheat, rye, barley and oats)

Investigation and Diagnosis

- We can do blood tests for both IgE- and IgG-mediated allergens, and then testing for small intestinal bacterial overgrowth is required, which we do at Breakspear: the lactulose breath test.
- We need to do a test for alactasia, which is a lactose breath test, also done at Breakspear.
- We can then do a fructose breath test to measure fructose intolerance. We can measure fructose by the Acumen test.

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Investigation and Diagnosis (cont.)

- Treatment programmes can be undertaken for small intestinal bacterial overgrowth with antibiotics that are not absorbed, to clear the small intestinal bacteria.
- If somebody has abnormal colonic flora, then we can treat that with a tailored programme of supplements.
- Often people with those problems will have increased gut permeability and many IgG antibodies.

Small Intestinal Bacterial Overgrowth

- From the time people began diagnosing disease, the aroma of the human breath has provided clues to various medical problems.
- For example, breath that emits a fishy smell is associated with advanced liver disease, whilst a sweet acetone odour is common in patients with acute diabetes.

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Lactose, Sucrose and Lactulose Breath Test

How the Breath Test Works

- In the human body, bacteria in the digestive tract ferment dietary carbohydrates, producing acids (such as butyric acid), water and gases as by-products.
- Since only bacteria are capable of producing hydrogen and methane gases, primarily through anaerobic bacteria, the presence of such gases indicates that the carbohydrate has been exposed to bacterial fermentation.

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Lactose, Sucrose and Lactulose Breath Test (cont.)

How the Breath Test Works (cont.)

- Some of the gas produced in the colon is re-absorbed into the bloodstream, and then travels to the lungs through the pulmonary alveolar membrane, which is a barrier separating air in the alveoli of the lung from blood in the capillaries.
- Breath testing is based on this physiological process.

Lactose, Sucrose and Lactulose Breath Test (cont.)

How the Breath Test Works (cont.)

- For non-fasting individuals, the breath hydrogen level is high early in the morning.
- Hydrogen accumulates because of reduced motility during sleep, as food is exposed to bacteria in the colon for longer periods of time.
- Further, reduced breathing (hypoventilation), typically during sleep, increases the level of hydrogen in the blood and alveolar air, because it is not eliminated efficiently.

Lactose, Sucrose and Lactulose Breath Test (cont.)

How the Breath Test Works (cont.)

- The breath hydrogen level falls until early afternoon, when it increases slightly until mid-afternoon, probably due to the effects of carbohydrates entering the colon from a meal eaten at lunchtime.
- Breath hydrogen falls slightly for the remainder of the day.
- In fasting individuals, breath hydrogen levels fall gradually during the entire day.
- This reflects the decrease in availability of carbohydrates to generate hydrogen.

Lactose, Sucrose and Lactulose Breath Test (cont.)

- If the enzyme lactase, which is secreted by cells that line the small intestine and breaks down the sugar in milk (i.e. lactose), is deficient or absent, undigested lactose will reach the colon (large intestine), where it is fermented by bacteria.
- This fermentation releases hydrogen and methane; hydrogen can be measured in the breath as it is released from the lungs.
- By taking sequential breath samples after a test dose of lactose is administered, the pattern of gas generation can be plotted.

Lactose Intolerance

- Symptoms of lactose intolerance include bloating, diarrhoea, flatulence, abdominal cramps and discomfort.
- This may lead, in time, to an imbalance of the normal gut flora, irritation of the intestinal lining, altered permeability (leaky gut), food allergies and other chronic illnesses.

Lactulose Intolerance

- The process used for determining lactose intolerance can also be used to determine sucrose intolerance by administering a challenge dose of sucrose to the patient.
- Lactulose is another carbohydrate that can be administered in the same manner, and is used to identify small bacterial overgrowth of the small intestine.

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Intestinal Antigenic Permeability Screen™

- Actomyosin IgA
- Occludin/Zonulin IgG
- Occludin/Zonulin IgA
- Occludin/Zonulin IgM
- Lipopolysaccharides (LPS) IgG
- Lipopolysaccharides (LPS) IgA
- Lipopolysaccharides (LPS) IgM

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Intestinal Antigenic Permeability Screen™ (cont.)

Clinical Use:

- Measure intestinal permeability to large molecules which inflame the immune system
- Identify the damaging route through the intestinal barrier

Recommended for Patients Who:

- Present multiple symptom complaints (including Chronic Fatigue Syndrome)
- Suffer from abnormal immune cell count and function (including autoimmune diseases)
- Complain of food allergy and intolerance

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Wheat/Gluten Proteome Reactivity & Autoimmunity™

- Wheat IgG
- Wheat IgA
- Wheat Germ Agglutinin IgG
- Wheat Germ Agglutinin IgA
- Native + Deamidated Alpha-Gliadin-33-mer IgG
- Native + Deamidated Alpha-Gliadin-33-mer IgA
- Alpha-Gliadin-17-mer IgG
- Alpha-Gliadin-17-mer IgA
- Gamma-Gliadin-15-mer IgG
- Gamma-Gliadin-15-mer IgA
- Omega-Gliadin-17-mer IgG
- Omega-Gliadin-17-mer IgA
- Glutenin-21-mer IgG
- Glutenin-21-mer IgA
- Gluteomorphin+Prodynorphin IgG
- Gluteomorphin+Prodynorphin IgA
- Gliadin-Transglutaminase Complex IgG
- Gliadin-Transglutaminase Complex IgA
- Transglutaminase-2 IgG
- Transglutaminase-2 IgA
- Transglutaminase-3 IgG
- Transglutaminase-3 IgA
- Transglutaminase-6 IgG
- Transglutaminase-6 IgA

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Wheat/Gluten Proteome Reactivity & Autoimmunity™ (cont.)

Clinical Use:

- Accurately identify Gluten Reactivity
- Measure antibody production against 9 wheat proteins and peptides and 3 essential structure enzymes

Recommended for Patients Who:

- Have non-response GI symptoms
- Present multiple-symptom complaints (including Chronic Fatigue Syndrome and Fibromyalgia)
- Suffer from depression or neuro-autoimmunity

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Gluten-Associated Cross-Reactive Foods & Foods Sensitivity™

- Rye, Barley, Spelt, Polish Wheat
- IgG + IgA Combined
- Cow's Milk IgG + IgA Combined
- Alpha-Casein & Beta-Casein IgG + IgA Combined
- Casomorphin IgG + IgA Combined
- Milk Butyrophilin IgG + IgA Combined
- Whey Protein IgG + IgA Combined
- Chocolate (Milk) IgG + IgA Combined
- Oats IgG + IgA Combined
- Yeast IgG + IgA Combined
- Coffee IgG + IgA Combined
- Sesame IgG + IgA Combined
- Buckwheat IgG + IgA Combined
- Sorghum IgG + IgA Combined
- Millet IgG + IgA Combined
- Hemp IgG + IgA Combined
- Amaranth IgG + IgA Combined
- Quinoa IgG + IgA Combined
- Tapioca IgG + IgA Combined
- Teff IgG + IgA Combined
- Soy IgG + IgA Combined
- Egg IgG + IgA Combined
- Corn IgG + IgA Combined
- Rice IgG + IgA Combined
- Potato IgG + IgA Combined

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Gluten-Associated Cross-Reactive Foods & Foods Sensitivity™ (cont.)

Clinical Use:

- Identify additional dietary proteins to which the Non-Celiac Gluten Sensitive (NCGS) or Celiac disease (CD) patient is sensitized
- Detect cross-reactions in the patient non-responsive on a gluten-free diet
- Categorize the 1-in-2 NCGS or CD patient who is also sensitive to dairy products

Recommended for Patients Who:

- Have Non-Celiac Gluten Sensitivity or Celiac disease
- Are experiencing limited improvements or are non-responsive on a gluten-free diet
- Have gut dysbiosis, which appears to be resistant to standard therapy

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Array 7X: Neurological Autoimmune Reactivity Screen™ – Expanded

Clinical Use:

- Detection of immune reactivity in pathogenesis of neuro-inflammatory, neuro-autoimmune and neuro-degenerative disorders
- Early detection of autoimmune reactivity of both peripheral and central nervous system
- Assist in monitoring the effectiveness of related treatment protocols

Recommended for Patients Who:

- Have idiopathic neurological conditions such as Cerebellar Ataxia or Peripheral Neuropathy
- Have Gluten-Reactivity, Dairy Sensitivity and/or enhanced permeability of the Gut and/or Blood-Brain Barrier

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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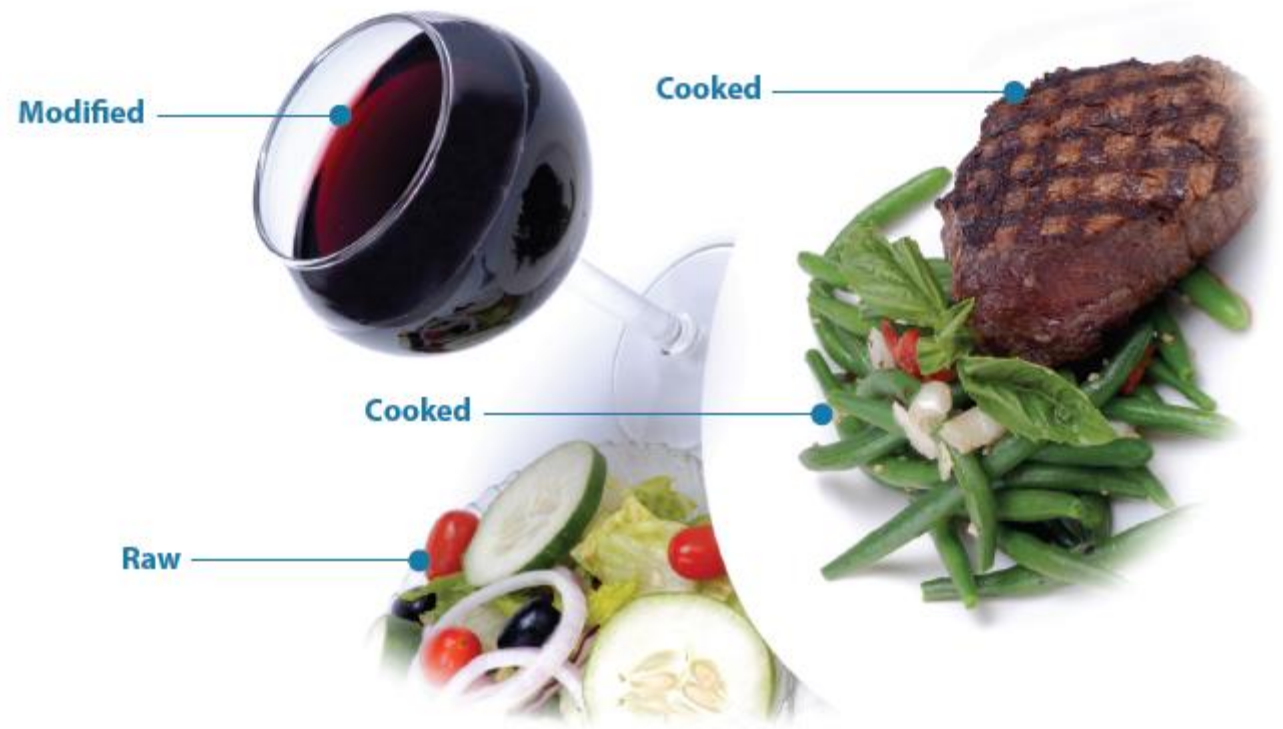
Multiple Food Immune Reactivity Screen™

- 180 Real-World Food Allergens:
  - Cooked
  - Raw
  - Modified



Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

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Multiple Food Immune Reactivity Screen™ (cont.)

