

# *International Day of* **Immunology**





# General Immunology



## What is the Immune System?

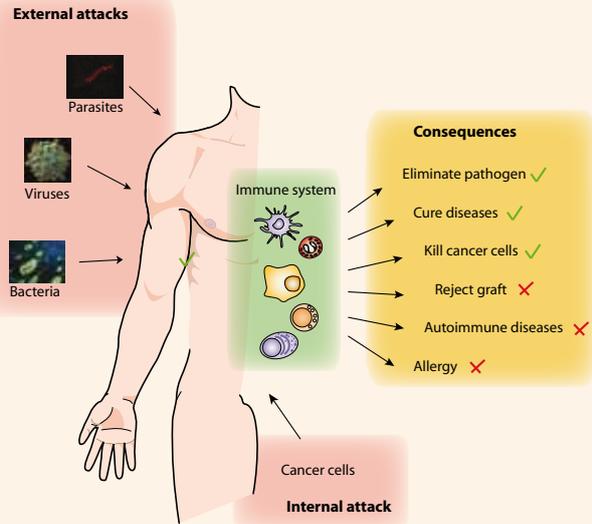
Every day your body is being attacked by foreign organisms such as bacteria, viruses and parasites that can cause disease. These are called **pathogens**.

Humans have evolved a complex system of cells and chemicals which are released from cells to protect you from these invaders. This is called the immune system.

Components of your immune system travel around your body through the blood and lymph fluids patrolling for invading pathogens. Once a pathogen is recognized, the immune system swings into action to eliminate it. Parts of the pathogen may be broken down and recognized by the immune system as foreign material. These are called **antigens**.

Your immune system can also protect you from your own cells that are either over activated and can cause autoimmune conditions or that have become mutated and can cause cancer.

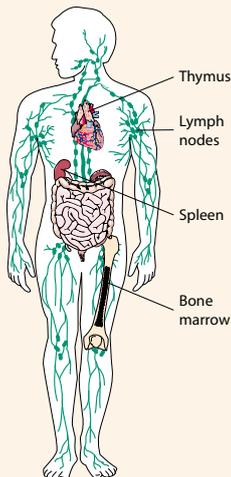
We can activate or suppress the immune system to protect ourselves from disease. Vaccines are used to boost the immune system against a certain pathogen. If the pathogen then attacks the body, the immune system is primed and ready to go. On the other hand, for organ transplants immunosuppressive drugs are used to quieten the immune system, so that the skin graft is not seen as foreign and is not attacked by the immune system and rejected.



## Organs of the immune system

The bone marrow generates cells of the immune system. From there, cells migrate to the peripheral lymphoid organs such as the spleen, thymus and lymph nodes and into the blood.

The lymphatic system (in green) drains the liquid away from the tissues of your body. This liquid, called **lymph**, carries antigens to the **lymph nodes**. Here antigens are presented by macrophages and dendritic cells to B and T lymphocytes. If the lymphocyte is able to recognize the antigen it will become activated and can aid in the destruction of the pathogen. Activation of lymphocytes can also occur in other areas of the body such as the spleen.



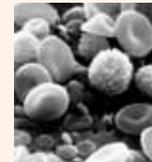
## Innate versus adaptive immune system

The immune system is composed of two different parts called the innate and the adaptive immune system. Both have different characteristics and complement each other.

Innate immunity	Adaptive immunity
Quick (few hours)	Slow (few days)
Non-specific, one cell recognize many pathogens	Specific, each cell recognizes only one antigen
Activates the adaptive immune system	Leads to immunological memory
Present in virtually all organisms	Only present in jawed vertebrates

## Cells of the immune system

Immune cells are diverse. White blood cells including lymphocytes and neutrophils, as well as red blood cells, can be seen.



## Actions of Immune cells

### Our immune system recognises pathogens by:

- **Pattern Recognition Receptors (PRRs).** These form part of the innate immune system and give a quick response.
- **Antigen presentation.** Certain immune cells can present (put on their cell surface) antigens (molecules unique to the pathogen) to activate other immune cells. This is important for pathogen detection by the adaptive immune system.
- **Antibodies.** These are secreted by cloned B cells and can bind to pathogens.

