

All you need to know about science and new perspectives on health and diseases

ALL YOU NEED TO KNOW ABOUT SCIENCE AND NEW PERSPECTIVES ON HEALTH AND DISEASES

All you need to know about health and diseases

Science and New Perspectives on

Immunology

Immune System

Lymphatic System

Acupuncture, Meridans and Traditional Chinese Herbs

Food incompatibilities and their relation to enzymes, gut microbiota and medication interaction

Systemic Candidiasis and fungi

Anne-Margré C. Vink, MD



Publisher Marsilea 4 B.V.
Almere, The Netherlands (Europe)

Author: Anne-Margré C. Vink, MD
Omslagontwerp: Anne-Margré C. Vink and Dion Spijk, Threii-Design te Amsterdam
Eerste Druk: in eigen beheer uitgegeven via bookmundo.com

© Uitgeverij Marsilea 4 B.V. in 2025

All rights reserved. No part of this book may be reproduced, stored in a database or retrieval system, or published, in any form or in any way, electronically, mechanically, by print, photoprint, microfilm or any other means without prior written permission from publisher.

Apart from any permitted use under the Copyrights at ground of articles 16h until 16m
Authorslaw 1912 jo by Decision of 27 November 2002, Stb 575.

Niets van deze uitgave mag worden gekopieerd of overgenomen daar heeft u voorafgaand schriftelijke toestemming voor nodig. Of men dient de daarvoor wettelijke verschuldigde vergoeding te voldoen aan de Stichting Reprerecht te Hoofddorp (Postbus 3060, 2130 KB Hoofddorp) of contact op te nemen met de uitgever voor het treffen van een rechtstreekse regeling in de zin van art. 161. Vijfde lid, Auteurswet 1912. Voor het overeenstemmen van gedeelte (n) uit deze uitgave is bloemlezingen, readers en andere compilatieweken kan men zich wenden tot de Stichting PRO (Stichting Publicatie- en Reproductierechten Organisatie, Postbus 3060, 2130 KB Hoofddorp).

Ondanks al de aan de samenstelling van de tekst besteede zorg, kan noch de auteur, noch de uitgever aansprakelijkheid aanvaarden voor eventuele schade die zou kunnen voortvloeien uit enige fout die in deze uitgave zou kunnen voorkomen

ISBN 978940382442

Email: info@medisynx.com

Index

All you need to know about Science and New Perspectives on health and diseases

Page	Chapter/ Paragraph	Title
10		Foreword
11		Introduction
12	Chapter 1	Immune system and Immunology, what is our immune system
13	1.1	Innate Immune system
15	1.2	Complement System
17		Classical,- Alternative-, Lectin Pathway
21		Other complement functions, phagocytes, macrophages, neutrophils
23	1.3	Adaptive- or Acquired Immune system
24		B-Cell and antibodies
25		How do we get our gene-segments?
27		B-Cell activation and class switching
27	1.4	Immunoglobulins and hierarchic structure
29		Cell-mediated reponses, chronic inflammations and autoimmune diseases
30	1.5	Cytokine network
31	1.6	Cell-mediated immunity of skin
33		Timeline from Day 1 to 0-8 weeks to develop a disease
39		How a brain tumor like Glioblastoma begins
41		Three different pathways to activate Complement System
42		Complements components in types of tumors
43		Lung Covid in relation to immune system
46	Chapter 2	Introduction to Lymphatic System
48	2.1	Lymphatic System, scans and devices to image
52		Scintographic methods, Fluorescence microlymphography
54		MRI, PET scan
56		Lymphatic System and Lymphatic Vessels
60		Biological functions of Lymphatic vessels and implications in diseases and edema
61		Cholesterol crucial for Homeostasis
62		Plasticity of Brush Border – the Yin and Yang- of Intestinal Homeostasis
64		Cholesterol uptake by Brush-Border Membrane (BBM)
65		Our Lymphatic Vessels are our Meridians
67	2.2	More about Lymph and Composition
68	2.3	Lymphatic transport System
69		Lymphatic connection point lateral of Umbilicus
69	2.4	Left Duct or Thoracic Duct and Right Duct of Lymphatic System
70	2.5	Lymphatic Organs and Lymphatic Tissues
72	2.6	Secondary Lymphoid Organs

73		Peyers Patches in Small Intestine
73	2.7	Lymphatic Vessels and skin
77	2.8	Other Lymphoid tissues: MALT, GALT, BALT and SALT
77	2.9	Diseases of Lymphoid System
79	2.10	Glymphatic Systems in Brains and Eye
81		Two Durameter Lymphatic Vessels in Brains
87		Seeing into the Brains
88		How quality of Sleep clears your Brains, your memory and Aging
90		Waste into your Brains
94		Gilles de la Tourette
95		Dopamine and Gilles de la Tourette Connection
96	2.11	Lymphatic System of Head and neck
97		Superficial Lymphnodes
98	2.12	Lymphatic System of Face
99	2.13	Lymphatic System of Ear
99	2.14	Lymphatic System of Eeye and Canal of Schlemm
102	2.15	Lymphatic System of Nose
103	2.16	Lymphatic System of Mouth and Tongue
105	2.17	Lymphatic System of Muscles
106	2.18	Lymphatic System of Bone marrow and Bone healing
107		Types of Bloodcells and Bone healing
107		Role of Lymphatic System in Bone healing
108		Lymphatic System can produce Bloodcells: Leucocytes and Erythrocytes
110	2.19	Lymphatic System and development of Tumors and Cancers
110		Two kind of Tumors: benign and malignant
111	2.20	Breast Cancer of mammae
112	2.21	Colon- and Colectoral Cancer
114	2.22	Lung Cancer (Pulmonary System)
116	2.23	Stomach Cancer 111 Pancreas- and Galbladder Cancer
119	2.24	Bladder- and Kidney cancer and riskfactors
120		Bladder Cancer relation to hair painting (hair dye products) and genetics
124	2.25	Thyroid- and Parathyroid Cancer
127	2.26	Oral- and Oropharyngeal Cancer (Mouth and Throat)
128		Relation of smoking and or HPV and Cancers
130	2.27	Uterine- and Cervix Cancer
133	2.28	Prostate- and Penis Cancer
136	2.29	Skin Cancers
138	2.30	Leukemias
140	2.31	Lymphoedema
142		Pathofysiology Lymphatics
143	2.32	Carteledge Degradation: Artrosis, Osteoarthritis by Lymphatics
145	2.33	Ankylosing Sponylitis or M. Bechterew
147	2.34	The Working of Lymphatic Vessels
148	2.35	Calcium and Electrical Dynamics on Lymphatic Endothelium
151		Controlling Neuro-activity states and Na^{+} - K^{+} Na^{+} / Ca^{2+}
152	2.36	Non-invasive and Invasive measurement Lymphatic Flow
153	2.37	Pumping Act of Lymphatic System
156	2.38	Intrinsic Pumping
157	2.39	Extrinsic Pumping
158	2.40	Heterogeneticity of Lymphatic Network Topology

159	2.41	Lymphatic System and relation to Cancers
161		Lymphatic System and Acupuncture
163	Chapter 3	Blood, Blood Vessels and Blood-Brain-Barrier (BBB)
163	3.1	Blood Vessels
164	3.2	Breakdown of BBB
165	3.3	How Drugs and Medication are brought into Brains
165	3.4	Blood-Brain-Barrier (BBB) Pathways
166	3.5	Our Blood Circulation System is fully depending on our Lymphatic System
168	3.6	Blood and Immune Elements
168	3.7	Medisynx BASIS Plus Research
169	Chapter 4	Acupuncture, Meridians and Wei Qi
169	4.1	Introduction
169	4.2	Our 12 + 2 Principal Meridians
171	4.3	Meridians and essential Acupuncture Points
172	4.4	Yin and Yang Explanation
174	4.5	Science of Acupuncture in relation to Lymphatic System
180	4.6	Effect of Stimulation with sound and ultrasonic waves on Meridians / Lymphatics
182	4.7.1	Probing the mystery of Chinese meridian channels
186	4.7.2	Quality of Acupuncture for effectiveness and Safety
186	4.8	Studies of Acupuncture and Case Reports
188	4.9	Visualization of Acupuncture and Meridians
189	4.10	Relationship between Acupuncture points and Blood and Lymph
189	4.11	Evolution of Acupuncture in 20th Century
190	4.12	History of Acupuncture
193	4.13	US President Richard Nixon and his wife Trade Trip to China and their discovery of Acupuncture
193	4.14	Acupuncture in The Netherlands (West-Europe)
195	4.15	Introduction of Western Medicine to China
197	4.16	Development of Scientific Acupuncture
197	4.17	Acceptance and Implementation of Acupuncture into Western Medicine
198	4.18	Studies of Acupuncture and Blood, Nerves, Lymphatics
199	4.19	Conclusions of Scientific Evidence of Acupuncture
199	4.20	Medisynx Research of Meridians, Acupuncture and Wei Qi
200	4.21	What is a Meridian?
202		Why using Sterling Silver Acupuncture Needles?
203	4.22	Acupuncture Points
204	4.23	Medisynx Method of Acupuncture
204	4.24	How to define which Medisynx Method Acupuncture Points are needed to insert?
206	4.25	Medisynx Basic Acupuncture Needling Setting
209		TCM Organ Clock
210	4.26	World Health Organization (WHO) acknowledged Acupuncture as safe and effective
213	4.27	WHO overview to recommend initially acupuncture treatment
215	4.28	WHO Nomenclature Acupuncture Points
216	4.29	Publication 'CAM-education in the Medical Curriculum: Attitude towards and acknowledge of CAM among Dutch Medical Students'

216	4.30	The 5 Essentials of Acupuncture
217	4.31	Diagnose in traditional Chinese Medicine (TCM)
222	4.32	Medisynx Method Treatment of Acupuncture
223	4.33	Medisynx Basic Acupuncture Points
244	4.34	Closer look into Knee and Lymphatics
246	4.35	Closer look into Arm- and Foot Supination and Pronation
247	4.36	Deformation or degeneratio of Bones, Cartilage and Ligaments
247	4.37	Neurological Disorders
247	4.37.1	Anxiety and Panic Attacks
248	4.37.2	Insomnia or Sleeping problems
248	4.37.3	Trigemius Neuralgy
248	4.37.4	Gilles de la Tourette
249	4.37.5	Schizophrenia, ghost talking and ghost seeing
249	4.37.6	Huntington Disease and Chorea
250	4.37.7	The Head, Migraines and Headache
251	4.37.8	Facial Paralysis
251	4.37.9	Epilepsy
251	4.37.10	TIA and CVA
251	4.38	Acupuncture of Eye
255	4.38.1	Cataracta
255	4.38.2	Glaucoma, and increase of Intra Ocular Pressure
256	4.38.3	Optic Nerve abnormalities
256	4.38.4	Lens Shape changes
256	4.38.5	Keratoconus
257	4.38.6	Strabismus
257	4.38.7	Nystagmus
258	4.38.8	Edema of Eyelids (Ptosis)
258	4.39	Acupuncture of Ear
260	4.39.1	Vertigo and Menière
260	4.39.2	Otitis Media and itchy in Ear
260	4.39.3	Tinnitus (Ear ringing)
266	4.40	Vocal Cords and Voice
266	4.41	Thyroid Disease
267	4.42	Urogenital- and Gynaecological Diseases
267	4.42.1	Cystitis and Interstitial Cystitis
267	4.43	Pulmonary Diseases (Lung diseases)
267	4.43.1	Asthma
267	4.43.2	Allergic Rhinitis
267	4.43.3	Pharyngitis
268	4.44	Cardiological and heart Diseases
268	4.44.1	Arrhythmias
268	4.45	Short Check list of manifestations in relation to Meridian System
269	4.46	Overview of The 5 Essentials of Acupuncture
269	4.47	Traditional Chinese Herbs or Chinese Materia Medica
271	4.47.1	TCM herbs are safe and effective and according to CITES Law
274	4.47.2	Neutralizing of certain toxic plants in plants by specific combinations and hydrolysis
274	4.47.3	Decoction (Tang) of Herbs by Hydrolysis
275	4.47.4	Chinese Medicine most ancient Healing System
275	4.47.5	Harvest natural or wild medicinal herbs
276	4.48	The Future of Acupuncture and Traditional Chinese Herbs

278 Chapter 5 Food incompatibilities, their relation to medicines, microbiota and Candida albicans and Systemic Candidiasis and Fungi