Clinical Use:

- Evaluate immune reactions to foods, raw and/or modified, food enzymes, lectins and food additives, including meat glue, artificial colourings and gums.
- Early detection of dietary-related triggers of autoimmunity reactivity.
- Monitor the effectiveness of customized dietary protocol in your patient.

Recommended for Patients Who:

- Seek a life-long health and wellness strategy.
- Present with unexplained symptoms whether gastrointestinal, neurological, dermatological or behavioural in nature.
- Are suspected of having increased intestinal permeability, which is the gateway for environmentally-induced autoimmune disorders.

Available from: https://www.cyrexlabs.com/ [Cited 2015 Nov 4]

Fructose Study

- At Breakspear, we are able to take measurements of the intermediary metabolism of fructose.
- Apart from measuring plasma levels of SCFAs and red blood cell fructose-6-phosphate levels to identify fructose intolerance, plasma lactate dehydrogenase activity can also be measured.
- This enzyme is responsible for the conversion of lactate to pyruvate, and may be indicative of ‘mild’ liver damage due to elevated fructose stressing pathways in the liver.

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Fructose Study (cont.)

We can measure:

- Fructose-6-phosphate
- Lactate dehydrogenase
- Short chain fatty acids

Lactic acid dehydrogenase gives us an indication of whether or not the liver has been involved in this degradation.

Food Allergy

- Food allergy and intolerance became very much acknowledged with the publication of Jonathan Brostoff's book, "Food Allergy and Intolerance".
- Investigation of food allergy had relied on looking for IgE antibodies, and certainly these are involved in peanut allergy, but large numbers of people have food intolerance without having IgE-mediated allergy.

Brostoff J, Challacombe SJ. Food allergy and intolerance. London: Baillière Tindall; 1987.

Food Allergy (cont.)

- Food allergies are very common.
- The immediately recognisable form of food allergies are called IgE mediated hypersensitivity reactions and result in swift responses of diarrhoea, vomiting, anaphylaxis, and sometimes rashes, eczema or asthma.

Protection

- Protection from this type of food allergy is primarily the avoidance of the food.
- If the individual is sensitive to many foods by this mechanism, sodium cromoglycate, which is a mast cells stabiliser, can be used prophylactically.

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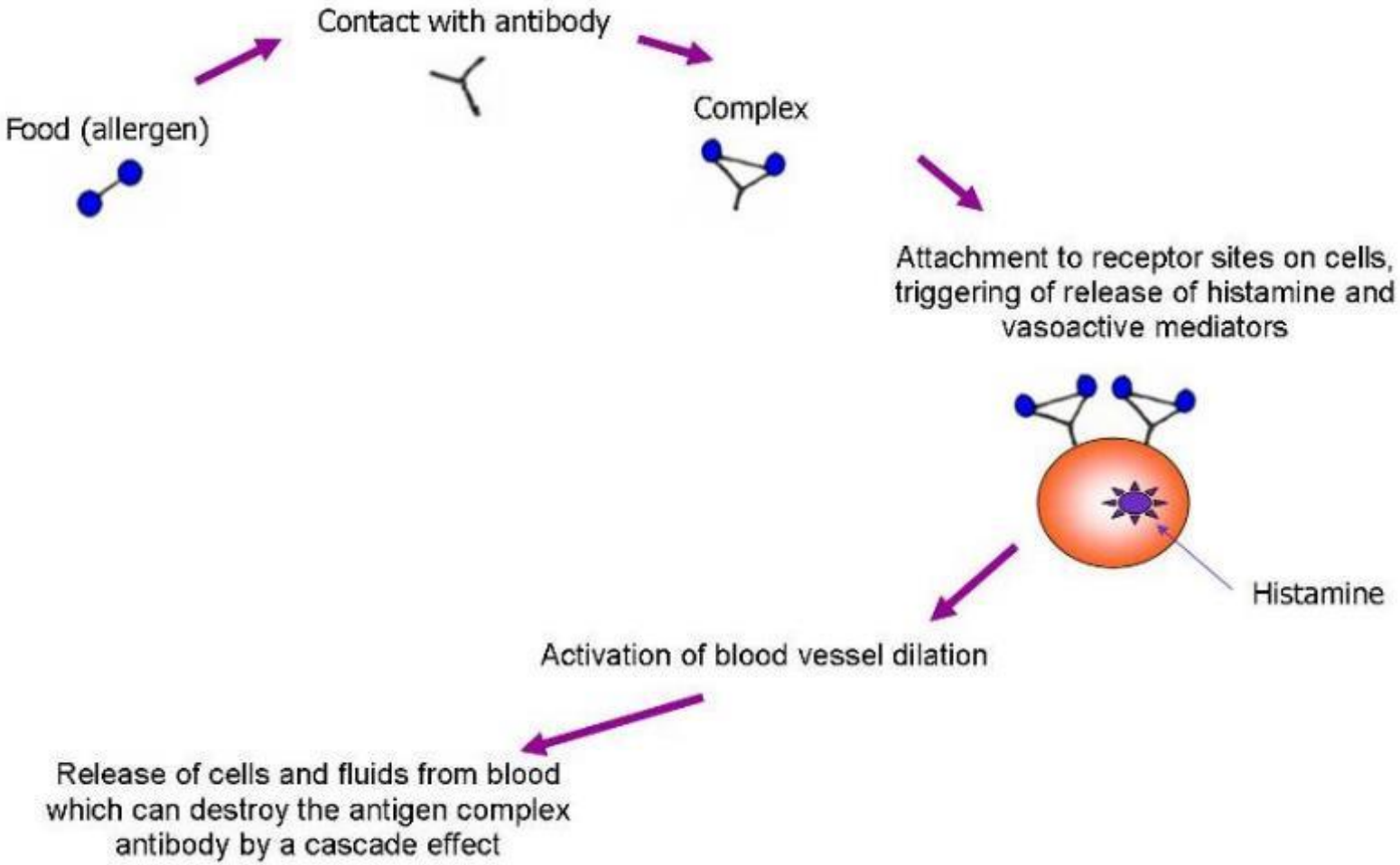
Chain of Events



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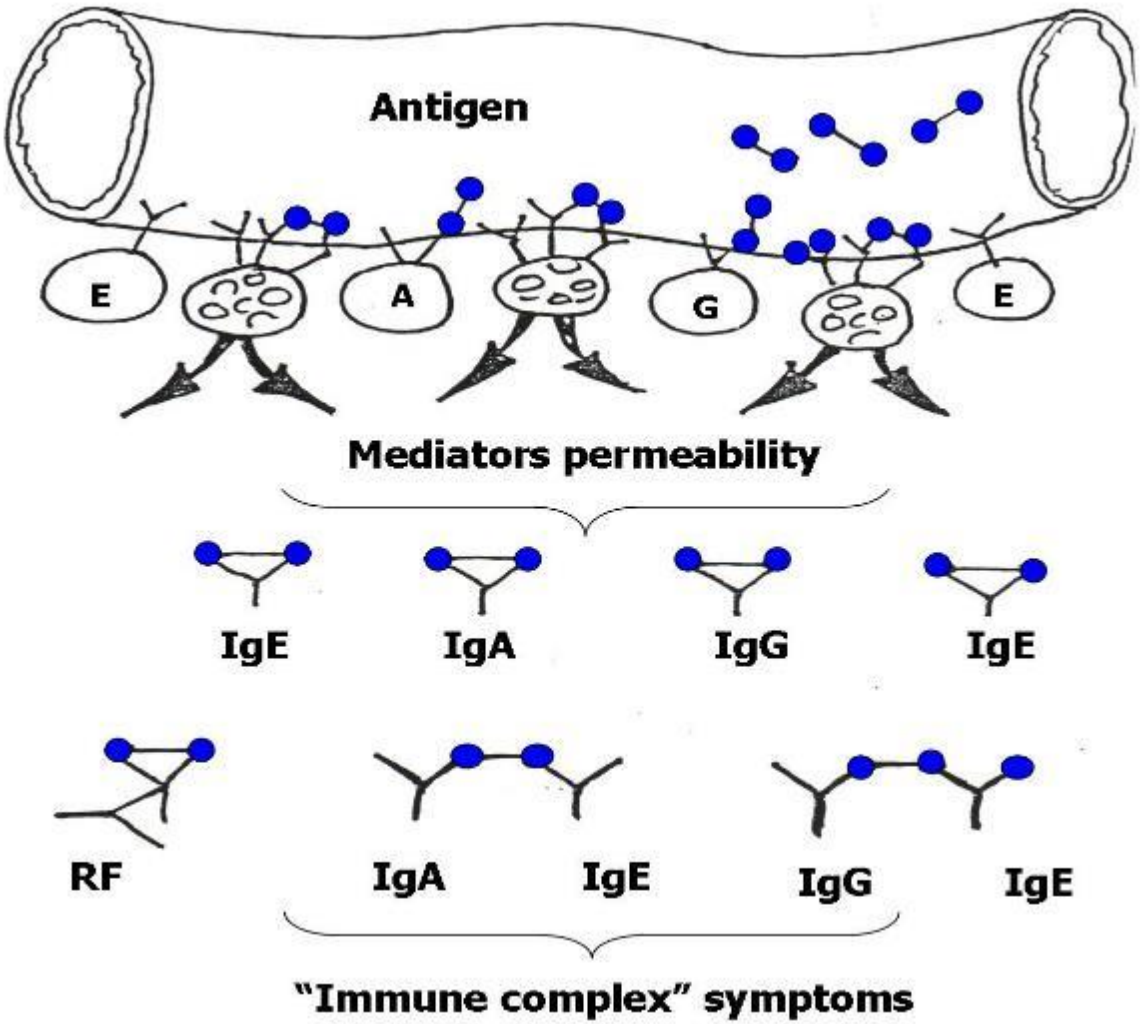
Gut