### Cells of the immune system communicate with each other through:

- **Signalling molecules.** Immune cells release molecules that activate other immune cells (eg cytokines) or attract other immune cells (eg chemokines).

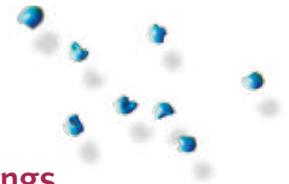
### Pathogens are killed in the following ways:

- **Phagocytosis.** Various immune cells ("phagocytes") engulf the pathogen to destroy it and allow antigen presentation.
- **Toxic molecules.** Immune cells release toxic molecules to destroy pathogens, for example, by degranulation (the release of molecules from granules).
- **Antibodies bound to pathogens can:**
  - (1) neutralise or damage
  - (2) stimulate phagocytosis
  - (3) activate complement
- **Complement.** A number of small proteins in the blood act following an activation cascade to help or "complement" the ability of antibodies or phagocytic cells to destroy pathogens. Complement proteins:
  - (1) cover the pathogen to enhance phagocytosis (opsonisation),
  - (2) attract phagocytes to the pathogen (chemotaxis), and
  - (3) rupture the pathogen (lysis).





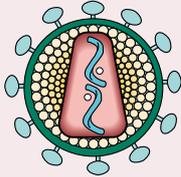
# Vaccination



Our immune system defends us from dangerous things

## Infectious Microbes (Pathogens)

Bacteria, viruses, fungi and parasites



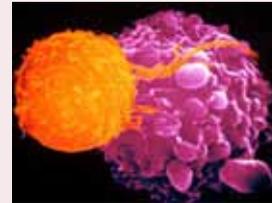
Influenza virus



Salmonella bacterium

## Cancer Cells

They were once our normal cells, then they mutated and forgot to stop dividing



Most of the time our immune system can keep up with these dangers, but sometimes it gets overwhelmed

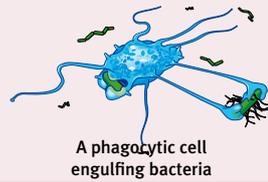
## The armed forces of the body

White blood cells (T-cells and B-cells)

Phagocytes

Complement

Antibodies



A phagocytic cell engulfing bacteria



A winter Flu

## Pandemic: Spanish Flu 1918–1919

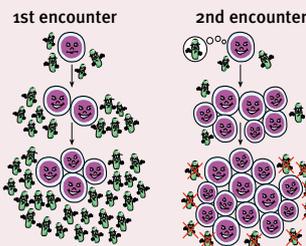


Estimated toll : 40 Million dead

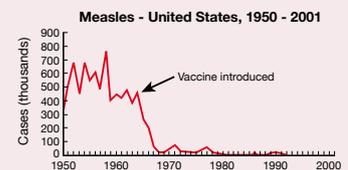
## Our B and T cells have good memories

They can remember a microbe for years so next time they see it, they can fight it off faster and more effectively. Rather than wait till we get sick, we can train the immune system to recognise a certain microbe by introducing it to a non-dangerous form of the microbe.

This is called vaccination



Vaccination has reduced the incidence of many diseases



## Vaccines

### History of vaccination.

Edward Jenner, a British doctor, is known as the father of vaccination.

He noticed that milkmaids rarely contracted smallpox and thought that cow pox infection (which is very mild in humans) may protect them from the vicious disease, smallpox.

He vaccinated his patients with cow pox, which protected them from small pox.

As a result of vaccination, small pox has been eradicated.

Who would have thought we owed cows for saving so much grief and eliminating a scourge of mankind?

Louis Pasteur coined the term vaccine in honor of Jenner's work from the Latin name for cow. Pasteur did ground breaking work on vaccines for all manner of infectious diseases.

### What have vaccines done for you?

#### The good:

Vaccines are one of the most effective and cost efficient medicines we have ever used.