278	5.1	Why we need to eat?
278	5.2	Enzymes are necessary to digest food
279	5.3	Gut bacterias or Microbiota or Microbiome
280	5.4	Accumulation of Waste of food incompatibilities
281	5.4.1	Our Small Intestine functions
281	5.4.2	Scavenger Receptors and Cholesterol
283	5.4.3	The Janus-Faced Role of SR-BI in Atherosclerosis
283	5.4.4	Villous Atrophy or Leaky Gut Syndrome
286	5.4.5	Publication of relationship E-Numbers in Food and serious Diseases
286	5.5	Microbiome and Microbiota and Central Nervous System (CNS)
291	5.5.1	Validation of level of Villous Atrophy
291	5.6	Publications of relation Food and Psychological, Psychiatry and Sleep disorders
291	5.7	Good Microbiota for Good Health
292	5.7.1	Bacteriophages
294	5.7.2	Antibiotic Resistance
295	5.7.3	Mechanisms of Resistance
296	5.7.4	Prevention and Drug Development
297	5.7.5	Bacteriophages or Phages are Viruses
298	5.7.6	Generalized Transduction
298	5.7.7	Specialized Transduction
299	5.7.8	Novel Nanoscale Bacteriophage-based-treatment
301	5.7.9	Vegetarians and Veganists
302	5.7.10	Bacteriophages improve effectiveness of Rhamnolipids
303	5.7.11	Medisynx Candida Albicans Assays
304	5.7.12	Candida Albicans and Systemic Candidiasis and other Fungi
306	5.7.13	Candida Auris
309	5.7.14	Candida Albicans and its Three-Morphic Stadia
311	5.7.15	Relation of using Medication and development of Systemic Candidiasis
313	5.7.16	Intestinal Colonization Phenotype
316	5.7.17	How Fungi and yeast cells reach Bloodstream?
323	5.7.18	Candida Albicans is found in Sperm of males
324	5.7.19	Men's Infertility in relation to Candida Albicans
326	5.7.20	Lung Covid and Systemic Candidiasis
329	5.7.21	Candida Albicans perturbs Gut-Brain-Axis
332	5.7.22	Mammalian Endocannabinoid System (eCB)
333	5.7.23	Obsessive-Compulsive-Disorder(OCD), Psychiatry Disorders
337	5.7.24	Gut-Brain-Axis
340	5.7.25	The Nervous Pathway and Parkinson Disease (PD)
340	5.7.26	The Immune Pathway, from Gut to Host
341	5.7.27	From Host Immune System to Gut Microbiota
341	5.7.28	Dysbiosis and Neurobiology Basis of OCD
342	5.7.29	Dysbiosis and Hyperactivity in CSTC
342	5.7.30	Serotonin
343	5.7.31	Glutamate
344	5.7.32	Dopamine
344	5.7.33	Dysbiosis and Immune Basis of OCD
344	5.7.34	Dysbiosis and genetic Basis of OCD
345	5.7.35	Dysbiosis and Environmental Basis and Food on OCD

346	5.7.36	Systemic Candidiasis and Mental and Psychiatry Disorders
349	5.7.37	Fungal Infections and Alzheimer Disease (AD)
351	5.7.38	Fungal Infections and Amyotrophic Lateral sclerosis (ALS)
351	5.7.39	Medisynx Method Treatment in ALS
352	5.7.40	Which nutrients are essential for us, our brains, our muscles and our regeneration?
357	5.7.41	Genetic Manipulated Organism and specific properties of food
359	5.7.42	Medisynx Clinics, Laboratory, Scientific- and Education Institute
360	5.7.43	Incompatible Food leads to oxidative Stress and DNA damage and shortening of telomeres
361	5.7.44	Compendium of Cross-Over-Reactions of Pineapple and specific Anesthetics, Analgetica and Anti-inflammatories
365	5.7.45	Medisynx Candida Albicans Assays
365	5.7.46	Summary, all-in short
367		References and Sources

Foreword

As a little child I already felt what some food did to me, sometimes I felt a heavy ache in my stomach after drinking a fresh glass of orange juice and explained to my mother 'it feels like having a stone here', pointing to my stomach area. She only laughed and said "no you can see it is liquid, it is not massive, so stop telling this it is ridiculous". I felt disappointed and sad not to be believed.

My great luck and happiness were my grandmothers, they believed me and said 'well you are unique, as your DNA is unique, so what is healthy for one can be unhealthy for another', that simple it is.

And that is no new science, Hippocrates (460 BC to 377 BC) he knew that already 2500 years ago, when he spoke his famous lines 'let food be thy medicine and thy medicine your food'.

My grandmother also told me the story of Galileo Galilei (1564 to 1642), a scientist in Physics, Astronomy and Mathematics, a visionary far ahead of the rest, he proved our planet is round not flat, but he was not believed either and not accepted, he was tried by inquisition of the church, the place for science in that time, forced to recant, cancelled as scientist.

Sadly so many more visionaries were not believed and cancelled as outcast, just because they had new insights and refused to cover up incorrect science and commercialism in scientific research.

Reason for me to carry out my scientific research fully independent without any direction than the truth the whole truth and nothing but the truth, no more no less. The rejection of my mother was my basics, not everybody in the world will or wants to believe you, as they can have other meanings and or other interests and or protect an industry or a business, but I kept on going unceasingly, cause I wanted to know why a vitamin and mineral rich fruit as orange was not healthy for me.

To get all knowledge and insights to discover that, I had to study hard, and so many different studies though, and even overcome strong resistances as a study Acupuncture and Chinese Herbs was not appreciated in Western Medicine clinicians.

My only goal was and still is to cure patients and to inform them how they can prevent becoming ill, and that in the most natural, effective and safest way based on objectives and subjective results and without profit interest. And then share all my knowledge and new insights with colleagues and all who are interested in, and to implement Medisynx Method intervention in hospitals and clinics worldwide so that it will become available for everybody worldwide. Exactly how Hippocrates said so already: 'let food be thy medicine and thy medicine your food' Together we can achieve so much more.....

Thank you so much for reading my book and do tell the world.

Warm regards,

Anne-Margré

Introduction

This book is all about Immunology, Immune system, Lymphatic System, concerning lymphatic vessels, lymph nodes and lymphatic organs, Acupuncture, meridians, Traditional Chinese herbs, and Food incompatibilities and Systemic Candidiasis and what is their relation to each other.

More than 40 years of scientific research brought new insights, 360° perspectives and knowledge on their relationship and pathogenesis of diseases, the way to become unhealthy, physically and or mentally.

In a healthy individual the homeostasis is in total balance. In medicine we use the definition – homeostasis-, homeostasis is the balance of all biological,- and immunological reactions and feedback reactions in whole body, head, brains and mindset. That homeostatic balance is crucial for a good health and an easy and peaceful mindset. An unbalance of homeostasis will immediately lead to manifestations, symptoms, features, illness and disease (s) as well acute as chronic and finally can even be fatal. It is therefore that this knowledge and insight is so important. In other words a good working relationship of all these systems together is The Basics for a stabile homeostasis in balance so for a good health.

There are different perspectives on these systems, a modern Western Medicine perspective based on objectives by microscopes and technical devices as laboratory research, röntgen and CT-, MRI- and PET scans, and on the other hand there is an ancient Traditional Chinese Medicine (TCM) perspective purely based on experience of action-reaction, as 4000 years ago there were no microscopes nor electric devices. All their knowledge was based on visuality of skin, hair, nails, tongue, and if manifestations disappeared, feeling pulse, tongue check and subjective reaction of patients and their health results. Simple but very adequate.

Nowadays we are also able to research what TCM perspective means and what it is all about and are we capable to translate TCM perspective and expressions into Western words and understanding. In short in modern Western Medicine we speak about immune system and lymphatic system where in TCM we respectfully use the words Wei Qi (pronounce – way chi) and Meridians. The conclusion is it is only a matter of two different languages hence it is a Babelonian speech confusion.

In following chapters we are going into these systems first shortly and rapidly, but enough to understand the most important. For professionals we go deeper into the matter.

This book has five chapters (1,2,3,4 and 5) and sub-chapters (1.1, 1.2, 1.3 etc), and each chapter is divided into two levels:

In level 1: a short text in simple words to understand the basics and

Level 2: a scientific paragraph to go deeper into the matter, this text is written in another letter type. If you understand level 1, it is more easy to read and understand level 2.

Chapter 1 Immune system and Immunology

Chapter 2 Lymphatic System, lymphatic vessels, lymphatic tissues, lymphatic organs

Chapter 3 Blood, blood vessels, Blood-Brain-Barrier

Chapter 4 Acupuncture, Meridians, Organs and Wei Qi

Chapter 5 Food and Food incompatibility, Cross-overreactions to drugs-medication, natural- and chemical substances and Systemic Candidiasis by Candida Albicans and other fungi, bacterias and viruses

Chapter I

Immune system and Immunology

What is our Immune system?

Level I:

The immune system is a complex defense system, a network of immune players cooperating together to get things done, and just looking at one player does not make much sense, you need an overall view. In this book you will get a short and rapid tour of the immune system in Paragraph I, to get the feeling how it all fits together and a deeper into the matter in Paragraph II.

Our immune system is developed to defense us against invaders, bacterias, viruses, parasites and incompatibilities like food incompatibilities. Any invader or body-strange-substance that breaches the physical barrier by mouth, gastro-intestinal tract (stomach and intestines), eyes, nose, urogenital tract, or skin mucosa will be detected and your immune system will set on a domino-effect (cascade) of defense reactions.

The study of the immune system is called Immunology.

Our immune system is like an army with a strict hierarchy, from top to down, from general to foot-warriors and guards and detectors. Each with their specific function and actions, their responsibilities and decision authority. As in the army only the high functions are allowed to sets on actions and a cascade of immunological reactions to attack and offend. Your immune system is everywhere in your body, especially at the 'doors' thus entrances of your body, so your mouth, your nose, your eyes, your urinary tract and for women their vagina and your skin.

We are born with an innate immunsystem, a natural defense system, all animals do have such a general defendsystem, and we also have an adaptive immune system, a defense system that actually can adapt to be able to protect us against new viruses and incompatibilities, a self-learning system, and this system is getting smarter by learning every day. Necessary as viruses can change relatively in short period so our immune system has to adept to recognize the 'new' virus to detect and to attack the virus. That is why a vaccination against an Influenza-virus is only effective temporally. The vaccin must be adapted too.

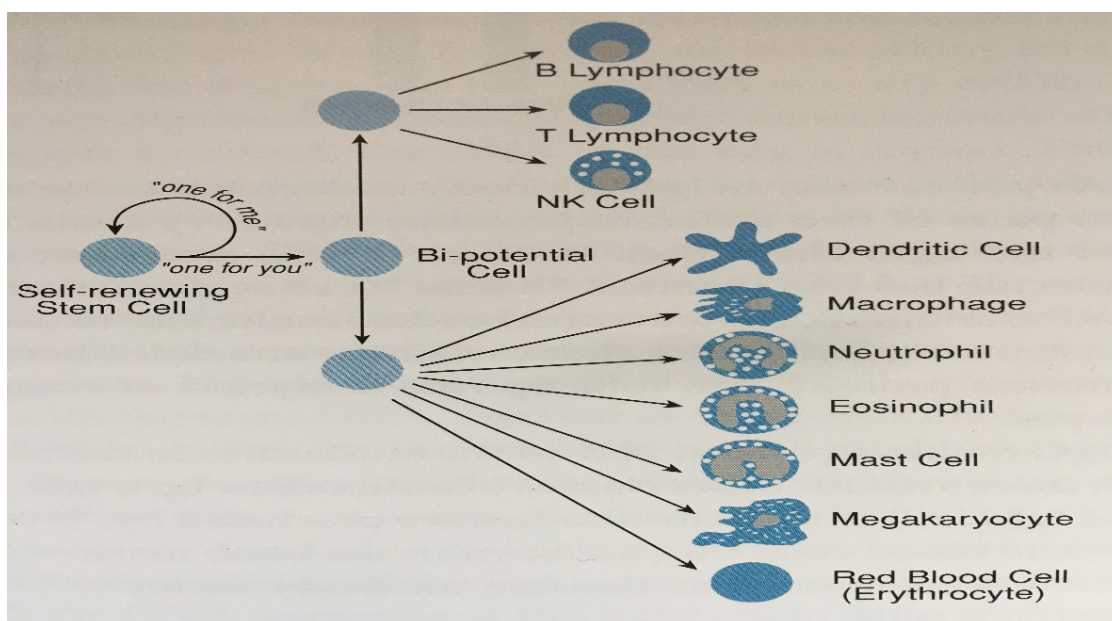


Fig. I Development from stemcell to different blood cells and immune-system cells

1.1 Innate immune system: defense system you are born with, inherited of your parents and ancestors

Level I

We are born with an innate defense system, we inherited this system from our parents and ancestors. It is a simple detecting-action system and invader like bacteria will be eaten up by special cells, called macrophages, in short MHC.