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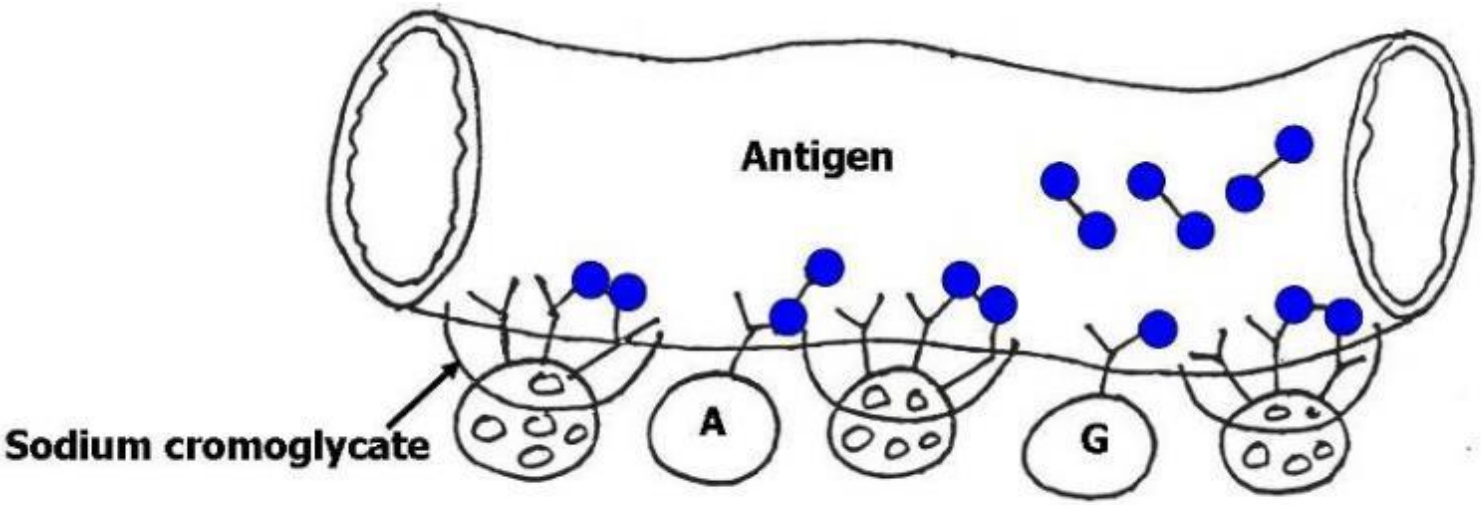
Gut (cont.)



No mediators

No complexes

No symptoms

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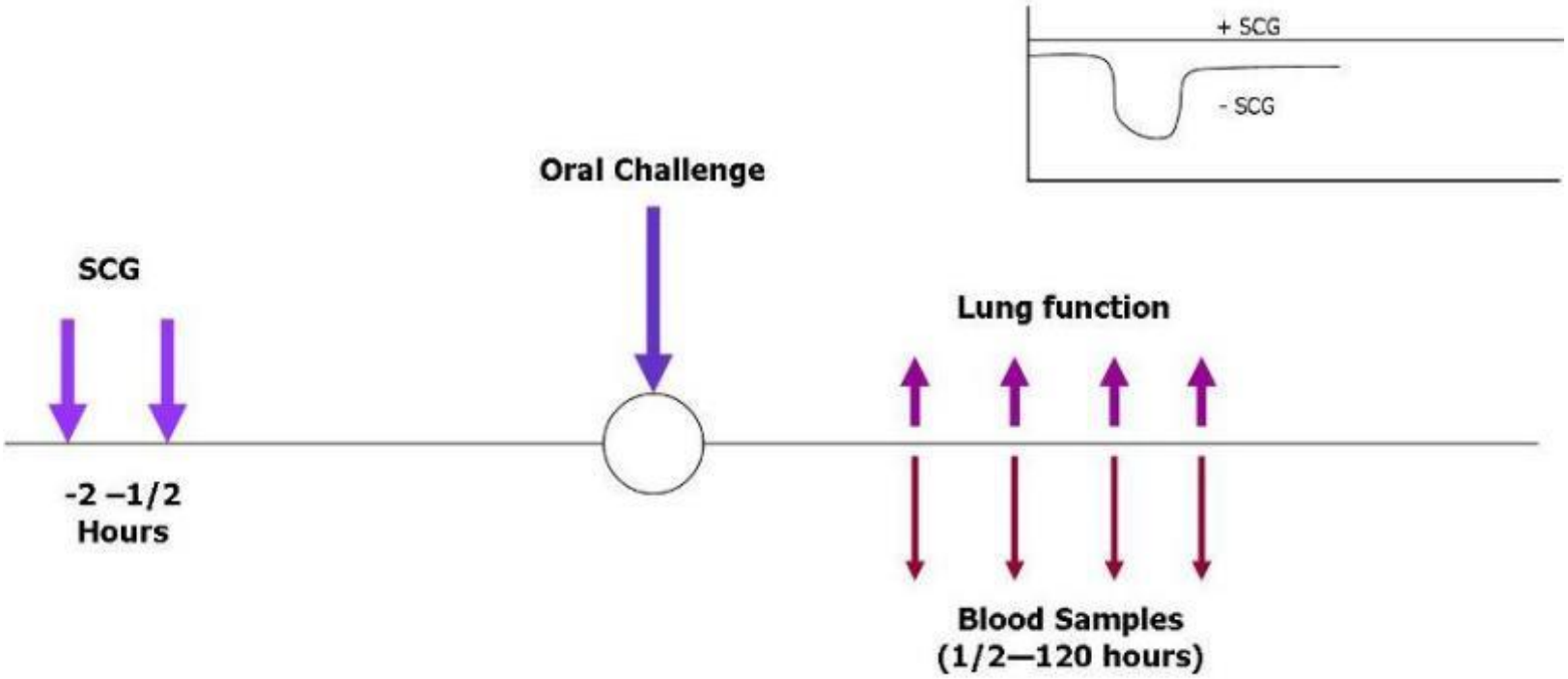
Protocol for Challenge



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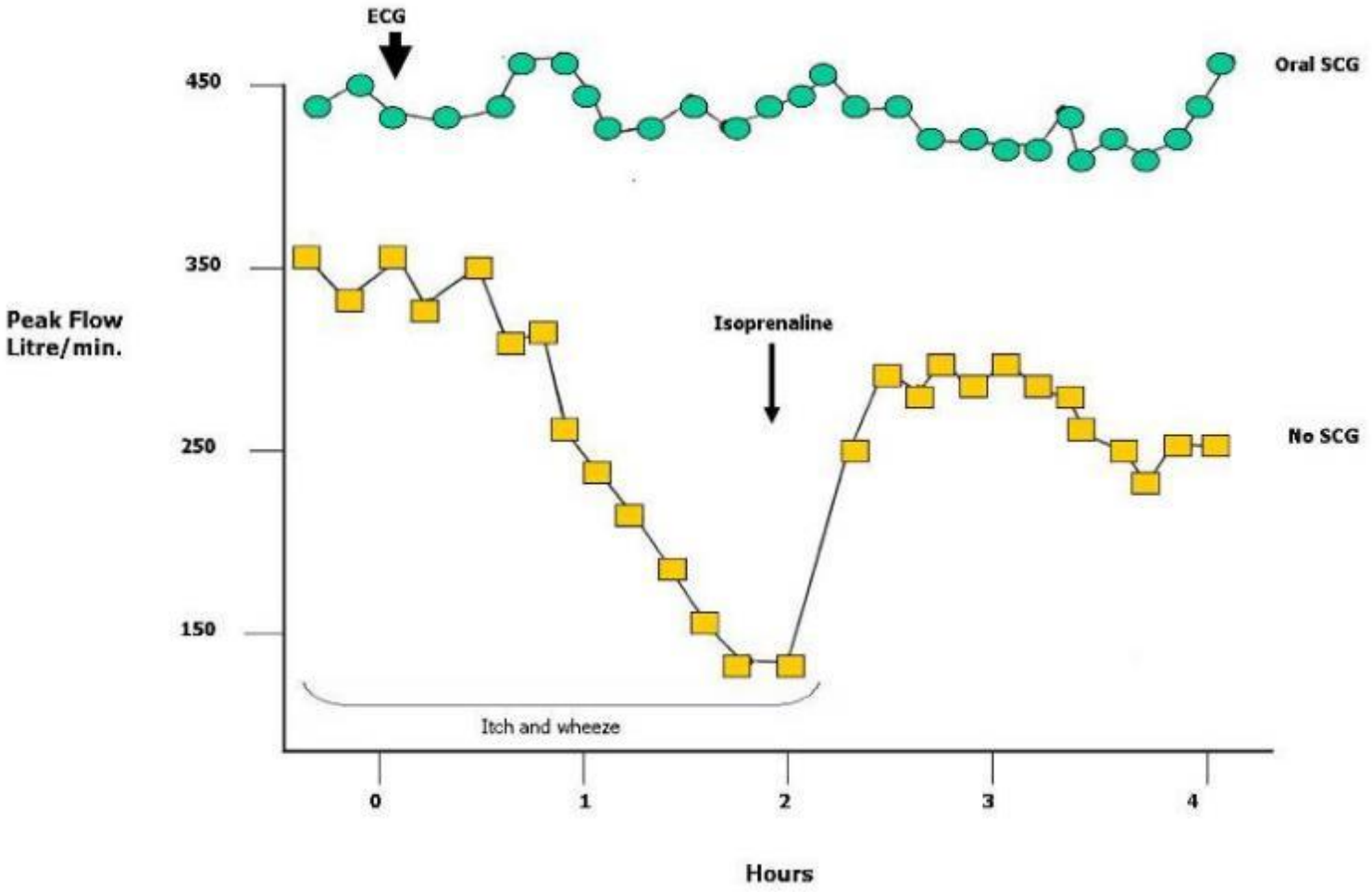
Peak Flow and Symptoms After Egg Challenge