They have eradicated smallpox and are extremely effective at limiting the spread and impact of many once common diseases.

Vaccines have dramatically reduced the prevalence of:

- Mumps
- Tetanus
- Measles/Rubella
- Polio

It is not just humans that have benefited from vaccination. Pets and livestock also receive life saving vaccines.

### The bad:

Early vaccines caused some side effects.

Modern vaccines have very minimal side effects. There remains a very small risk of serious complications. It is personal preference to vaccinate your child but there is no doubt that mass vaccination has a much lower complication rate than the diseases they cure.

### Australian cancer vaccine

Professor Ian Fraser while working in Melbourne and Brisbane developed Guardasil™.

This is the first vaccine that has been licenced and marketed as a cancer vaccine.

It protects you from a number of strains of the Human Papilloma Virus which can cause cervical cancer. Other anti-cancer vaccines are being developed.

### Why aren't there vaccines for every infection?

Some pathogens are very good at evading the immune system, making it difficult for the immune system to recognize or remember them. It is very hard to develop a vaccine that offers protection from such pathogens.

Examples include many parasites including the malaria parasite, human immunodeficiency virus (HIV), and rhinoviruses and coronaviruses which cause the common cold. This is also why you need a new flu vaccine every year, as the influenza virus changes each year and can evade the immune response.

### Examples of diseases caused by viruses

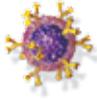
Disease	Virus	Vaccination
Influenza	Influenza virus	Available
Hepatitis A	Hepatovirus	Available (eg: Havrix)
Poliomyelitis	Poliovirus	Available (eg: OPV)
Common cold	Rhinovirus Coronavirus	Not available
Diarrhoea	Rotavirus	Not available
HIV	Human Immunodeficiency Virus	Not available

### Examples of diseases caused by bacteria

Disease	Bacteria	Vaccination
Diphtheria, Pertussis, Tetanus	Corynebacterium diphtheriae Bordetella pertussis Clostridium tetani	Available (eg: DPT)
Tuberculosis	Mycobacterium tuberculosis	Available (eg: BCG)
Salmonellosis	S. serovar typhimurium	Not available
Legionnaires/ Legionellosis	Legionella pneumophila	Not available

### Examples of diseases caused by fungi/parasites

Disease	Parasites/Fungi	Vaccination
Malaria	Plasmodium spp. including falciparum	Not available
Athlete's foot (tinea)	Trichophyton rubrum	Not available



# Autoimmune Disease

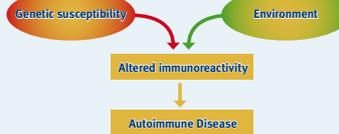


## Autoimmunity

Examples of autoimmune disease include:

- Type I diabetes (pancreas)
- Rheumatoid arthritis (joints)
- Coeliac disease (intestine)
- Multiple sclerosis (brain and spinal cord)
- Systemic lupus erythematosus (multiple tissues)
- Sjogren's syndrome (mucous membranes)

**It is also important to know how we can turn an over-active immune system OFF!**



- Autoimmune disease affects about 4% of the population
- Type 1 diabetes affects about 0.4% of the population
- Sjogren's Syndrome affects about 0.5% of the population



Factors that can influence the prevalence of autoimmune diseases

- Infections: e.g. parasites ↓, perinatal ↓ ("hygiene hypothesis")
- Food: quantity ↑, altered composition (lipid, fructose etc)
- Exercise: ↓
- Climate: ambient temp ↑, UVR/vitamin D ↓
- Sleep: ↓
- Drugs: antibiotics (infants) ↓
- Modifiers: culture, education, wealth, access to technology, family size, maternal age...