Innate immunsystem works relatively simple, when a bacteria gets in, your white bloodcells (leucocytes, as -leuco- means white) will detect it, as a bacteria tissue wall consists of proteins and fats that are not present in our human body. And immediately these white bloodcells will activate macrophages (macro means -large- and phage means -to eat-). Macrophages will devour the bacteria, it looks like a 'Packman cell' that 'eats' the invader. Then step by step macrophage will become a phagosome and later it will fuse with a lysosome and lysosomes have powerfull chemicals and enzymes to destroy bacteria. This proces is called phagocytosis.

Macrophages and all other blood cells are made in bone marrow from stemcells. When macrophages 'eat' bacteria they release chemicals to increase the flow of blood to vicinity the wound and it will also produce cytokines. Cytokines are hormon-like messengers facilitate communication between cells of immune system. But the innate team has more players to 'eat' invaders including complement proteins and Natural Killer cells to be able to destroy parasites and virus-infected cells, and some cancer cells.

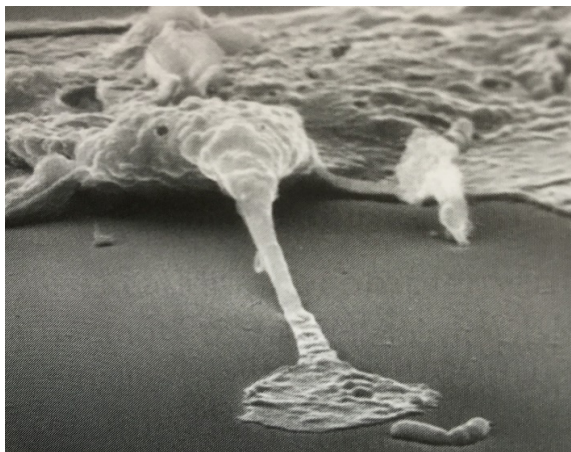


Fig. 2 Macrophage 'foot' to grab bacterium

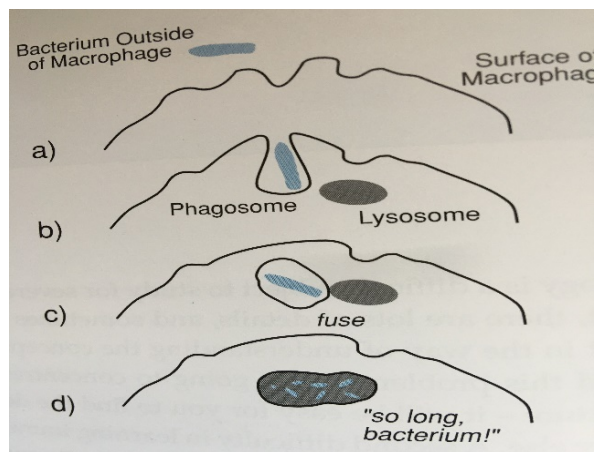


Fig. 3 Macrophage encounters a bacterium

Phagocyte cells, consist of macrophages and neutrophils are the most important parts of innate system, detecting and eating invaders whole day and night long.

Macrophages (MHC) are abundantly found in your skin, to protect you against penetrating invaders, when you have a wound or a burn. Macrophages are also present in your lungs to defend against inhaled microbes and in the tissues of your intestines waiting for ingested microbes. You can call macrophages the garbage cleaners of your body, they also clean up dead cells, cancer cells and cellular debris.

Level II

Ilya Metchnikoff (1845-1916) first discovered macrophages.

Macrophages were first discovered and named by *Ilya Metchnikoff* (1845-1916), a Russian zoologist and later he became a famous researcher in immunology and diseases. He was awarded with Nobel Prize in Physiology-Medicine in 1908. He also proved Macrophages can be identified using – flow cytometry- or – immunohistochemical- by their specific expression of proteins such as – CD14, CD40, CD11b, CD64, F4/80, EMR1, Lysosome M, MAC-1/MAC-3 and CD68.

Level I

Ilya Metchnikoff also discovered the – orthobiosis- that certain bacteria are necessary to produce, in collaboration with our intestines. These bacteria in particular *Lactobacillus delbrueckii* subsp. *Bulgaricus* are essential to be able to produce the enzyme – *lactase*- to digest Lactose. By cutting *lactose* (milk sugar) into a *galactose* and *glucose*, to be able to absorb them in our small intestine.

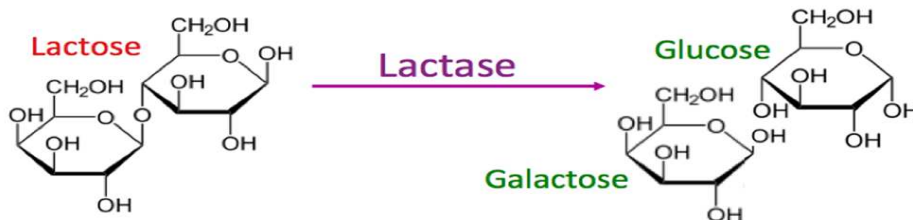


Fig. 4 Cutting Lactose into a Galactose and a Glucose by enzyme Lactase (-ase- means enzyme)

Ilya Metchnikoff proved that only a few people originate from Caucasian race are having such a recipe of an enzyme-programme on their DNA Blue Print. Only if you have such a recipe on your DNA Blue-print and have these bacteria in your intestine too, then you are able to produce the enzyme – Lactase-

Therefore only these humans are able to digest the milksugar called- lactose-. Reason why only they can drink safely animal milks (dairy) and eat animal milk products like Yogurt, Cheese, Ice and desserts, without becoming ill or having manifestations. If you are not able to produce Lactase you cannot cut Lactose into a Galactose and Glucose and that will lead to acute manifestations like: bloating, hiccups, stone-like feeling in stomach, slowed emptying of stomach and diarrhea and finally leading Leaky Gut Syndrome and inflammations and to chronic diseases. For this crucial knowledge Metchnikoff received the Nobel Prize, not just a simple award. But where do they inform you about this important information in a supermarket or in dairy advertisements or our National Health department?

Other races as Black or Africans, Asian, American Indian or Alaska natives, Hispanic or Latino, Native Hawaiian or other Pacific Islander and some Caucasian white people are NOT capable to produce this enzyme Lactase, hence they cannot digest animal milk and dairy products but who tells them!

Read more about it in Chapter 5 Food and Foodincompatibility

Level II to go deeper into Macrophages (MHC)

When a large amount of invaders enters the body the immune system detect and receives signals which alerts them and will become activated ('primed' as immunologists usually say) and macrophages get an expression class II MHC molecules in their surface and are able to function

as antigen presenting cells (APC) to show these to helper T cells. Also a number of different signals can prime a resting macrophage into action like cytokine an interferon gamma (IFN- γ) which is produced by helper T Cells and natural killer (NK) cells. It is all about alarming.

Beyond increasing inflammation (M1 macrophage) and stimulating the immune system, macrophages also play an important anti-inflammatory role (M2 macrophage) and can decrease immune reactions by releasing cytokines.

M1 macrophage have the ability to metabolize – arginine- to – nitric oxide-.

M2 macrophage can metabolize -arginine- into a repair molecule – ornithine-.

Hyperactivated macrophages also produce and secrete another cytokine a – tumor necrosis factor - (TNF), it can kill tumor cells and virus-infected cells and even help activate other immune system warriors. Inside a hyperactivated macrophage the number of lysosomes increases so that invaders can be destructed better. Hyperactivated macrophages produce – reactive oxygen molecules like hydrogen peroxide, you recognize this aggressive substance from de-colouring your hair at your hairdressor. Therefore a hyperactivated macrophage is a real killer-machine and can also become overpowered and need to be stopped by neutrophils. Neutrophils can be called foot soldiers, to kill invaders and break them like armed forces. We have approx. 20 billion neutrophils. Neutrophils live only for a short time they die by suicide called – apoptosis- after about 5 days. In contrary to macrophages they have a long life span from months to years.

1.2 The Complement system with its complement cascade (domino-effect) by about 20 different proteins is part of our innate defense system.

Level I

Our Complement system is composed of about twenty different proteins working together to destroy invaders and to warn other immune system players that an attack is going on.

The complement system is very old, even a sea urchins (Echinoidea) an simple sea-animal, which evolved about 700 million years ago have such a complement system.



Fig. 5 Sea urchins (Echinoidea)

In humans, complement proteins begin to develop in first trimester of fetal development, obvious that Mother nature wants this important system to be ready to go, even before baby is born. In case a baby is born with a defect in one of major complement proteins it will die due to infections.

The Complement system is a simple but perfect working system of defense.

At the moment an invader enters your body. An invader like a bacterium, this bacterium will be

detected immediately and a cascade of reactions (domino-effect) will be activated to unharm that bacterium. But our Complement system can also defend us against other invaders as parasites and viruses.

The Complement system is a major component of both the innate and acquired immune or adaptive systems. Complement proteins are found in normal serum.

The Complement system is activated by different pathways by enzymes

There are two innate pathways: the Alternative Pathway and Lectin Pathway.

The Complement system is also activated by antibodies bound to antigen, this is called Classical Pathway. The Classical Pathway is an evolutionary recent Pathway activated by antibodies, also called Immunoglobulins. These antibodies bound to the surface of an organism and thus works only in association with our Acquired Immune responses.

Complement components, especially C3b bind to invading microbes or bacterias and opsonize (so eat) them. Complement system may form a membrane-attack complex and punch holes in microbes. The Complement system plays a key role in triggering (activating) inflammation, by releasing a potent chemoattractant C5a. Deficiencies of some complement components lead to increases susceptibility to infections.

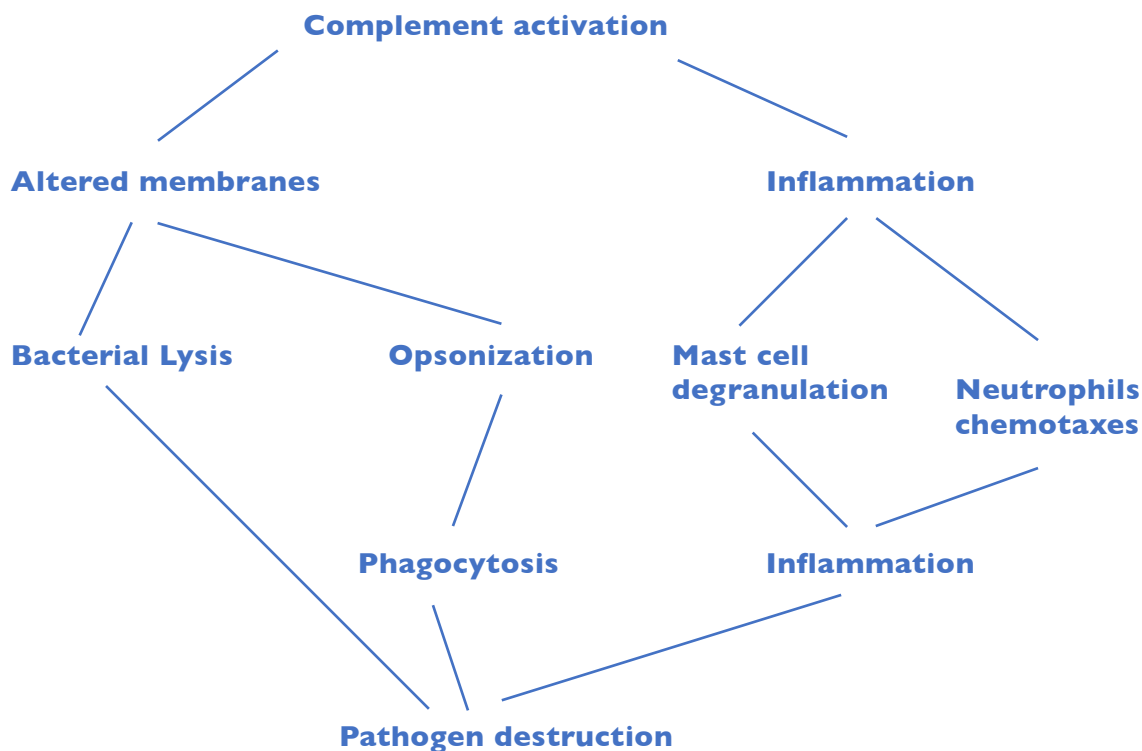


Fig. 6 The functions of the Complement system. Complement may either alter microbial membranes or alternatively trigger inflammation. Either way, it hastens the elimination of microbial invaders like bacterias and therefore it is the key player of the innate immune system.

Level I

Our complement system has three action ways.