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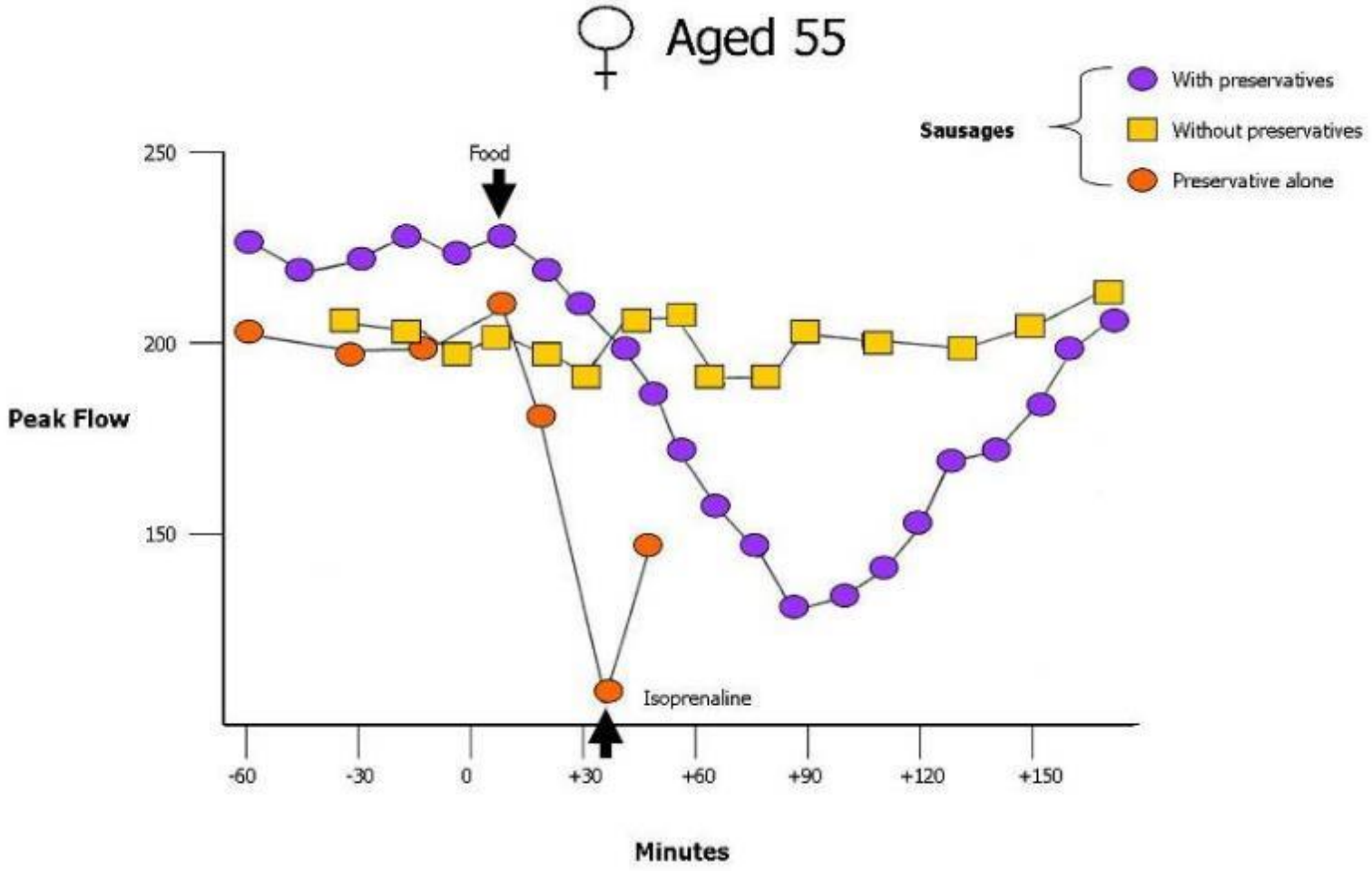
“Intrinsic” Asthma Food Challenge



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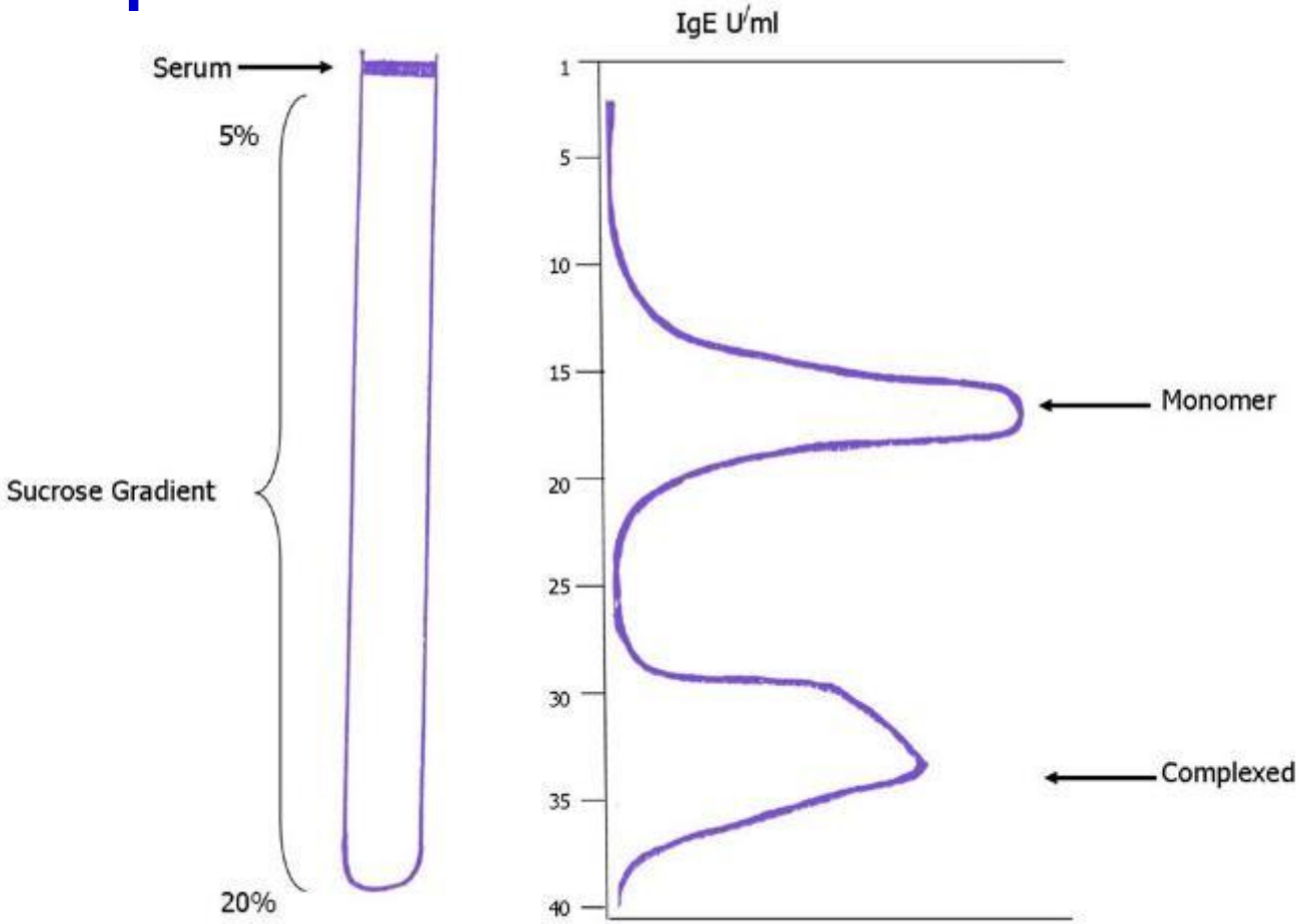
Analytical Ultracentrifugation of Atopic Serum: IgE Complexes



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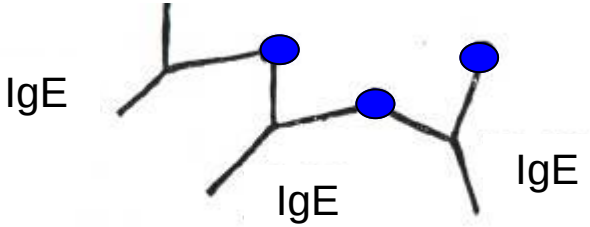
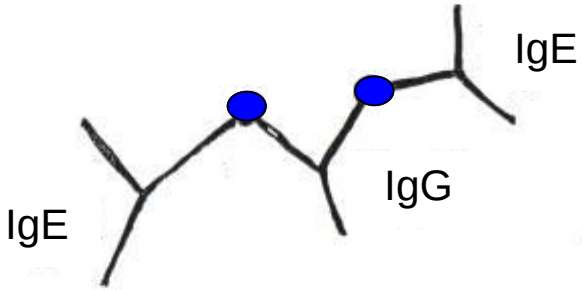
Possible Components of Complexed IgE



1. Allergen: IgE

3. Rheumatoid factor



2. IgG: Allergen: IgE

4. Anti idiotype

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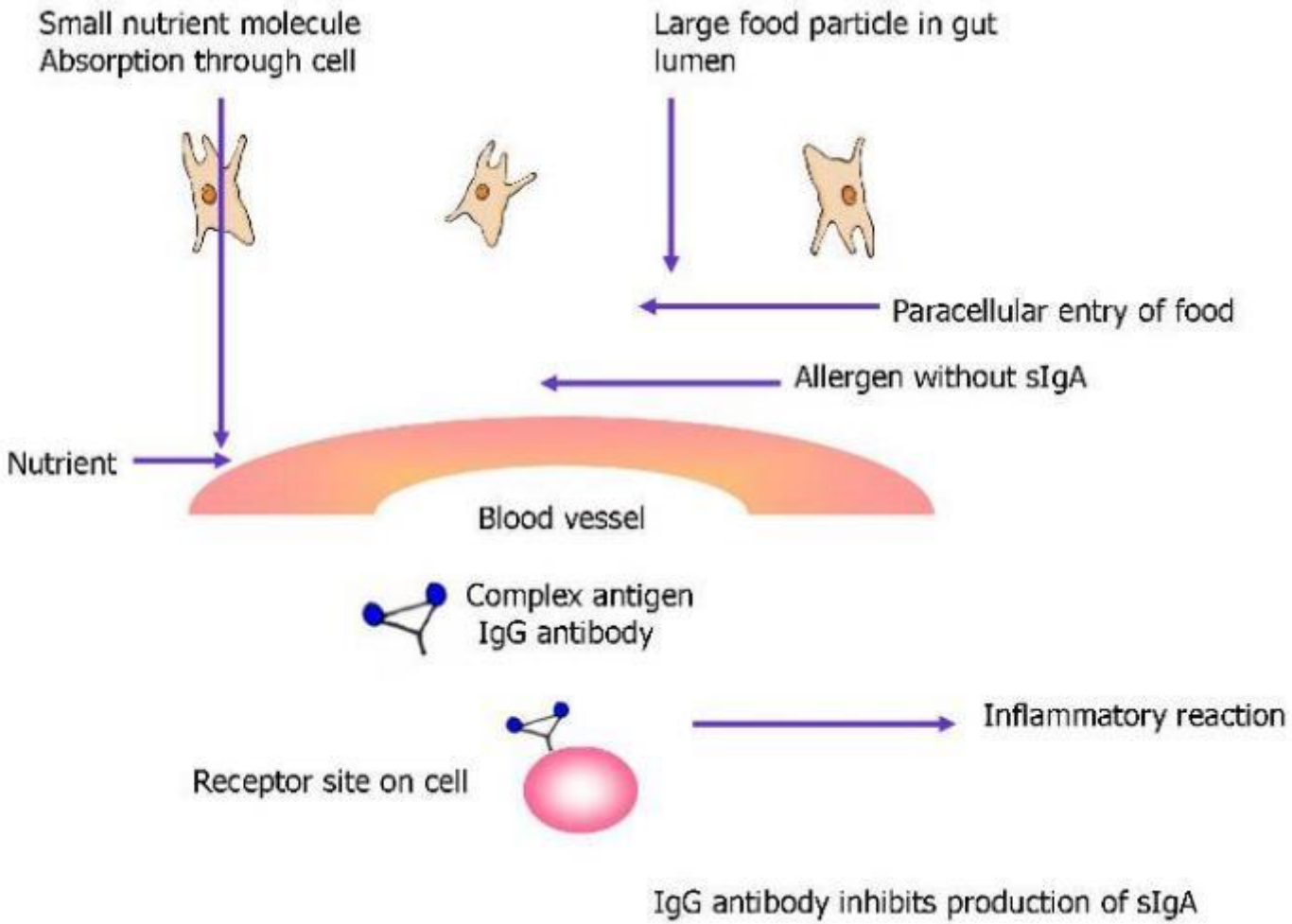
Reactions