## Rheumatoid Arthritis

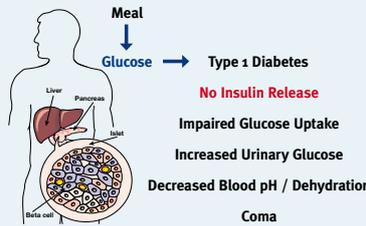


- Common autoimmune-mediated inflammatory disease
- Chronic synovial joint inflammation & eventual joint destruction
- Extra-articular features eg. vasculitis & cardiovascular disease



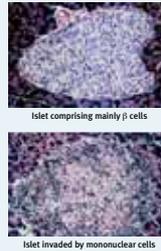
## Type 1 Diabetes

Endocrine disruption due to autoimmunity

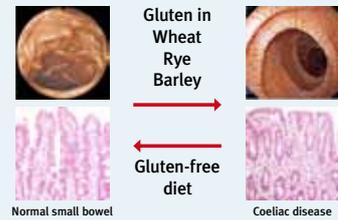


## Type 1 diabetes

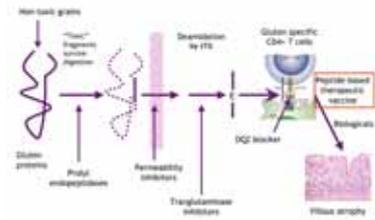
- Juvenile-onset 1:200 pop.
- Adult-onset 1:200 pop. (10% of adult diabetes)
- Immune cells infiltrate the pancreas
- Pancreas β-cell (beta-cell) destruction
- insulin deficiency
- hyperglycaemia



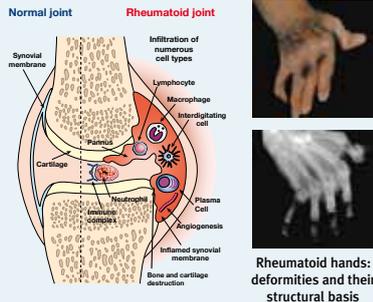
## Coeliac Disease



## Targets for drug development



## Comparison of normal and rheumatoid joint



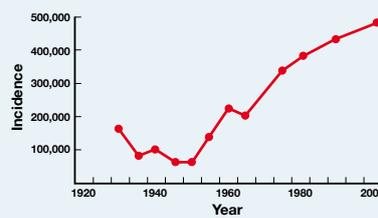
Rheumatoid hands: deformities and their structural basis

## Treatment



TNF is a signalling chemical that can stimulate the immune system. Anti-TNF antibody treatment has revolutionised the treatment of chronic inflammatory disease for some patients

## The rise and rise of diabetes



## Treatment for diabetes



- Daily Insulin injections (Insulin Pump/Pen)
- Pancreatic/Islet transplantation
- Nasal insulin delivery for diabetes prevention (in development)

## Treatment Options

Currently the only treatment is a gluten-free diet

- this is expensive, difficult and
- fails in 50% of adults

Treatment in development

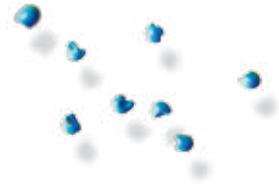
- peptide immunotherapy (similar to allergy desensitisation)



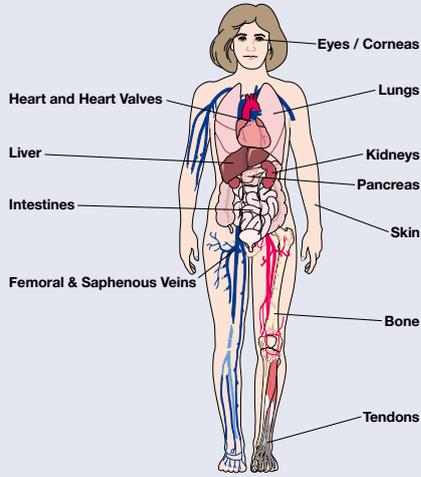
Scientists from Melbourne's The Walter and Eliza Hall Institute of Medical Research, Dr Jessica Stewart, Dr Bob Anderson and Dr Jason Tye-Din discuss the progress of a coeliac disease experiment



# Transplantation



## Organs and Tissues for Donations



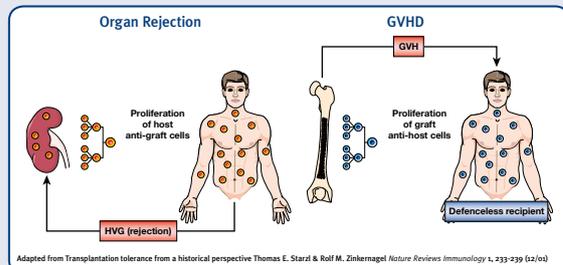
People in end stage organ failure require transplantation to survive. Over 30,000 Australians have received organ and tissue transplants since the 1960s. Transplanted organs include kidneys, heart, lungs, liver and pancreas. Tissues include corneas, skin, bone, heart valves and bone marrow.