- 1. Classical Pathway**
- 2. Alternative Pathway**
- 3. Lectin Pathway**

Each pathway activates other reactions but all three pathways will finally lead to activation of C5b-9, you will feel manifestations and become really ill and activation of C5b-9 will lead to membrane damages and DNA changes and tumors.

Level II to go deeper into Complement System and its Pathways to activate actions and deactivate by feed-backs.

The complement system must be activated before it can even function and there are three ways this can occur, in short:

1. Classical Pathway, depending on and mostly triggered by antibodies bound to the surface of a foreign organism (bacteria, viruses and parasites) and body-strange foreign substances, like food and nutrients, drugs and medication.
2. Alternative Pathway, evolved before the classical pathway. By immunologists called – antibody-dependant activation-. The proteins that make up the complement system are produced mainly in the liver and are present at high concentrations in blood and tissues. The most abundant complement protein is called C3 and in humans C3 molecules are continually being broken into two smaller proteins: C3a and C3b.
3. Lectin Pathway on pathogen surfaces activating C4

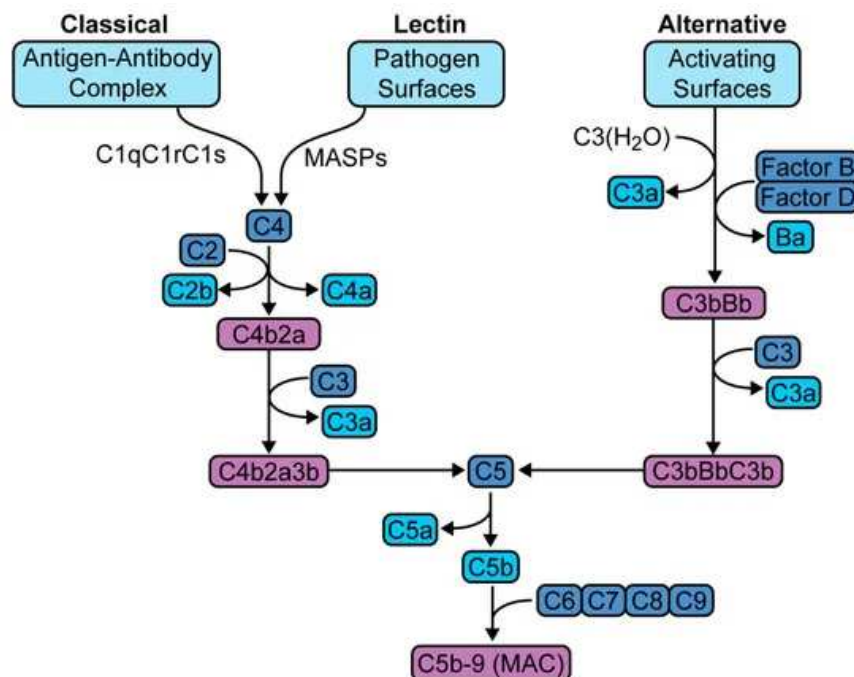


Fig. 7 Complement cascade of pathophysiology, or domino effect of your immune system, the way you will become ill at final stage of C5b-9 (MAC)

Note: What do you see?

Have a closer look and see that there 3 different Pathways (Classical, Lectin and Alternative Pathway) and all three pathways lead to C5 and then to C5b-9 (MAC). Underway to C5 you will feel manifestations sometimes mild sometimes bit more severe and then at end of cascade your immune system arrives at C5b-9 (MAC) surely then you will know 'I am ill'.

Fig. 8 Complements components and their weight and concentration in $\mu\text{g/ml}$

Complement components

Name	MW (kDa)	Serum concentrations ($\mu\text{g/ml}$)
Classical Pathway		
Clq	460	80
Clr	83	50
Cls	83	50
C4	200	600
C2	102	20
C3	185	1300
Alternative Pathway		
D	24	1
B	90	210
Terminal Components		
C5	204	70
C6	120	65
C7	120	55
C8	160	55
C9	70	60
Control Proteins		
CI-INH	105	200
C4BP	550	250
H	150	480
I	88	35
Ana INH	310	35
P	4 x 56	20
S	83	500

NB: have a closer look to these figures of Classical Pathway, what do you see?

Component C3 with a concentration of 1300 $\mu\text{g/ml}$ is most abundant in serum, probably cause this C3 is allowed to act as feed back action, to stop cascade in Classical Pathway.

You need to know too that all average concentrations are based on general situations and defined in people who could be ill due to food incompatibilities. In healthy people we see much lower C3 concentrations. We have seen that also other immune components are much lower in our patients who are on a strict diet. That is logic as to make these components you need to use stem-cells and why wasting stem-cells when it is not necessary, it is better to use stem-cells for regeneration of cells and tissues, recovery of injuries and damages, and ofcourse for anti-aging. A perfect working body and head though.

Complement activations can be activated by three different Pathways. Level II

1. Classical Pathway

2. Alternative Pathway

3. Lectin Pathway

I. Classical Pathway

Classical Pathway, depending on and mostly triggered by antibodies bound to the surface of a foreign organism (bacteria, viruses and parasites) and foreign or body-strange substances, like food and nutrients, drugs and medication. These immunological reactions to food, nutrients and drugs we call – *incompatibilities* - and -food incompatibilities -.

As this reaction is triggered by antibodies, which may occur as late as 7-10 days after contact. Once it is activated it is a very efficient complement-activating pathway.

When antibody molecules bind to an antigen they change their molecular shape and expose active sites on their Fc-regions. If several antibody molecules are bound to an organism or particle of food or drug, multiple activities will be exposed within a small area. These multiple active sites trigger Classical Complement Pathway activation.

The first component of Classical complement pathway is a multimolecular protein complex called C1. C1 consists of three proteins (C1q, C1r and C1s) bound together by calcium. C1q looks like a sixstranded whip when viewed by electron microscopy. Two molecules of C1r and two of C1s form a figure-of-eight structure located between the C1q strands. C1q is activated when the tips of at least two strands bind to complement-activating sites on immunoglobulin Fc regions. Binding to the immunoglobulin causes a conformational change in C1q that is transmitted to C1r. Resulting that C1r reveals an active proteolytic site that splits a peptidebond in C1s to convert that molecule to an enzymatically active form. Single antigen-bound molecules of immunoglobulin M (IgM) or paired antigen-bound molecules of IgG molecules are needed to activate C1. The penta-form and polymeric IgM structure readily provides two closely spaced complement-activating sites. While in contrary two IgG molecules must be located very close together to have the same effect. Therefore IgG is much less efficient than IgM in activating the Classical Pathway.

C1 may also be activated directly by some viruses or bacteria i.e. *Escherichia coli* and *Klebsiella pneumoniae*.

Activated C1's cleaves C4 into C4a and C4b. C2 then binds to C4b to form C4b2.
Activated C1's then splits the bound C2, generating a small peptide C2a and C4b2b.

C1's cannot act on soluble C2; the C2 must first be bound to C4b before it can be split up, this is another example of substrate modulation.

The C4b2b complex as described above is a potent protease (-ase- an enzyme though), that splits C3 and is therefore called classical C3 convertase (again – ase- cause it is done by an enzyme)

C3b generated in this way binds and activates C5. Subsequent reactions lead to formation of the MAC and microbial killing.

The close relationship between Lectin Pathway and Classical Pathway shows that some lectins can also activate the classical pathway. Like a lectin called specific intracellular adhesion molecule-grabbing nonintegrin (SIGN) R1 is found on the surface of macrophages binds to bacteria such as *Streptococcus pneumoniae* and so acquires the ability to activate C1 and trigger the classical pathway directly.

The consequences of complement activation are clearly potentially dangerous that all of the activation pathways must be carefully controlled by regulatory proteins: Factors, C1-INH, H and I and CD55 and CD59.

Where C1-INH is the most important one as it is able to block the activities of an active C1r and C1s. Other regulatory proteins control the activities of the C3 and C5 convertase. In example CD55 (decay accelerating factor) is a glycoprotein expressed on the surface of red blood cells, neutrophils, lymphocytes, monocytes, platelets and endothelial cells. CD55 binds to the convertases and accelerates their decay. It is necessary to protect normal cells from complement attacks. Also other proteins that accelerate degradation of the convertases include factor H and C4-binding protein (C4BP) found in plasma and CD35 (CR1) and CD46 found on cell membranes.

The C5b6789 complex is controlled and is mediated by three glycoproteins: CD59 (also called protectin) is most important, and Vitronectin and clusterin. These three inhibit C5b678 insertion and C9 polymerization in normal cell membranes. Assuming this is enough into the deep, if you like to go more broad look it up in Immunology books.

2. Alternative Pathway

The Alternative Pathway of complement activation is an evolutionary pathway that is even found in some invertebrates. It is triggered when microbial cell walls come into contact with complement components in the bloodstream and is thus a key component of innate immunity.

The most important complement protein is called C3. C3 is a disulfide-linked heterodimer with α and β chains synthesized by liver cells and macrophages and is the complement component of highest concentration in serum.

The Alternative Pathway can be activated by proteins mainly produced in the liver and are present at high concentrations in blood and tissues. The most abundant complement protein is called C3, and in the human body C3 molecules are continuously being broken into two smaller proteins: C3b and C3a.

C3b is very reactive, and can bind to either of two common chemical groups of amino- or hydroxyl groups. Cause many surfaces of invaders like bacteria consist of amino- or hydroxyl groups, there is a lot of work for these C3b molecules. If C3b is not able to react within 60 microseconds it is neutralized by binding to a water molecule, and its attack is over. Therefore C3b has to be close to the surface of the invading cell to set on the Complement cascade.

Once C3b is reacting with a molecule on cell surface another complement protein B binds to C3b and complement protein D comes along and hold off part B to yield C3bBb.

Once a bacterium has this C3bBb molecule fixed to its surface, the game begins, cause C3bBb acts like a 'saw' that can cut and connect other C3 molecules which are close in the area (convertase) so is very efficiently. In this way it can bind to many amino- or hydroxyl groups on surfaces of bacteria. All this attacking and cutting sets up a positive feedback loop, and become a snowball effect and complement cascade goes on as C3bBb and C3b can grab protein C5 and cut it into two pieces: C5b which can then combine with other complement proteins (C6, C7, C8 and C9) to make a membrane attack complex (MAC) and can anchor the complex in the bacterial cell membrane. These C9 proteins are able to make a channel to open up a hole in the surface of bacterium. As soon as a bacterium has a hole in its surface it is a delicious snack, to

be eaten up. Our complement system can also defend us against viruses and parasites in the same way.

You now probably think why our complement is not enough for our defense? Well Mother Nature was not sure about that as so many proteins in a body is not easy to control and C3b fragment can also easily bind to a protein in the blood and can fix to the surface by an enzyme MCP that is present on the surface of human cells. Or can accelerate destruction of convertase by Decay Accelerating Factor (DAF) and destruct other blood proteins. And this will block the positive feedback loop to start up. For that reason we have another cell-surface protein CD59, called protectin, these security-guards prevents the incorporation of C9 molecules into nascent MAC's. This knowledge is important in cases of a transplantation of an organ of an animal instead of a human organ (xeno-transplantation)

Xenotransplantation (*xenos*- from the Greek meaning "foreign" or strange, or heterologous transplant, is the transplantation of living cells, tissues or organs from one species to another. Such cells, tissues or organs are called xenografts or xenotransplants.

It happened once in a surgery of a baboon, who received an organ of a pig, when baboon's immune system started up immediately and attacked the organ, within minutes this pig organ became a bloody pulp. Caused by complement system, as the pig version of DAF and CD59 is not compatible to control a primate complement. Conclusion the complement is working very fast and attacks any invader with a surface of amino- or hydroxyl group. Besides this can happen to any cell surface which is not protected so Mother Nature knew that very well that our complement system is not enough.

3. The Lectin Pathway

Next to Classical Pathway (by antibody-dependant) and Alternative Pathway (by anti-independant) there is a Lectin Activation Pathway. This third pathway may be even the most important activation pathway. The central player is a protein that is produced mainly in the liver, and is present in blood and tissues. This protein is called mannose-binding lectin or MBL.

This lectin protein can bind to a carbohydrate molecule and as mannose is a carbohydrate molecule and can be found on the surface of many pathogens, like MBL can bind to yeasts such as *Candida albicans*. But also to a HIV-I virus and Influenza viruses. And to bacteria like Salmonella, Streptococcus, and to parasites as Leishmania. At other hand MBL does not bind to carbohydrates on healthy human cells and tissues. That is an important strategy carried out by the innate system, as innate system mainly focuses on patterns of carbohydrates and fats found on surfaces of common pathogens but not on surfaces of human cells.