IgA Antibodies

- IgA antibodies are the protective antibodies in the gut lumen.
- They also have the function of protecting the gut lining from being attacked by bacteria.

IgA Antibodies (cont.)

- IgA antibodies stop bacterial adhesion to gastrointestinal cells.
- They can also attach to food particles and transport them into the portal circulation.
- When transported to the liver they become detached from the food particles which are further metabolised by the liver and which are then disseminated through the systemic circulation as nutrients.

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IgA Antibodies (cont.)

- IgA – class of immunoglobulin bearing alpha chains
- Make up 10-15% of immunoglobulins in serum (1.5 – 3.5 mg/m)
- Secretory IgA in fluids of:
  - mucous membranes
  - tears
  - saliva
  - colostrum
  - milk
  - respiratory, gastrointestinal and genitourinary tracts
- IgA1 80-90% in blood
- IgA2 secretions AM1
  AM2 allotypes
- They do not fix complement by classical pathway.

IgA Deficiency

- 1:700 people - the most common immuno-deficiency disorder
- IgA deficient individuals have increased incidence of connective tissue disease & pyogenic infections

Secretory IgA

- Inflammation can significantly increase intestinal permeability and compromise assimilation of nutrients.
- The extent of inflammation, whether caused by pathogens or inflammatory bowel disease (IBD), can be assessed and monitored by examination of the levels of biomarkers such as lysozyme, lactoferrin, white blood cells and mucus.

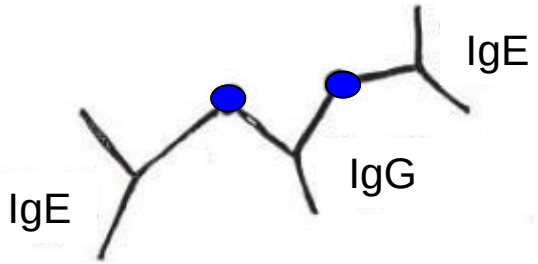
Available from: http://www.doctorsdata.com/comprehensive-stool-analysis-w-parasitology-x3/ [Cited 2015 Nov 4]

Secretory IgA (cont.)

- These markers can be used to differentiate between inflammation associated with potentially life threatening inflammatory bowel disease (IBD), which requires life long treatment, and less severe inflammation that can be associated with irritable bowel syndrome (IBS) which is frequently due to the presence of enteroinvasive pathogens.
- Lactoferrin is only markedly elevated prior to and during the active phases of IBD, but not with IBS.

Available from: http://www.doctorsdata.com/comprehensive-stool-analysis-w-parasitology-x3/ [Cited 2015 Nov 4]

IgG Reactions



- The majority of food allergy reactions are, however, not due to IgE mediated reactions but to IgG reactions.
- IgG antibodies are formed when food has gained access to the tissues in large enough amounts for an antibody response to be marked.
- Normally food is broken down adequately by digestion in the gastrointestinal tract and then absorbed and enters the blood stream in small particles, often attached to IgA.

IgG Antibodies

- If, however, large food particles, without IgA antibody adhesion to them, enter the systemic circulation, IgG antibodies are formed.
- The complexes that are produced (IgG antibodies plus antigen) have to be broken down and in this process a cascade of chemical reactions occur which cause the disintegration of the antigen.

IgG Antibodies (cont.)

- If complexes latch on to tissue cells in sufficient numbers, an inflammatory reaction at that site occurs.
- Tissue can then be destroyed by cytokine responses and disease at that location can ensue.
- IgG antibodies also inhibit the formation of IgA antibodies by Peyer's patches in the gastrointestinal tract wall.
- Hence, food-mediated responses can be perpetuated.

IgG Antibodies (cont.)

- Treatment for these must be to protect the gastrointestinal lining from triggering foods, and food avoidance, which is not usually possible if a large number of IgG food reactions should occur once there has been increased intestinal permeability.

IgG Antibodies (cont.)

75% of total immunoglobulin is IgG

- 1 – 66% +/- 8
- 2 – 23% +/- 8
- 3 – 7% +/- 4
- 4 – 4% +/- 2.5

Fix complement cross placenta. Bind to Fc gamma receptors (IgG4 does not activate classical pathway).

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The Role of IgG4 in Food Allergy

- Interest in the role of IgG4 in allergic disease stems from the capacity of this subclass to bind to basophils and presumably to mast cells.
- Several studies have shown that IgG4 can bind to basophils in such a way that subsequent challenge with an anti-IgG4 antibody causes cell degranulation and histamine release.

Brostoff J, Challacombe SJ. Food allergy and intolerance. London: Baillière Tindall; 1987. p.898.

IgE Deficiency

IgE (epsilon chains)

- Anaphylaxis
- Receptors on basophils and mast cells
- Degranulation releasing histamine and serotonin
- Attract eosinophils which can damage parasites

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IgM

- (mu Chains) – 5-50% of immunoglobulins
- Early response – fix complement

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Environmental IgE Allergy Tests and Panels

- Inhalant allergy IgE test selection is based on regional allergen prevalence, allergen cross-reactivity, home or occupational exposure with special consideration of symptoms and history.
- Individual inhalant allergens include airborne pollens from grasses, trees, and weeds; animal danders, molds, dust mites and occupational allergens are available.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Food Allergy Panels

- Food allergies and food sensitivities are abnormal responses to a food component triggered by the immune system in the form of immunoglobulins (IgE, IgG, IgA, IgM), representing either an immediate or delayed response.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Food Allergy Panels (cont.)

- Specific IgE food panels include the major food allergens known to be responsible for immediate type reactions and are grouped for pediatric, adult, basic or comprehensive panels. Individual specific IgE foods can be ordered from the lab's inventory of over 100 different foods as needed.
- Specific IgG, IgA or IgM ELISA food panels are arranged in comprehensive panels of 96 foods consumed in the typical western diet, or 184 foods which include many of the substitute foods typically found in rotation / elimination diets.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Yeast and Intestinal Immunity Panels

- Yeast and intestinal immunity panels are used to help identify the cause of patients suffering from the effects of gut dysbiosis, a disturbance of the gut microbiome.
- Microbial dysregulation within the gut is an important contributing factor in a wide range of disorders.
- Food sensitivities, environmental toxins, stress, prolonged use of antibiotics and genetic predisposition may contribute to gut dysbiosis.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Intestinal Flora Immunity Panel

- The normal microbial flora of the intestines facilitates the digestion of food, biosynthesis of certain vitamins and may even help prevent colonization and infection by invasive pathogens.
- The populations of bacteria that live in the gut are a combination of both beneficial or harmful bacteria.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Intestinal Flora Immunity Panel (cont.)

- A balance of both beneficial or harmful bacteria is considered the healthiest.
- One of the most important roles bacteria play is keeping undesirable bacteria and yeast in check.
- Harmful bacteria and yeast grow when there is not a strong population of good bacteria around.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Intestinal Flora Immunity Panel (cont.)

- Good bacteria compete for food and seek sites in the gut where they can implant themselves.
- Toxins are produced that are harmful to invading bacteria. This keeps the population of bad bacteria at a low.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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Intestinal Flora Immunity Panel (cont.)

- The integrity of the gut can become compromised causing the overgrowth of yeast, bacteria, viruses and parasites. This causes microflora imbalance and enhances gut permeability.
- Consequently, bacterial, fungal, food antigens, as well as microbial toxins, may pass into the blood, inducing the formation of IgM, IgA and IgG antibodies.

Available from: http://foodallergy.com/tests/available-tests/ [Cited 2015 Nov 4]

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IgE Allergy Profile 1 (Food and Inhalants)

- Allergy, asthma and autoimmune diseases are increasing around the world, especially in industrialized countries and affect all ages. Since every country has their own dietary habits there are noteworthy differences in the allergens causing food allergy.

The Doctors Laboratory. Laboratory Guide 2015.

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IgE Allergy Profile 1 (Food and Inhalants) (cont.)

Total IgE with individual IgE allergens for:

Grass Mix, including:

- Cocksfoot
- Meadow Fescue
- Meadow
- Rye
- Timothy

Weed Mix, including:

- Common Ragweed
- Giant Ragweed
- Western Ragweed

Dust Mix, including:

- Blatella germanica
- Dermatophagoides pteronyssinus
- Dermatophagoides farinae
- Hollister-Stier Labs

Mould Mix, including:

- A. alternate
- Aspergillus fumigatus
- Candida albicans
- Cladosporum herbarum
- Helminthosporium halodes
- Penicillum notatum

Tree Mix, including:

- Box Elder
- Common Silverbirch
- Hazel
- Oak
- London Plane
- Maple
- Sycamore

Available from: http://www.tdlpathology.com/test-information/profiles-allergy [Cited 2015 Nov 5]

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IgE Allergy Profile 1 (Food and Inhalants) (cont.)