The Mannose-binding lectin activates complement system in the blood by binding a MBL to a protein MASP, and when the mannose-binding lectin grabs its target (mannose on the surface of a bacterium) the MASP protein functions like a convertase to clip C3 proteins to make C3b. And C3b can bind to the surface of the bacterium and the complement chain reaction will be stopped.

So the alternative activation pathway is spontaneous and can be set on randomly like a 'mine' to destroy any unprotected surface, but lectin activation can be seen as a 'smart bomb' that are targeted by mannose-binding lectins.

Other complement system functions

The complement system has two other important functions besides membrane attack complexes. When C3b has fixed itself on to the surface of an invader it will produce a serum protein of a smaller fragment: iC3b. The -i- prefix means that this cleaved protein is inactive for making MAC's, but will be stayed attached to the invader and can prepare invader for phagocytosis, to be opsonized (eaten up)

by antibodies. On the surface of phagocytes like macrophages are receptors that can bind to iC3b and will facilitate phagocytosis. Reason why many invaders do have a slimy surface to try to become slippery to make binding more difficult. However when these slithery invaders are coated with complement fragments phagocytosis is even more easy. So its second function is to 'paint' the surface of invaders to easy opsonization.

The third function of complement system is that the fragments of complement proteins can act as chemoattractants, chemicals that recruit other immun system players to battle and attack. Like C3a and C5a are parts of C3 and C5 that are clipped off when C3b and C5b are produced, never spoil rich elements or fragments! Especially C5a is a powerful chemoattractant for macrophages, and can activate them to become strong killers. These C3a and C5a are also called anaphylatoxins, cause they can contribute to anaphylactic shock in an allergy.

Thus complement system is a very multifunctional system it can destroy invaders by building membrane attack complexes, it can tag invaders for destruction and phagocytes and warn other cells that we are under attack and can direct them to the battlefield and activate them to destruct, and that all even very fast within minutes.

Phagocytes

Phagocytes is an important arm of innate system, it is their main task to eat up invaders, the most important phagocytes are macrophages and neutrophils.

Macrophages

Macrophages are found under your skin, where they protect you against invaders which are penetrated into the body through the skin, i.e. by a wound or burn. Macrophages are also present in your lungs, to protect you against inhaled microbes. And they are abundantly in the tissues that surround your intestines, waiting for microbial invaders you have ingested.

Macrophages can have three stages of readiness. In tissues they are usually just relaxed waiting and have a slow proliferation. In this state they are function primary as garbage collectors, keeping our tissues free of debris from continuous dying cells of more than a million a second in a adult human being it is still though a lot of work. Dying cells give a signal to macrophages to attract them and – eat me up please- by a signal on their surface of dying cells. Or they warn macrophages that they are only resting by expressing a very few class II MHC on their surface, like a flag - leave alone I am resting- and presenting antigen to helper T cells will not come into action. Macrophages only live for a couple of months in tissues and in healthy humans do not have a lot of work to do until they get warned that the barrier defense has been penetrated, then they come into action, they get primed as immunologists say. At that moment macrophages will produce class II MHC molecules and can function as a antigen presenting cell and activate helper T cells to recognize invaders.

A number of different signals can prime a resting macrophage but from studies we know that cytokine called Interferon Gamma (IFN- γ) mainly produced by helper t cells and Natural killer cells (NK) is able to set such activation on rapidly.

Sometimes a hyperactivation can occur, when macrophages receive a signal from an invader by a molecule called Lipopolysaccharide (LPS), a component of outer cell membrane of Gram-negative bacteria such as Escherichia Coli (E. Coli) when it detects this bacteria it will stop proliferating process immediately and switch on to a killing mode. In this state macrophages will become larger and more phagocytic so that they are able to eat up even bigger invaders like parasites. Hyperactivated macrophages also produce and secrete another cytokine called Tumor Necrosis Factor (TNF). This cytokine can kill tumor cells and virus infected cells and can help to activate other immune system soldiers.

Inside of a hyperactivated macrophage the number of lysosomes increase and destruction of ingested invaders becomes more efficient. Although hyperactivated macrophages will produce more reactive oxygen molecules such as hydrogen peroxide, you know this substance of bleaching and discolouring your hair and how aggressive it is. Indeed a hyperactive macrophage is a real killing machine.

All actions happens in sizes and level of forces, all depends on the type and strength of activation signals what is necessary.

Neutrophils

In our veins and arteries circulate about 20 billion of neutrophils, they only live for a short time and have to set on to die after approx. 5 days, and can be seen as foot-warriors, their only job is to kill and to break down stuff on call. Neutrophils are produced in bone-marrow. When they get released from the blood it takes half an hour to become activated and then they are very phagocytic.

Neutrophils also produce cytokines like TNF to alert other immune system cells and can produce destructive chemicals which they keep inside the cell, and can turn tissues into a toxic substance to kill microbes. They are the only ones that are allowed to liquify both cells and connective tissue by creating pus.

1.3 Adaptive or acquired immune system, our defense system that can adapt so can learn day by day to become better and better in defending us. You were not born with a complete Adaptive Immune system, however you will get some antibodies of your mother during pregnancy by placenta (passive immunity) and by gene segments on DNA. However passive immunity provides only a temporal immunity of several weeks to months. Babies own immune system will start up to make own antibodies after 7-8 months.

Level I

For most animals the innate immune system is enough to defend them, however vertebrates, like us, Mother Nature gave us also an adaptive immune system, probably first designed to protect us against viruses, as innate system was not that effective against viruses.

As Bacteria multiplies rapidly the innate system is not fast enough, in fact a single bacterium can double their number every 30 minutes so roughly 100 trillion bacteria in one day, then we are really in big trouble. Besides microbes like viruses and bacteria are always mutating, so they change their 'outlook', and your immune system cannot recognize them anymore. Reason why your immune system has to learn to adapt itself to re-recognize them again. Just as mutations in bacteria can render them resistance to certain antibiotics. Mutations also can change microbes in ways that make them better able to resist immune defenses. Your immune system has to create new counter-weapons to be able to keep the mutated microbe from taking over. For millions of years our immune system and that of animals has to learn to upgrade immune responses to these mutated (changed) microbial attackers. This adaptive immune system started to become upgraded in fish, but in humans the ultimate innovated defense system was created. A smart immune system that can adapt to deal with each unusual invader, to defend ourselves against a specific invader, without we cannot survive.

The adaptive or acquired immune system is defending against one specific invader, by using antibodies. To attack one specific virus you need one specific antibody. So an antibody is not a multitasker. Whereby the agent that caused the antibodies to be made was called an antigen. So an antigen makes an antibody. We call an antibody also an immunoglobulin.

Antibodies are Immunoglobulins (Ig's), consisting of one heavy chain (Hc) and two light chains (Lc) working like 'arms and hands' to bind to antigens.

B cells and antibodies

The most important components of adaptive immune system is a B cell. We call it a B cell because it is 'born' in Bone marrow. Like all other blood cells B cells are born in the bone marrow, where they descend from stem cells. Each day we produce more than a billion B cells and that during our entire life of a human. Even elderly people do so, they also need to make fresh B cells every day.

During their early days in the bone marrow B cells select gene segments coding for the two proteins that make up their B cell receptors (BCR's) and those receptors take up their positions on the surface of the B cell. The antibody molecule is almost the same as the B cell receptor, except that it lacks the protein sequences at the tip of the heavy chain which anchor the BCR. In this way the B cell is able to fix to the B receptor. If it does not have this anchor the antibody molecule will leave the B cell and is free to travel around the body to do what it has to do.

How do newborn babies get their passive immunity of antibodies?

Immunity in newborn babies is only temporary and starts to decrease after first few weeks until couple of months. Babies can also inherit antibodies against nutrients of food, we call it a food incompatibility. Babies receive these antibodies of IgG classes (IgG1, IgG2, IgG3 and IgG4) by placenta of their mom, see fig. 10 passage by placenta, further on in this chapter.

These inherited antibodies can be temporal but sometimes their own immune system takes over and will copy these antibodies and become permanent. This passing over can happen by placenta during pregnancy in last trimester of pregnancy and by gene segments on DNA.

As in our research we test babies by their umbilicus blood to define their first inherited incompatibilities and after 7 months we test them again with their own venous blood and this is how we were able to determine which antibodies are inherited or which are produced later by their own immune system. Very interesting though.

We had even the richness to test babies at birth and later at 7 months and older of families from 3 to 5 generations so we obtained a lot of knowledge and a good vision on inherited antibodies thus to their inherited food incompatibilities.

When baby reaches 8 months their own immune system is mature and ready to take over its own defense and is able to produce antibodies themselves.

Breast milk especially colostrum, the first mothermilk, contains antibodies, therefore breastfed babies have a longer period of passive immunity. Premature babies are at higher risk of developing an illness because their immune system is not yet as strong as it needs to be as they did not receive enough antibodies as they were born too early, as these antibodies are brought over from mother to fetus by placenta during last three months of pregnancy.

Mothers can pass their immunity over to their babies during last three months of pregnancy, this is passive immunity, for that reason it is also important to vaccinate mothers during pregnancy like against whooping cough (Pertussis) as whooping cough is very dangerous for babies, they

become dyspnea and most babies need to be hospitalized.

At end of 7 months babies own immune system will start up making own antibodies against invaders like viruses for that reason babies need vaccinations. But babies will also start up to make own antibodies against nutrients in food and drugs / medication, there is no possibility to prevent that to happen and babies get manifestations and symptoms and get ill and will get acute and or chronic diseases like gastroparesis, eczema, asthma and bronchitis.

Read more about food incompatibilities in Chapter 5.

Level II

How do we get our gene segments?

Lets get closer to the process of selecting gene segments to make a B cell receptor.

The B cell receptor is made up of two kinds of proteins, the heavy chain (Hc) and the light chain (Lc) and each of these proteins is encoded by genes that are assembled from gene segments inherited of your mom and dad.

The gene segments that are chosen to make up your final Hc gene are located on chromosome 14. And each B cell has two chromosomes 14's one from your mom and one from your dad. At moment of conception, when the sperm (spermatozoid) from father enters the egg (ovum) from mother, this selection of segments are made, which of our four separate gene segments: D, J, V or C segment will be chosen. Immunologists call this joined-together gene segments a – gene rearrangement-. This rearrangement is about cutting and pasting to create the best one. It is almost like a 'game', which chromosome 14 wins, and the winning chromosome 14 is used to construct the winning Heavy Chain protein so Hc protein. This Heavy Chain protein is then transported to the cell surface, where it signals to the losing chromosome that the game is over. How it does stop this game over is not yet discovered, so we still need more research. Until now we assume it has something to do with changing the conformation of the cells's DNA so that it is no longer accessible to the cut-and-paste process.

Well then you think what happens if both chromosomes fail to assemble gene segments to set a productive rearrangement? Then this B cell commits suicide, called apoptosis.

As the whole completed Heavy Chain and Light Chain must fit together perfectly to make a complete antibody. If it fails, so Hcs and Lcs donot match together correct way, the B cell commits suicide.

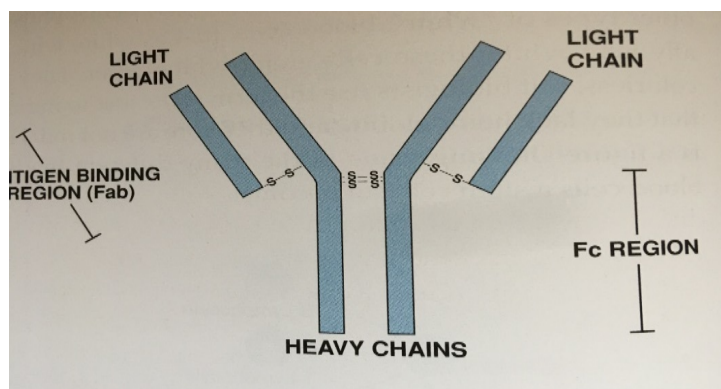


Fig. 8 An Immunoglobulin consists of one heavy chain and two light chain

How B cells are activated?

B Cells must be activated first to be able to produce antibodies. Most B cells have never encountered their cognate antigen, we call these 'naive or virgin' B cells. In the situation a B cell recognize a smallpox virus in a human who never had been exposed to smallpox. At the other hand B cells that did have such an exposure before and do have a their cognate antigen, these we call 'experiences' B cells. There are two ways that such naive B cells can be activated to defend us against invaders. One is completely dependant on the assistance of Helper T Cells (T cell-dependant activation and Th cell). These naive B cells then need two signals: one signal of the clustering of B cell's receptors and their associated signalling molecules. And a B cell second signal is needed. Immunologists call that – co-stimulatory- signals. The best-studied co-stimulatory signal involves direct contact between a B cell and a TH cell, on the surface of a activated Th cells are proteins called CD40L. When such a CD40L plugs in to a protein called CD40, on the surface of a B cell, the co-stimulatory signal will be sent and B cel gets activated. This interaction bewteen CD40 and CD40L is very important fro B cell activation. People with an genetic defect in one of these protein are unable to sets on a T cell-dependant antibody defense.

Level I

T cell comes from Thymus, as these T cells are produced in your Thymus, an organ. Your Thymus is a small gland in the lymphatic system that makes and trains special white blood cells called T cells. These T cells will help your immune system to defense you against diseases and infections. Your Thymus gland produces most of your T cells before birth. The rest are made in childhood and you will have all the T cells you need for whole life by time you reach puberty.

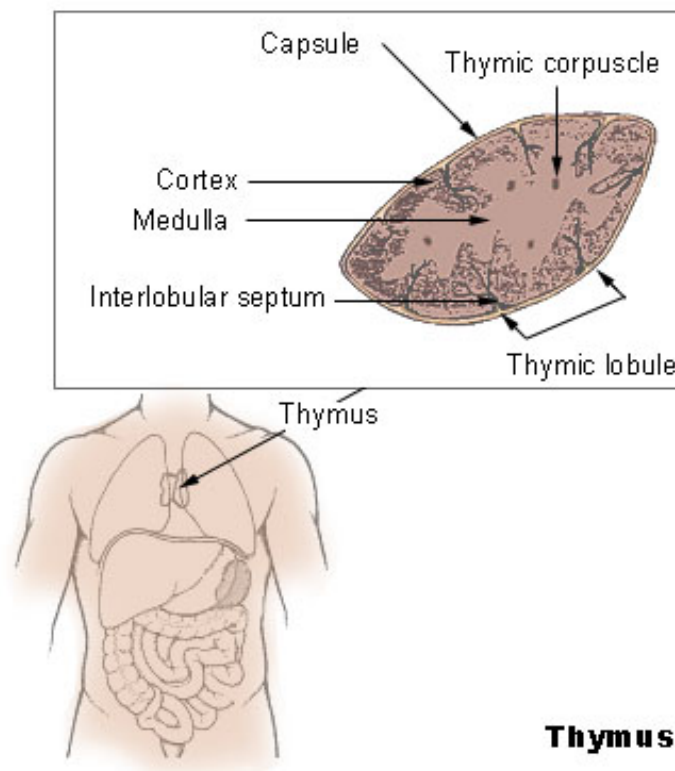
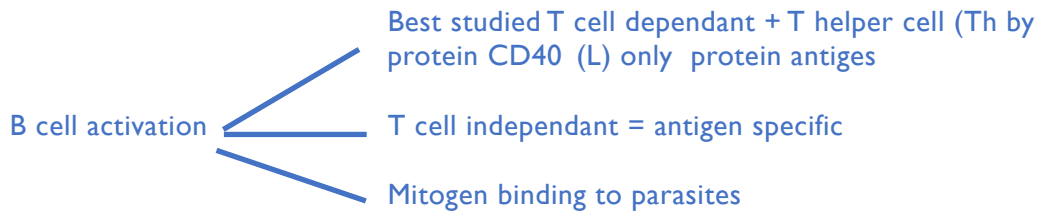


Fig. 9 Thymus gland of the lymphatic system.

B Cell Activation



If all B cells would need T cell help, the entire Adaptive system would be focused on proteins. By allowing some antigens to activate B cells without T cell help, Mother Nature did a perfect action and increased the universe of antigens to come into action also to non-proteins, like to carbohydrates and fats. Mitogens are immunologist's favorites as they can be used to activate B cells and hence easier to study.

Once B cells are activated and have proliferated to build up their quantity, they are ready for the next stage of Maturation in three steps:

- 1. Class switching**
- 2. Somatic hypermutation**
- 3. Career decision, to decide to become an antibody factory (a plasma cell) or a memory B cell for the future.**

Class Switching

When a virgin B cell is activated for the first time it produces mainly IgM antibodies. B cells can also produce IgD antibodies. We did not discover yet what is its function. Although IgM and IgD share the same Heavy Chain messenger RNA (mRNA).

B cell has the opportunity to change the class of antibody: IgG, IgA or IgE. By cutting and pasting it can change and is located on chromosome 14.

An IgM antibody is like a five-fold IgG antibody molecules, all fixed together.

Producing a huge amount of IgM antibodies in infections is very clever, because IgM antibodies are very efficient in activating the Complement cascade, immunologists call this 'fixing complement'. And they are good in neutralizing viruses too, by binding and preventing them from infecting cells, thus IgM is the perfect antibody to defend against viral and bacterial infections. From my research I know IgM is also triggered to come into action against yeasts like *Candida albicans*. However IgM cannot eliminate nor kill yeasts, however that situation can lead to an excessive and overproduction of IgM, finally this overproduction can cause misformed IgM productions. Discovering that, our hypothesis is there is maybe even a relation to M-protein in Waldenström, as that is what we noticed in our Waldenström patients. More research is needed.

1.4 Immunoglobulins

The immune system with its immunoglobulins has a hierarchic structure, like an army from foot-warriors to general, whereby each type of immunoglobulin has a specific task and authority.

Overview: most important functions of humane antibodyclasses and subclasses and their specific tasks and authority

Effectorfunctions	Immunoglobulins							
	IgG I	IgG2	IgG3	IgG4	IgM	IgA	IgD	IgE
Complement fixation by Classical Pathway	++	+	+++	-	+++	-	-	-
Passage by placenta	+	+	+	+	-	-	-	-
Binding to Staphylococcus protein A	+++	+++	-	+++	-	-	-	-
Binding to Staphylococcus protein G	+++	+++	-	+++	-	-	-	-

Fig. 10 Shows the hierarchic structure of immunoglobulins: only IgG3 and IgM have the main authority to activate Complement fixation, whereby IgG1 and IgG2 have less authority:

IgG1, IgG2, IgG3 and IgG4 are only able to pass placenta to foetus and new born baby. Notice also that IgG3 has NO task in defending against bacterium Staphylococcus, for that task there are foot-warriors IgG1, IgG2 and IgG4, thus we may conclude IgG3 is the leader in hierarchy and may be called the general.

What else shows this overview of fig 10 to us?

- IgG3 has the maximum authority to activate Classical Pathway, reason why we call it The General. Whereas IgG1 and IgG2 have less authority to activate Classical Pathway, call these two Secondants.
- IgE the one we know in relation to an onset of allergy, seems not so important in hierarchic way, cause IgE is not allowed to pass placenta, hence an allergy is not inherited by IgE nor is an IgE authorized to activate complement-fixation, so may not start an immunological cascade-effect in case of an invader or body-strange-substance. Eventhough allergists keep on saying that an allergy can be inherited, there is no prove.
My thesis is that baby's get their Gene-segments, Classical Pathway from their parents and IgG1, IgG2, IgG3 and IgG4 from their mother, and these primary reactions due to food incompatibilities can finally activate secondary reactions like an allergy (IgE mediated) and intolerances (IgA mediated).
Read more about it in Chapter 5 Food incompatibilities.

NB: Further you can see that IgM is not able to pass placenta to a foetus and new born baby, this is because IgM is a 'big' pentamer, a 5-arms form immunoglobulin, due to this penta form IgM is not able to pass intestine-barrier (unless in case of a Leaky-Gut-Syndrom), and with this penta form it is able to fold around and to grab and hold an invader in intestine.

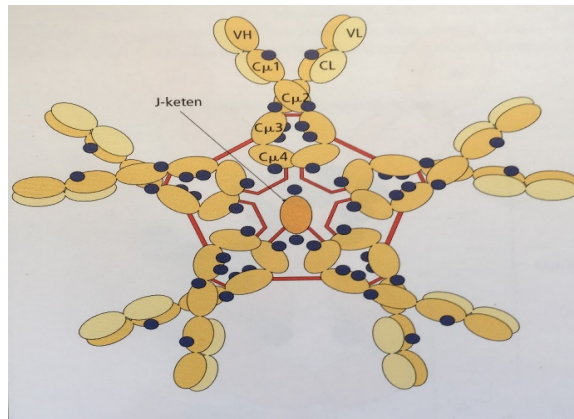


Fig. 11 IgM is a pentamer, present in intestines and its gene segments

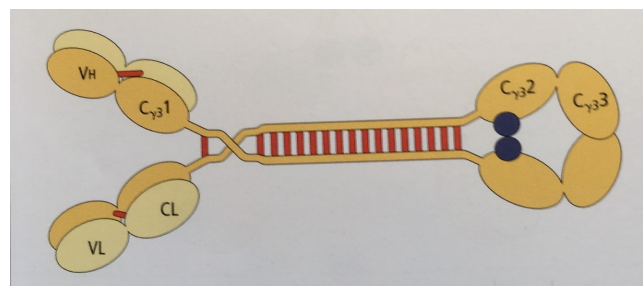


Fig. 12 IgG3 has a prolonged hinge-area, that provides it a more molecule-weight and possibly increased biological activity.

Cell mediated responses, chronic inflammation and auto-immune diseases

Level II

In cell-mediated responses can be pointed against auto-antigen or unidentified hidden infections or commensal individuals like *Candida albicans* a yeast and fungus but can also cause chronic tissue damages like Rheumatic Arthritis, Crohn Disease, Sarcoidose, Psoriasis and Multiple Sclerosis and even have a role in auto-immunity as in 'destruction'*) of Islands of Langerhans in Pancreas and individual becomes insulin- dependant in Diabetes Mellitus type I.

*) We rather speak about – dormant- cells and tissues, so sleeping cells and tissues as that proces is reversable by regeneration when patient follow up a strict diet of only compatibel food, beverages, creams and shampo according Medisynx Method.

Not to spill a huge amount of biological 'energy' Mother Nature evolved a multilayered system in which layer includes mechanisms that should swipe out most self-reactive cells, with lower layers catching cells that slipped through layers above. Normally that strategy works well but occasionally there is so much chaos and panic in the body due to presence of too much incompatibilities like food incompatibilities causing 'mistakes will be made', and instead of defending us against frein invaders our weapon of immune system are turned back on us on our own tissues. Autoimmune disease results when such breakdown in the mechanisms fails and causes a pathological condition itself.

NB Recently in the scientific magazine *The Lancet* is published that 22 million of people worldwide, so one on ten people, suffer from some form of autoimmune disease (publication of Nathalie Conrad, PhD of 3rd of June 2023)

Despite in what is postulate in medicine that autoimmune diseases are chronic, we demonstrated that a diet based on only compatible nutrients and specific acupuncture according Medisynx Method to clean up and to reset immune system is significant effective, curatively and preventively. See also Chapter 5 Food incompatibilities.

1.5. Cytokine Network

The Cytokine Network is a complex communication network, the research of molecular genetics brought a lot of insight in this specific network and its possibility to a genetic 'knock-out' of a cytokine or a receptor in a mouse, that provide that all noses in unity into same direction. Especially important to understand immunity and inflammations.

Some cytokines like IL-7 (Interleukin 7), TNF-alpha and TNF-beta (called lymphotoxine) are important for development of the immune system before birth. These cytokines have direct effects on Hypothalamus, Hypophyse and adrenal-ax and is used by nerve-system too, the ax nerve system and endocrine system. Absent of others i.e. IL-2, IL-4, IL-12 and IFN γ shows clearly that and individual with an infection comes under stress.