Total IgE with individual IgE allergens for (cont.):

Single allergens (19)

- Beef
- Bermuda Grass
- Cat Dander
- Clam
- Common Silver Birch
- Cows Milk
- Crab
- Dog Dander
- Egg White
- Egg Yolk
- Fish (Cod)
- Hazel Nut
- Horse Dander
- Latex
- Nettle
- Peanut
- Shrimp / Prawn
- Soya Bean Wheat

Available from: http://www.tdlpathology.com/test-information/profiles-allergy [Cited 2015 Nov 5]

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Antistreptolysin Titre

The ASO [Antistreptolysin O] test is primarily used to help determine whether a recent strep infection with group A Streptococcus:

- Is the cause of a person's glomerulonephritis, a form of kidney disease
- Caused rheumatic fever in a person with signs and symptoms

The ASO test is ordered when a person has symptoms that a health practitioner suspects may be due to an illness caused by a previous strep infection. It is ordered when the symptoms emerge, usually in the weeks following a sore throat or skin infection when the bacteria are no longer present in the throat or on the skin.

Available from: https://labtestsonline.org/understanding/analytes/aso/tab/test/ [Cited 2015 Nov 5]

Lymphocyte Sensitivity Test

- Patients sensitive to food and chemicals have their cells examined under a microscope.
- Cells are visualised using a fluorescent probe. Once a reaction occurs at the cell's surface, calcium flows into the cell and this disruption occurs with various foods and chemicals.
- This technique is a standard method in cell biology and is being undertaken by Dr John McLaren-Howard.

Lymphocyte Sensitivity Test (cont.)

- We recommend a panel of substances to be tested, including:
  - Sodium benzoate
  - Nickel
  - Sodium metabisulphite
  - Salicylates
  - Formaldehyde
  - Petrol
  - Natural gas
- Others can be added, up to a total of 12 items. The cells tested are the lymphocytes from whole blood. Intracellular calcium is measured before and after these exposures.

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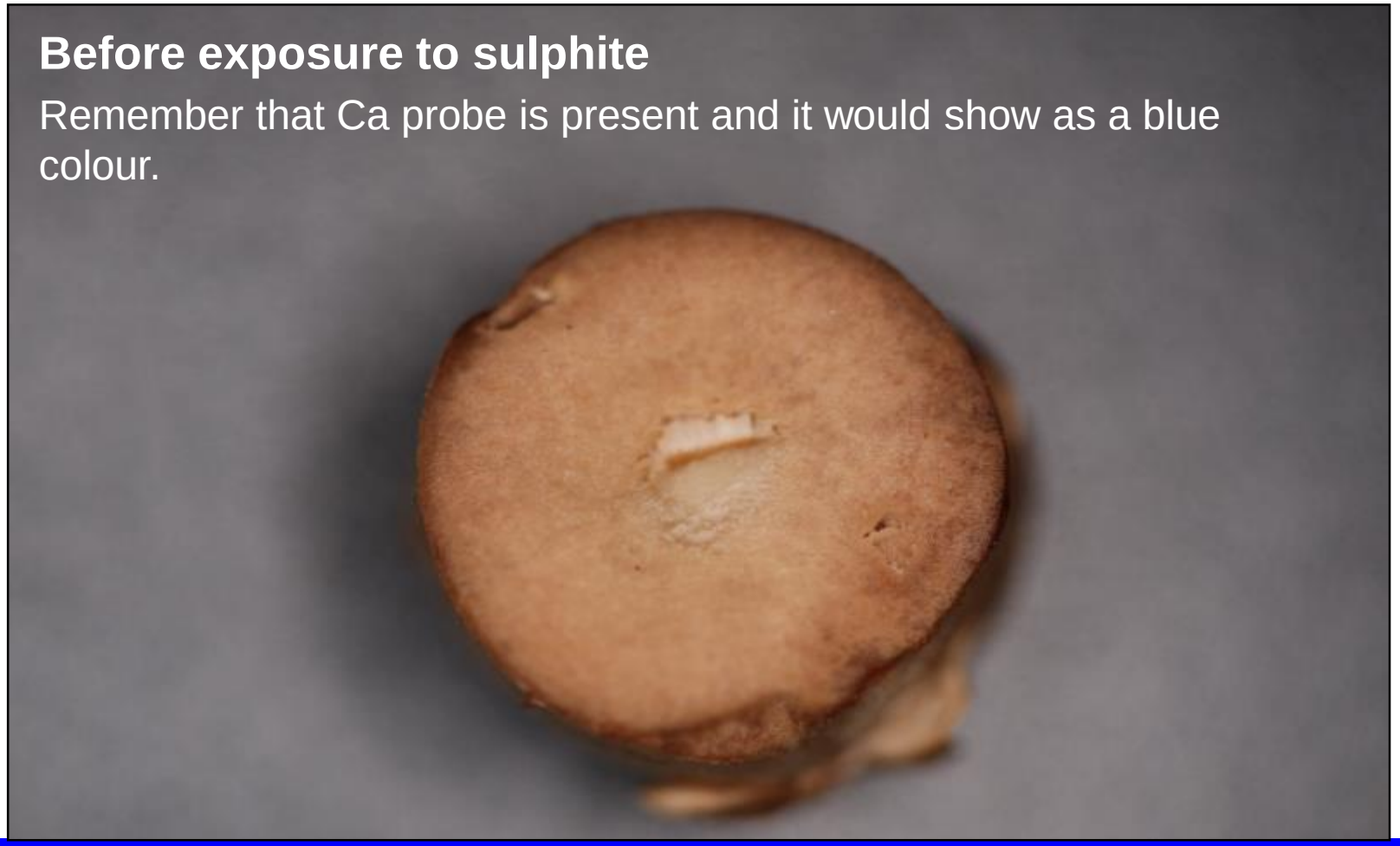
Lymphocyte (Slice): Sulphite-Sensitive Patient



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Lymphocyte (Slice): Sulphite-Sensitive Patient

Blue is calcium-sensitive fluorescent dye.

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Lymphocyte (Slice): Formaldehyde-Sensitive Patient

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Lymphocyte (Slice): Formaldehyde-Sensitive Patient

Recommended Treatment

- Use of sodium cromoglycate.
- Neutralizing vaccines which have a cell wall stabilising effect, not only in the gastrointestinal tract but throughout the body.
- Assessment of gastrointestinal function; improvement of integrity; production of secretory IgA and restitution of normal flora.
- Treatment for the ingestion of food has to be the utilisation of antihistamines, or if anaphylaxis occurs, adrenaline to combat shock, and perhaps resuscitation might be required.

Recommended Treatment (cont.)

- Dietary measures to ensure that there is limitation of artificial ingredients in the diet which can irritate and perpetuate food sensitivity states.
- Restitution of metabolic performance which has often been impaired because of chronic inflammatory responses calling on resources.

Oral Tolerance

- Oral tolerance is a state of specific immunological unresponsiveness induced by prior oral administration of antigen and is antigen-specific.

Oral Tolerance (cont.)

- Intestinal cells induce systemic tolerance
- Mediated by T cells
- Neonates - not tolerant
- With gastrointestinal tract infections - decrease
- With gastrointestinal tract flora diminution - decrease

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History of Allergy and Low-Dose Immunotherapy

- Noon published a paper on hay fever desensitisation in the Lancet in 1911.[1]
- Dr John Freeman employed allergen-specific immunotherapy in which increasing doses of allergen were used to force the body to accept these challenges: desensitisation.[2]
- It is not currently used, except in some centres where a very limited range is employed, in particular, grasses and wasp and bee venoms.

[1]*Noon L. Prophylactic inoculation against hay fever. Lancet. 1911;1:1572-3.*

[2]*Freeman J. Vaccination against hay fever. Lancet. 1914;1:1178-80.*

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History of Allergy and Low-Dose Immunotherapy (cont.)

- This technique was refined in the 1960s by Dr J B Miller.[1] It is a safe, effective treatment for sensitivities of all kinds, food, chemical or inhalant.
- The "vaccines" which are used for treatment must first be individually tested by injection into the skin (intradermal testing), or by using drops under the tongue (sublingual testing).

[1]*Miller JB. Relief at last! Springfield (IL): C C Thomas; 1987.*

Low-Dose Immunotherapy

- The American Academy of Environmental Medicine (AAEM) uses immunotherapy as a form of treatment across the United States and, in its practice guidelines, promotes the use of immunotherapy. The AAEM is an internationally recognised organisation and all the courses run by the AAEM are accredited by the American Medical Association.
- A compilation of nine references is given on the following slide and a fuller version of this reference list is available on request.

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Low-Dose Immunotherapy (cont.)

- Aboshady OA, Elghanam KM. **Sublingual immunotherapy in allergic rhinitis: efficacy, safety, adherence and guidelines.** Clin Exp Otorhinolaryngol. 2014;7:241-9.
- Akdis CA, Akdis M. **Mechanisms of allergen-specific immunotherapy.** J Allergy Clin Immunol. 2011;127:18-27. Available from: http://www.jacionline.org/article/S0091-6749(10)01850-6/pdf Accessed 18 December 2014.
- **American Academy of Environmental Medicine. Practice guidelines**.
- Calderon MA, Demoly P, Gerth van Wijk R, Bousquet J, Sheikh A, Frew A, et al. **EAACI: A European Declaration on Immunotherapy. Designing the future of allergen specific immunotherapy.** Clin Transl Allergy. 2012 Oct 30;2:20.
- Fujimura T, Okamoto Y, Taniguchi M. **Therapeutic effects and biomarkers in sublingual immunotherapy: a review.** J Allergy (Cairo). 2012.
- Moingeon P, Mascarell L. **Induction of tolerance via the sublingual route: mechanisms and applications.** Clin Dev Immunol. 2012; 2012; 623474.
- Moldaver D, Larché M. **Immunotherapy with peptides**. Allergy. 2011;66:784-91.
- Rodríguez del Río P, Díaz-Perales A, Sanchez-García S, Escudero C, do Santos P, Catarino M, et al. **Oral immunotherapy in children with IgE-mediated wheat allergy: outcome and molecular changes**. J Investig Allergol Clin Immunol. 2014;24:240-8.
- **World Health Organization. Allergen immunotherapy: therapeutic vaccines for allergic diseases.** WHO Position Paper**.** Allergy. 1998;53(44 Suppl):1-42. Low-dose immunotherapy: food sensitivity/multiple chemical sensitivity – references 190615 6.

Low-Dose Immunotherapy (cont.)

- Low-dose immunotherapy can be used to treat food, chemical and inhalant-particulate sensitivities.
- The person is tested for their allergies with individual injections of the antigen as an injection under the skin (intradermally) or by using drops under the tongue (sublingually).

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Low-Dose Immunotherapy (cont.)

- Testing begins with a solution of a substance to which allergy is suspected, which is assessed after 10 minutes.
- A series of weaker solutions may then be tested, until the correct therapeutic strength is reached.
- Treatment vaccines are provided for use at home, regularly, as they have been assessed for safety in the hospital.

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Low-Dose Immunotherapy (cont.)