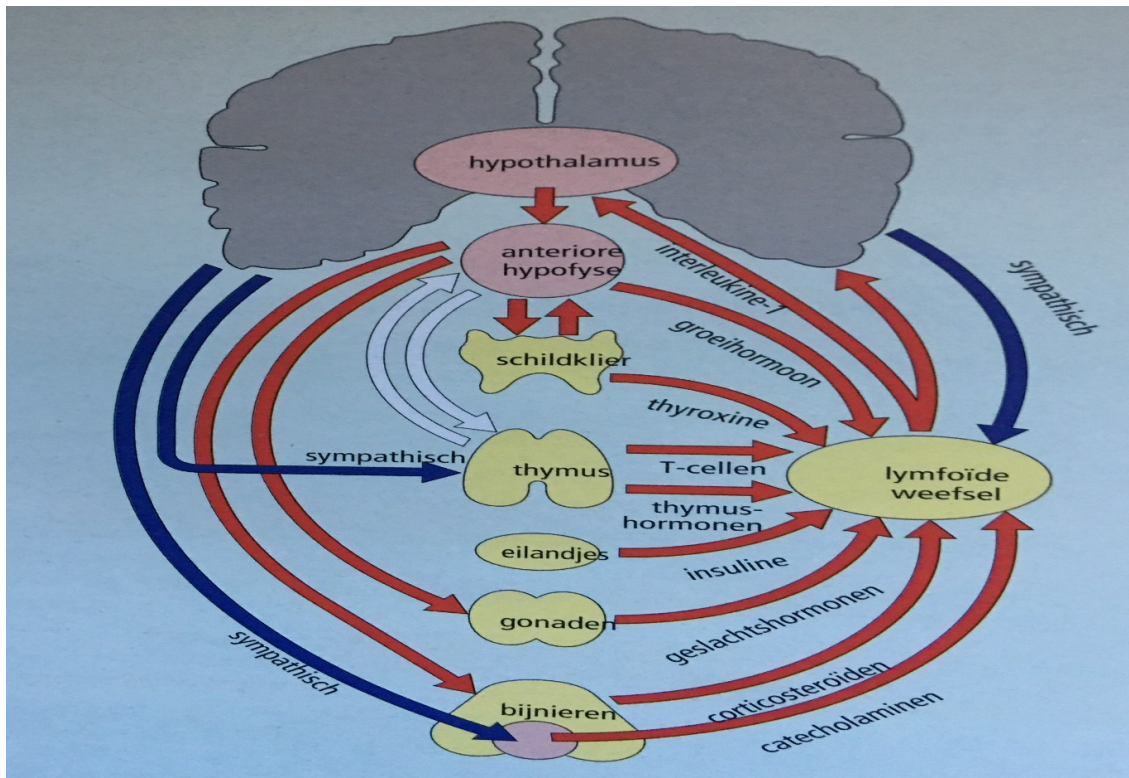


Fig. 13 Neuro-endocrine interactions with immune system: blue arrows shows nerve-connections, red arrows are hormonal interactions and white arrows are not determined definitely, but probably induced by lymphatic system, as Thymus is a lymphatic organ.

1.6 Cell-mediated immunity is the base of our defense of skin

Response against bacteria can result into immunological tissue damage and over-activating cytokine release can lead to an endotoxic-shock. Endotoxine (septicemic) shock will occur if an enormous production of cytokines take place, mostly due to Gram-positive bacterias, causing a life-threatening fever, circulatory collapse, diffuse intravascular coagulation and hemorrhagic necrosis, finally to organs failures.

Also invasion of yeasts and fungus (mycoses) can lead to cell-mediated immunity and responses.

1.7 What happens when your immune system comes into contact with an incompatibility, by food and nutrients, or drugs and medication?

Level I

Your immune system has detectors everywhere, at all entrances from skin to mouth, to protect you against invaders of bacteria and viruses and incompatibilities, as these are body-strange foreign substances, thus dangerous for our health.

When an incompatible substance is detected by your immune system you will feel it. You will feel manifestations and symptoms as soon as it gets into contact with your skin, mouth, nose, eyes, respiratory system (by breathing in to your lungs), Gastro-Intestinal tract (so into your oesophagus, stomach and intestines), and or urogenital system (so your vagina, penis, bladder and kidneys). Thus by all openings of your body.

First you will notice vague to more heavy Non-Systemic manifestations, these are acute manifestations like hiccups, bloating, choking, coughing, pressure or stone feeling in your stomach, nausea, vomiting, no appetite, anorexia, diarrhea, cramps in intestine (Irritated Bowel Syndrome / IBS), need to urinate very often (polyuria and pollakiuria), arrhythmias or extra systoles of your heart, itching in your ears, and more.

The timeline of Non-Systemic manifestations runs from a few seconds up to 8 weeks. During these 8 weeks you notice several different manifestations. Each incompatibility will give you a pattern of manifestations and in a personal time line.

These incompatibilities and undigested food in your small intestine will cause accumulation of waste products. This will cause maceration, your wall of the fingers of your small intestine (gut villi) becomes weak and more permeable, we call this a Leaky Gut Syndrome and leads inflammation of gut wall, that means your intestine is not absorbing only essential nutrients but all incompatibilities and pathogens will leak into your system. This will lead to Systemic manifestations and Systemic- and chronic diseases.

When these incompatibilities leak into your body and become systemic. These incompatibilities will pass your small intestine into the system and become systemic and at that moment your immune system will activate a cascade of immunological secondary reactions, we call these Systemic manifestations and will lead to systemic- and chronic diseases, DNA mutations, tumors and ageing and fast degenerating cells.

More about this in Chapter 5 Food incompatibilities.

Have a close look to this schedule of Fig. 14, below, it all starts with an invader such as also an incompatibility. This incompatibility will be detected by your immune system and activates two reactions:

1. IgG3 activation, and this IgG3 will then activate secondary reactions by Complement activation to Alternative Pathway and Classical Pathway to C5b9 causing Systemic manifestations and pathogenesis (route to make you ill) of chronic diseases, inflammations, tissue damages, auto-immune reactions and diseases and activation of immune elements.
2. IgG2 and IgG1 detects incompatibility that activates B7 on surface APC inducing allergy reactions and CD28 activation and it can activate Th0 to Th1 to start up to stimulate Growth factor CTL and NL cells, B cells switch to IgG3, activate macrophages and NK cells causing leaking blood vessels into tissue, edema and septic shock.

In short when your immune system detects an incompatibility that comes into contact with your skin or enters into your body it will immediately activates immunological reactions. You feel these reactions right away, within seconds to minutes but some also after 6-8 weeks. However you are not aware this is coming from your delicious food or drink or from your medication. Read more about in Chapter 5 Food incompatibilities.

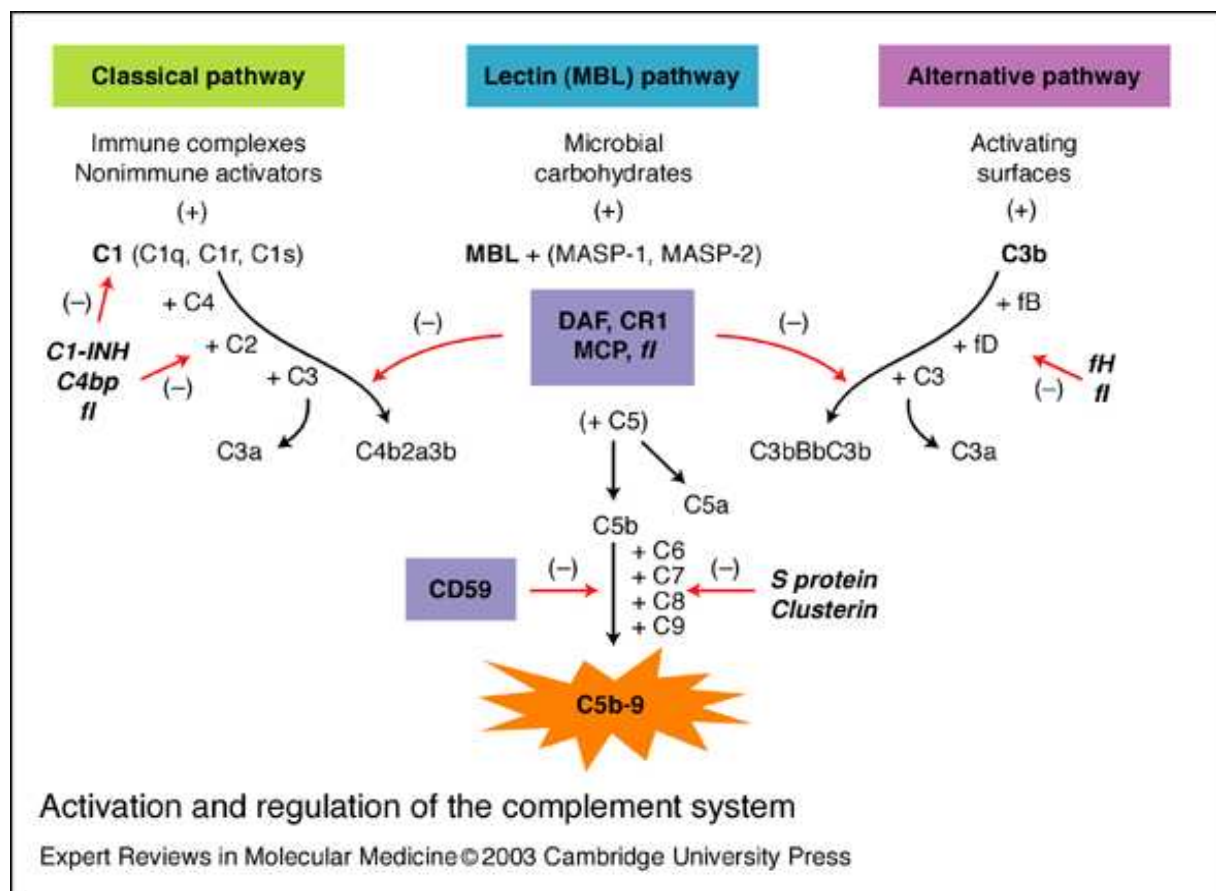


Fig. 14 All three Pathways lead to **C5b-9**

Time Line from Day 0 to 8 weeks

NON-Systemical manifestations and diseases

Systemical diseases and manifestations

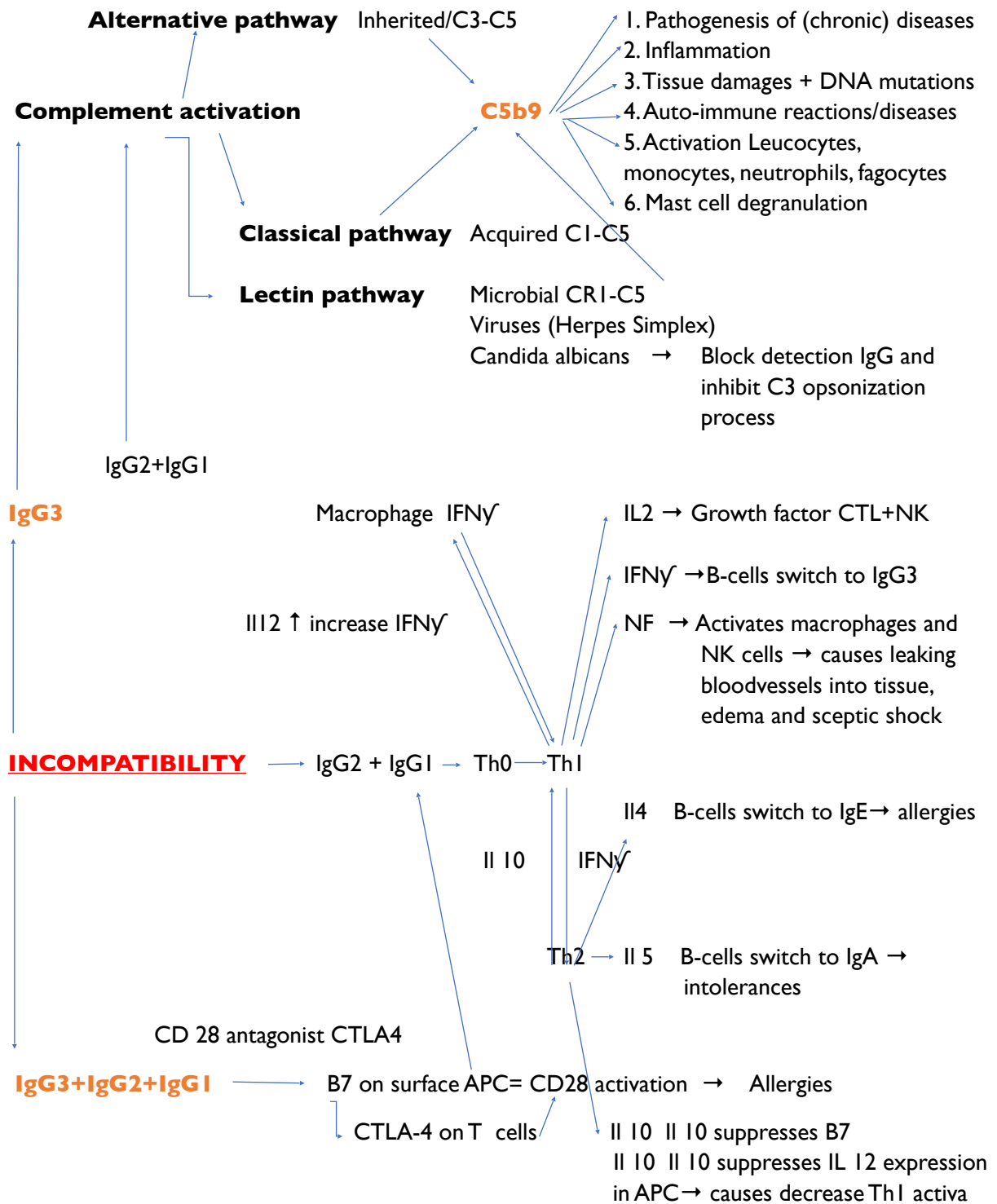


Fig. 15 Schedule and time line of Non-Systemical manifestations to Systemical manifestations and diseases in only a few seconds until 8 weeks later.