- The vaccines stabilise the responses of the body when exposed to provoking foods, chemicals or inhalants, and have no deleterious effects on the patient.
- The technique has been used on approximately 20 million people worldwide without serious adverse effect.
- Our low-dose immunotherapy for allergies is based on products from our laboratory, which produces vaccines based on 0.9% saline without preservatives.

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Low-Dose Immunotherapy (cont.)

- We also supply other hospitals in the UK, Germany and Australia.
- We have used this type of immunotherapy since 1980.
- It has been the subject of a paper published in the journal 'Clinical Allergy'[1] and, in expert hands, it is completely safe.

[1]*Scadding GK, Brostoff J. Low dose sublingual therapy in patients with allergic rhinitis due to house dust mite. Clin Allergy. 1986;16:483-91.*

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Immunological Mechanisms of Allergen-Specific Immunotherapy

A review article on allergen-specific immunotherapy states:

> Allergen-specific immunotherapy (SIT) involves repeated administration of the sensitizing allergen (usually by subcutaneous injection or, more recently, by sublingual application). SIT was first reported at the beginning of the last century and has been shown to be a robust and clinically effective allergen-specific form of treatment that induces active immunity to the allergen. SIT is disease modifying, rather than palliative, and has a duration of action that exceeds the treatment period.

Larché M, et al. Immunological mechanisms of allergen-specific immunotherapy. Nat Rev Immunol 2006;6:761-71.

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Immunological Mechanisms of Allergen-Specific Immunotherapy (cont.)

It has been shown to prevent the onset of new sensitizations to different allergens and to reduce the development of asthma in patients with allergic rhinitis caused by inhaled allergens. SIT improves the quality of life of the treated individuals, through the reduction of symptoms and medication usage. More specifically, it has been shown to reduce seasonal increases in specific IgE and in the nonspecific airway hyper-reactivity that occurs in individuals with asthma. Bronchial responses to an inhaled allergen challenge, and late-phase responses to an allergen challenge in the skin or nasal mucosae, are also reduced.

Larché M, et al. Immunological mechanisms of allergen-specific immunotherapy. Nat Rev Immunol 2006;6:761-71.

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Reversing Allergies

- Immunotherapy is the only type of treatment that reverses allergies.
- The WHO position paper* is encouraging the use of this:

  "Drugs provide symptomatic treatment, whereas allergen avoidance and immunotherapy are the only therapeutic modalities which have the potential to modify the natural course of the disease."

- 38 peer-review studies show the benefits of the use of low-dose immunotherapy.

**WHO Position Paper. Allergen immunotherapy: therapeutic vaccines for allergic diseases. Allergy. 1998;53:suppl.*

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Autonomic Nervous System and Allergy

- Where the autonomic response is abnormal, it returns to normality after one week's treatment with immunotherapy. Dr Peter Julu, Consultant Autonomic Neurophysiologist, does the tests for our patients at Breakspear Medical.
- The autonomic nervous system is the neural pathway for allergy.[1]

[1]*Shepherd AJ, Downing JEG, Miyan JA. Without nerves, immunology remains incomplete – in vivo veritas. Immunology. 2005;116:145-63.*

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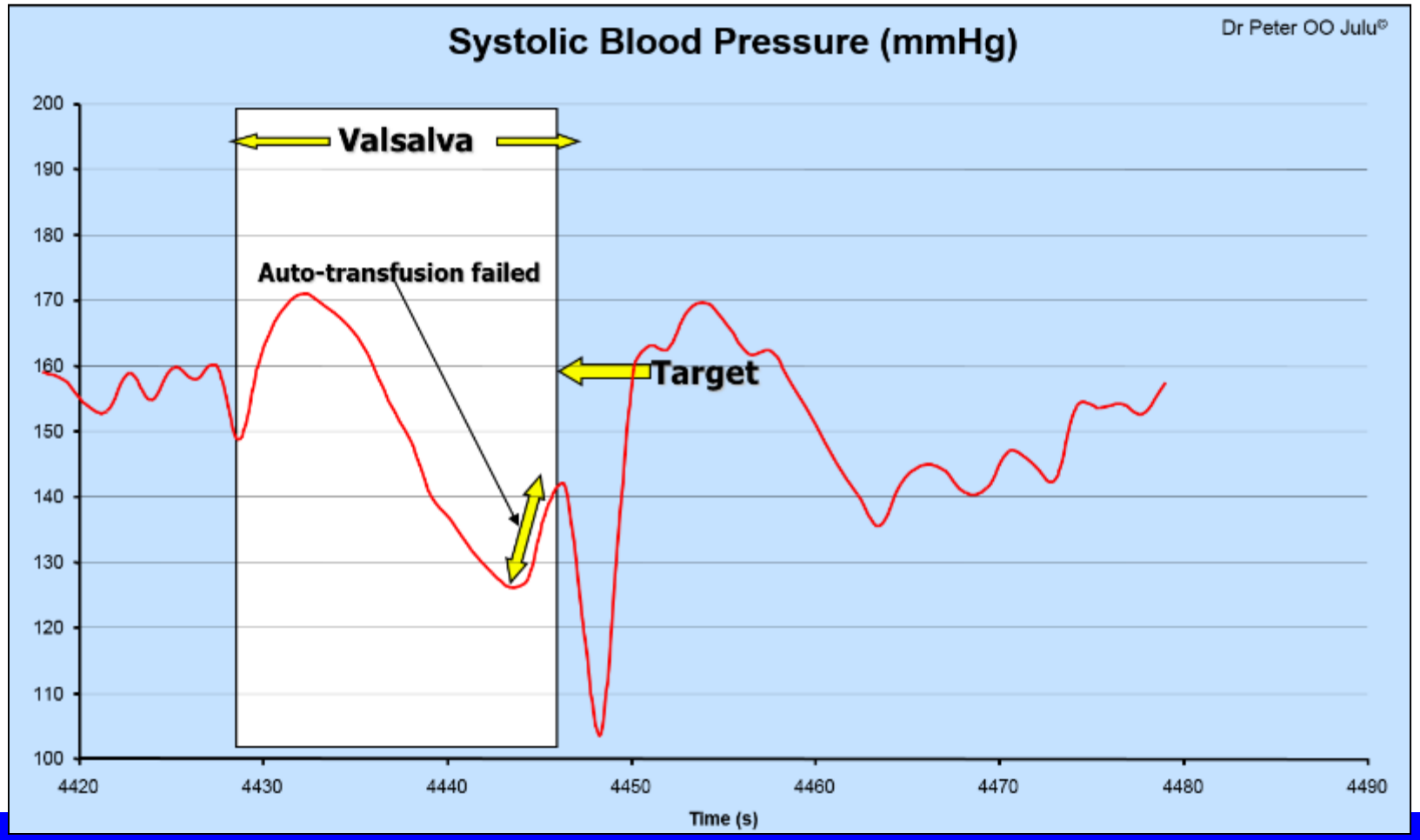
Autonomic Responses in Valsalva's Manoeuvre Before Low-Dose Immunotherapy



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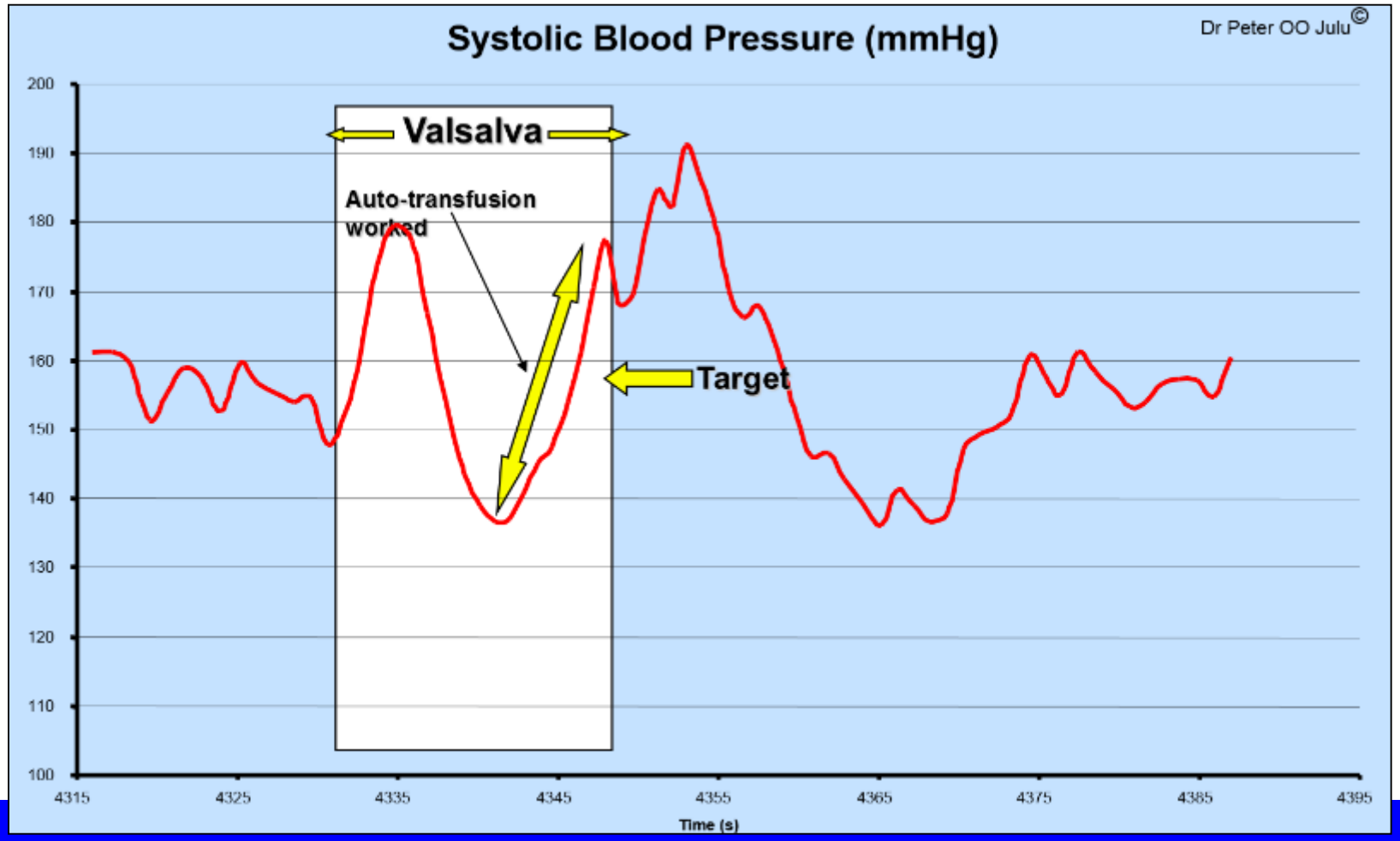
Autonomic Responses in Valsalva's Manoeuvre After Low-Dose Immunotherapy