What do you see in this Time Line?

At the moment of Day 0 you come into contact with an incompatibility you feel reactions, called manifestations or symptoms. Such a reaction can be innocent like bit of itch of your nose or in your ear or stomach reflux. However when the pathway get activated you will feel bit more severe manifestations like a nose bleeding (Epitaxis), dyspnea, arrhythmias or extra systoles, but it can even lead within seconds to very severe manifestations like choking, severe arrhythmias, when your heart starts to beat irregularly. And can even lead to a Cardiac Arrest, your heart stops beating suddenly and that is fatal.

We have seen a Cardiac Arrest to happen even in healthy professional sporters, like Abdelhak Nouri, a football player of Ajax encountered in 2017, when that happened Ajax' medical team did not act immediately to start to use a defibrillator and that caused hypoxia in the brains, with serious brain damages as consequences. Five years later Nouri made a little progress and his family found a way to communicate with him but almost certain he will never come back to how he was.

This Cardiac Arrest can be caused due to a food incompatibility, therefore it can happen to everybody at any time even with a good healthy condition. And after such an incident we cannot proof what is the exact cause, and the conclusion will be it is Idiopathic. However from our clinical research we know a food incompatibility can cause such heavy arrhythmias and extra systoles and indeed even a Cardiac Arrest.

What does B7 protein do in this schedule?

Level I

B7 is a protein that is on the surface of an Antigen Presenting Cell (APC). Of all cells of immune system this APC is an important cell of Adaptive Immune system, a self learning immune system. These APC's present an antigen to T cells and therefore they play an important role, a central key role in a cascade of immunological reactions.

This B7 protein can be activated by a T helper cell (Th cell) such in case of contact to an incompatibility and or food incompatibility. This T helper cell will set on a secondary reaction after contact with an incompatibility. IgG3, IgG2 or IgG1 will activate B7 and that sets on an allergy reaction, whereby mastcells starts to release - *histamine*- . Histamine causes the widening of blood- and lymph vessels to try to drain these incompatibilities away and spread it as soon as possible. But this widening (dilatation) causes an uncontrolled rapid blood pressure drop, what we call an anaphylactic shock. That can even be fatal. This is why allergy patients always need to have an Epi-injectionpen with them to inject Epinefrine (Adrenaline) as soon as possible to raise blood pressure again.

Level II

Antigen Presenting Cells (APC)

Before a killer T cell can even kill or a helper T cell can even help, it must be activated.

First a T cell must recognize its cognate antigen presented by an MHC molecule and need a second co-stimulatory signal. Only certain cells are equipped to provide both class I and class II MHC display and co-stimulating.

Cause these APC are to activate killer T cells and helper T cells, we call them T cell-activating cells. The term antigen presenting cells always refers to those special cells which can provide the high levels of MHC and co-stimulatory molecules required for T cell activation.

To Co-stimulation is often a protein B7 involved. This B7 on the surface of an APC can plug into a protein called CD28 on the surface of a T cell.

There are three (3) types of Antigen Presenting Cells:

- activated dendritic cells (DC) and can initiate immune response by activating virgin T cells. Also dendritic cells express some B7 and relatively low levels of MHC molecules on their surface. A dendritic cell can check about 500 T cells per hour; a complete activation of a naive T cell takes between 4-10 hours. Although mature dendritic cells express MHC and co-stimulatory molecules like B7, when they first enter lymphnode the expression level of these proteins increases when CD40 proteins on the APC are engaged by CD40L proteins on a Th cell. Besides that a dendritic cell's CD40 can cause the DC to secrete cytokines, like IL-12 and can prolong the lifetime of a dendritic cell. That provides that dendritic cells are presenting a T cell's cognate antigen and can stay long enough to activate a lot of T cells. Hence DC and T cells are working mutually.
- activated macrophages, these are very adaptable cells which can function as garbage-collectors or antigen presenting cells or strong killers, depending on the signals they receive from their micro-environment where they stay as they do not travel. They are soldiers who must wait on one spot and fight there.
- activated B cells., this one is not as good in antigen presentation, cause it only expresses a low level of class II MHC molecules and a little or no B7. However once a B cell has been activated it will increase levels of class II MHC dramatically, by proteins on its surface. In a serious danger B cells they can play an important role and they can concentrate antigen for presentation. After a B cell's receptor has bound to their cognate antigen, the whole complex of BCR plus antigen is removed from the cell surface

These three types all originate from a white blood cell produced in bone marrow. From there they migrate in to the rest of the body and first need to be activated to come into function. As new blood is made continuously also APC's need to be replenished as well.

We did broad research to B7 proteins.

B7 is a type of integral membrane protein found on activated antigen-presenting cells (APC) that, when paired with either a CD28 or CD152 (CTLA-4) surface protein on a T cell, can produce a co-stimulatory signal or a co-inhibitory signal to enhance or decrease the activity of a MHC-TCR signal between the APC and the T cell, respectively. Binding of the B7 of APC to CTLA-4 of T-cells causes inhibition of the activity of T-cells.

There are two major types of B7 proteins: B7-1 or CD80, and B7-2 or CD86. It is not known yet in how far they differ significantly from each other. So far CD80 is found on dendritic cells, macrophages, and activated B cells, CD86 (B7-2) on B cells. The proteins CD28 and CTLA-4 (CD152) each interact with both B7-1 and B7-2.

There are several steps to activation of the immune system against a pathogen and food incompatibilities. The T-cell receptor must first interact with the Major Histocompatibility Complex (MHC) surface protein. The CD4 or CD8 proteins on the T-cell surface form a complex with the CD3 protein, which can then recognize the MHC. This is also called "Signal 1" and its main purpose is to guarantee antigen specificity of the T cell activation.

However, MHC binding itself is insufficient for producing a T cell response. In fact, lack of further stimulatory signals sends the T cell into anergy. The co-stimulatory signal necessary to continue the immune response can come from B7-CD28 and CD40-CD40L interactions.

When CD40 on the APC binds CD40L (CD154) on the T cell, signals are sent back to both the APC and the T cell. (1) The signal from the APC to the T cell informs the T cell that it must express CD28 on its surface. (2) The signal from the T cell to the APC informs the APC to express B7 (which can be either B7.1 or B7.2). It is the B7-CD28 interaction that leads to activation of the T cell. Importantly, the B7-CD28 binding additionally instructs the T cell to produce CTLA-4 (the competitor for CD28). Since CTLA-4 also binds to B7 it decreases the B7 that can bind to CD28. The B7-CTLA-4 binding suppresses T cell activation. The balance between the opposing signals generated by B7-CD28 and B7-CTLA-4 binding regulates the intensity of the T cell response.

There are other activation signals which play a role in immune responses. In the TNF family of molecules, the protein 4-1BB (CD137) on the T cell may bind to 4-1BB ligand (4-1BBL) on the APC.

The B7 (B7-1/B7-2) protein is present on the APC surface, and it interacts with the CD28 receptor on the T cell surface. This is one source of "Signal 2" (cytokines can also contribute to T-cell activation, called "Signal 3"). This interaction produces a series of downstream signals which promote the target T cell's survival and activation.

Blockage of CD28 is effective in stopping T cell activation, a mechanism that the immune system uses to down-regulate T cell activation. T cells can express the surface protein CTLA-4 (CD152) as well, which can also bind B7, but with twenty times greater affinity for B7 proteins, and lacks the ability to activate T cells. As a result, the T cell is blocked from receiving the B7 protein signal and is not activated. CTLA-4-knockout mice are unable to stop immune responses, and develop a fatal massive lymphocyte proliferation.

Researchers financed by pharmaceutical Industry are focused to develop an B7-inhibitor, but why? As it is a food incompatibility reaction activated by IgG3, IgG2, IgG1 isn't it better to eliminate the cause by adapting the diet?

Besides B7-1 and B7-2 there are also other proteins belonging to the B7 family, see below:

Name	alternative names	will binds to
B7-1	CD 80	CD28, CTLA-4, PD-L1
B7-2	CD 86	CD28, CTLA-4
B7-DC	PDCD1LG2, PD-L2, CD273	PD-1
B7-H1	PD-L1, CD274	PD-1
B7-H2	ICOSLG, B7RP1, CD275	ICOS
B7-H3	CD276	
B7-H4	VTCN1	
B7-H5	VISTA, Platelet receptor G24, SISPI	
B7-H6	NCR3LGI	NKp30
B7-H7	HHL3LGI	NKp30

Class I MHC molecules

APC's actually do present the Class I and class II MHC molecules. Class I molecules have a binding groove that is closed at both ends, thus the small protein peptide fragments they present must fit within the confines of that groove. Mostly of them are eight to eleven (8-11) amino acids in length. These peptides are anchored at the ends, and their little variation in length will accommodate the bulge out a bit in the center. Humans have three genes for class I MHC proteins, HLA-A, HLA-B and HLA-C, located on chromosome 6. And as we have 6 chromosomes 6's one from mom and one from dad, we have totally six class I MHC genes.

We have at least 370 variants of the gene for the HLA-A protein and 660 different HLA-B genes, so it is polymorphic.

Each class I MHC molecule can bind to and present a large number of different peptides, each of them fits the particular amino acids, present at the ends of its binding groove.

Class II MHC molecules

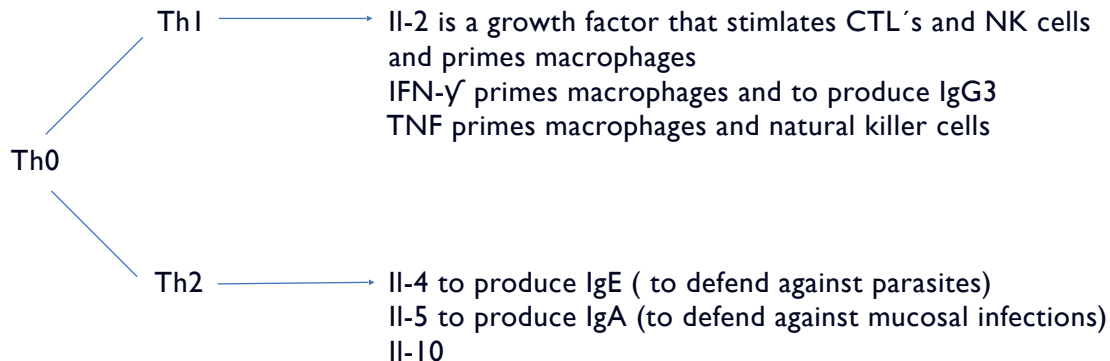
Also class II MHC molecules are encoded by genes in the HLA-D region of chromosome 6 and are also polymorphic. Within humans we see many different versions of class II molecules. But in contrary to class I MHC, these class II MHC molecules are open at both ends, thus a peptide can hang out of the groove. Also these peptides are longer and have a range of thirteen to twenty-five amino acids (13-25).

Almost every cell in the human body expresses class I molecules on its surface, although the number of molecules varies from cell to cell. Killer T cells, we call them cytotoxic lymphocytes or in short CTL's, inspect the protein fragments displayed by class I MHC molecules. So CTL's can check them, to check and to determine if a cell has been invaded by a virus or other parasite and should be destroyed.

A risk is that when mRNA is translated into protein in the cytoplasm of a cell mistakes are sometimes made and will lead to a production of useless proteins that don't fold up correctly. Besides these proteins suffer damage due to normal wear and tear. For that reason that we are not filled up with defective proteins we need to destroy them by chippers, called proteasomes. Most of these peptides will be reused to make new proteins.

Cytokines secreted by Th cells

When virgin helper T cells are first activated, the major cytokine they secrete is IL-2. They can also be restimulated to secrete other cytokines such as IFN- γ , IL-4, IL-5 and TNF.



The Th1 cytokines are the perfect package to help to defend against invaders which attack blood and tissues, cause Th1 cytokine instruct as well as the Innate Systems as also Adaptive systems to produce effective cells and antibodies.

So helper T cells use cytokines to direct the immune response, for that they need to decide which cytokines they need to make, for that they need to determine who is the invader, is it a bacterium, a virus, a parasite or a body-strange foreign substance so an incompatibility? And where are these 'invaders', in which area or tract? For that they need an observer to collect information continuously, indeed surely the dendritic antigen presenting cell. They can act as observer and knows how to react and sets on actions, we call them 'the brains of the immune system' and they are therefore stationed under all surfaces with an outside connection, there they wait, they check identity of invaders and go nearby lymph nodes and sets activation on.

There is also a negative feed back at work, IFN- γ made by Th-I cells decreases the rate of