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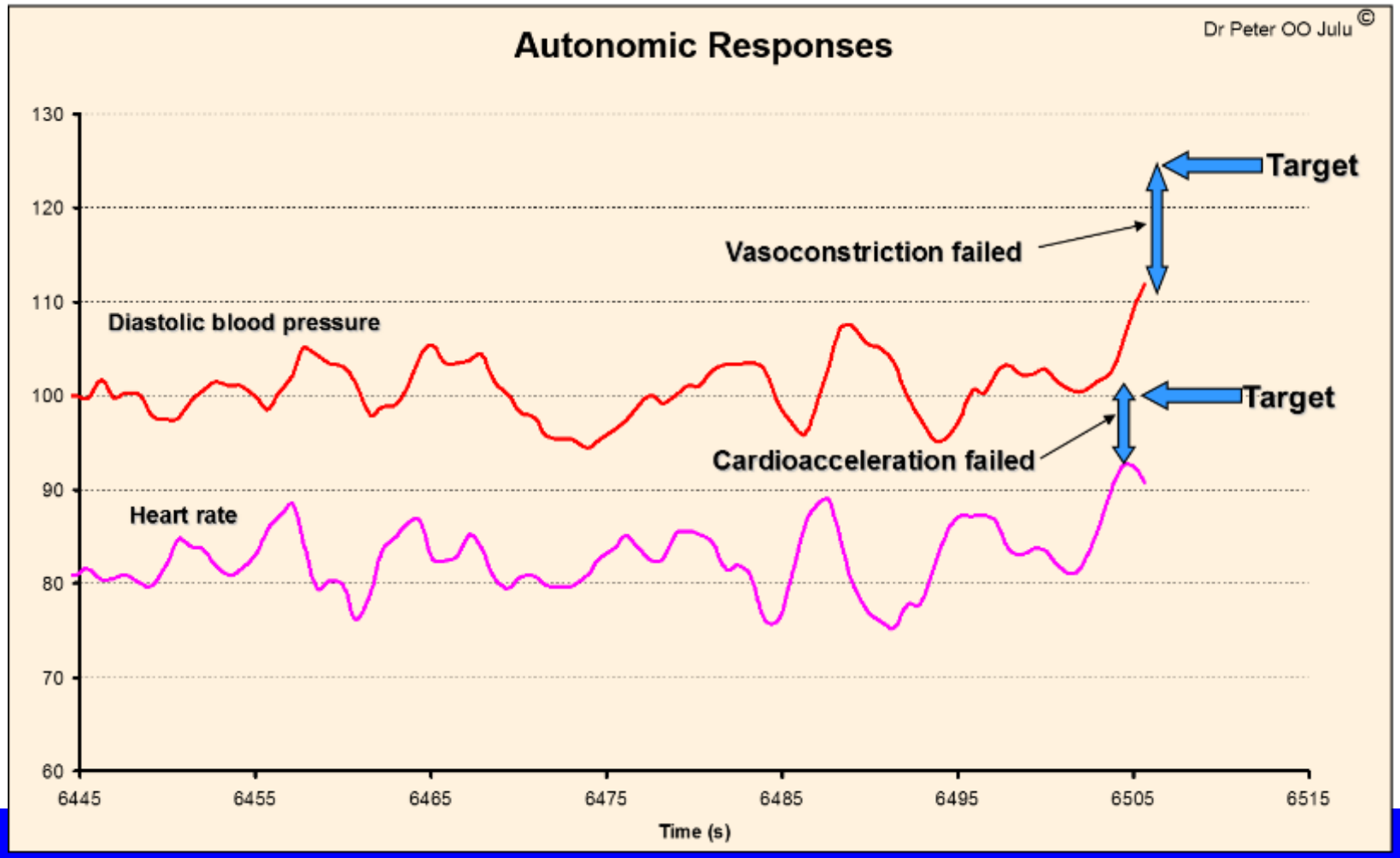
Autonomic Responses to Isometric Exercise Before Low-Dose Immunotherapy



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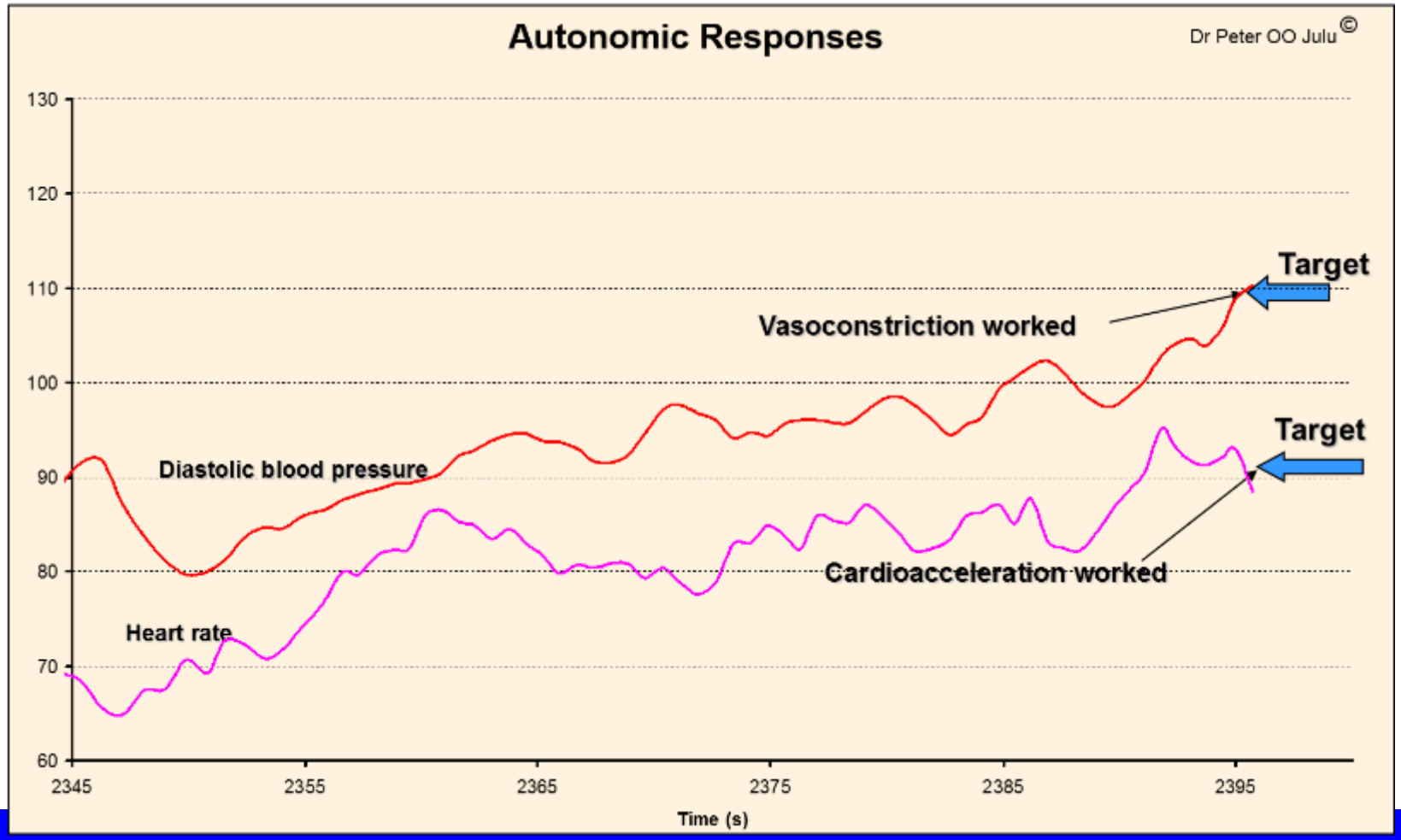
Autonomic Responses to Isometric Exercise After Low-Dose Immunotherapy



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Lymphocyte Sensitivity Test Before and After Low-Dose Immunotherapy

- A Lymphocyte Sensitivity Test was carried out before and after Low-Dose Immunotherapy.
- When sensitised lymphocytes are exposed to a low level of an allergen, the responses include a rapid passage of calcium into the cells.
- Intracellular calcium levels are quantified using a calcium-sensitive fluorescent probe pre-loaded into the lymphocytes.
- As not all lymphocytes carry the same sensitivity information, an integrated result is obtained using microplate technology and a Thermo Labsystems Multiscan Multisoft instrument.

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Lymphocyte Sensitivity Results

Percentage of decrease in intracellular calcium levels pertaining to sensitivities after low-dose immunotherapy

	Percentage of decrease in level	P-value	Number of patients analysed
Metabisulphite	25%	< 0.0004	44
Salicylate	16%	< 0.01	43
Benzoate	24%	< 0.01	42
Formaldehyde	32%	< 0.0001	43
Petrol exhaust	18%	< 0.003	43
Natural gas	21%	< 0.001	41
Nickel	16%	< 0.05	45
Organophosphates	28%	< 0.01	18
Nitrosamines	16%	< 0.05	15
Intracellular calcium	14%	< 0.0001	42

Methods of Immunotherapy Administration

- Subcutaneous injection is the most common method.
- The transcutaneous route is being used by allergists throughout the UK.
- Immunotherapy is now also being administered via an epicutaneous route.
- Sublingual immunotherapy (SLIT) is another route of administration and there are seventeen peer-reviewed studies. In Italy, treatment with sublingual immunotherapy is commonplace.

The Career of the Food Allergy Sufferer

- Dr Alison Bunnin reported a detailed study of 30 patients in her PhD thesis. She found that before their problems were correctly identified as food allergies, between them they had:
  - visited their family doctors 1,936 times
  - been to 822 hospital appointments
  - spent 422 days in hospital
  - taken 7,200 days off work
  - consumed drugs costing £17,500
  - attended specialists for consultations costing £27,200

Bunnin A. The career of the food allergy sufferer. London; Allergy Research and Education; 1989.

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The Career of the Food Allergy Sufferer (cont.)

- In her opinion, food allergy sufferers have two wars to fight. They have to face symptoms, including arthritis, headaches, asthma, skin and digestive disorders, and they have to battle against failure of recognition of their basic condition.

Bunnin A. The career of the food allergy sufferer. London; Allergy Research and Education; 1989.

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Food Intolerance, Allergy and Sensitivity: Rationale, Investigations and Treatment

Dr Jean A Monro

MB BS, MRCS, LRCP, FAAEM, DipIBEM

Breakspear Medical, Hertfordshire House, Wood Lane, Hemel Hempstead, Hertfordshire, HP2 4FD, UK

'Lifting the Veil' Part II – Chronic Disease: What's REALLY Going On?

Academy of Nutritional Medicine (AONM)

Sunday, 15th November 2015, London

END