## History of Transplantation

1933	First human-human kidney transplant	Yu Yu Voronoy, Soviet Union
1954	First successful living donor kidney transplant	Dr. Joseph Murray and Dr. David Hume, Brigham Hospital, Boston
1962	First successful deceased donor kidney transplant	Dr. Joseph Murray and Dr. David Hume, Brigham Hospital, Boston
1963	First successful lung transplant	Dr. James Hardy, University of Mississippi Medical Center, Jackson, MS
1967	First successful liver transplant	Dr. Thomas Starzl, University of Colorado, Denver, CO
1967	First successful heart transplant	Dr. Christiaan Barnard, Groote Schuur Hospital, South Africa
1981	First successful heart/lung transplant	Dr. Norman Shumway, Stanford University Medical Center, Palo Alto, CA
1988	First successful small intestine transplant	Dr. Eberhard Deltz, Kiel, Germany
1989	First successful living donor liver transplant	Dr. Christoph Broelsch, University of Chicago Medical Centre, Chicago, USA

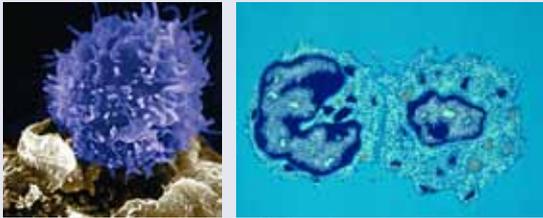
## Graft versus Host Disease

After bone marrow transplantation, sometimes the transplanted marrow can attack the recipient in a process called "graft versus host disease" (GVHD).



## Organ Rejection

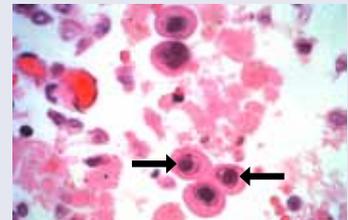
Rejection occurs when the immune system of the recipient attacks the transplanted organ or tissue. This is a normal response of a healthy immune system which can detect foreign tissues and destroy them.



Killer T Cells attacking "foreign" cells

## Infection

Unfortunately, drug induced immunosuppression can lead to opportunistic infections by normally harmless organisms. One organism is called cytomegalovirus (CMV).



CMV in the lung (black arrows)

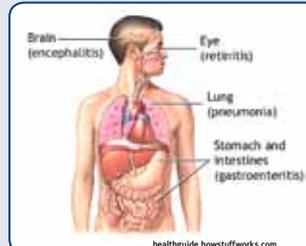
www.asnm.org

## Immunosuppression

Rejection can be reduced by tissue matching of donors and recipients, and by giving the recipient drugs that suppress their immune response.



## CMV Disease



healthguide.howstuffworks.com

CMV is a virus commonly found in healthy people but can cause serious infections in people with impaired immunity. The infection can result in pneumonia, gastroenteritis, retinitis or encephalitis. Antiviral medications may stop the replication of the virus but will not destroy it.

CMV disease can affect many organs

## Organ Transplantation in Australia

- Australia currently has one of the lowest organ donation rates in the developed world. Every organ donor can assist up to 10 recipients to enjoy renewed or improved life. People of all ages can be organ or tissue donors. There is effectively no age limit for corneal (eye tissue), bone tissue, kidney or liver donations.
- You can register online at **The Australian Organ Donor Register** to be an organ donor at <http://www.medicareaustralia.gov.au/>

## Organ Transplantation in Australia

- Australia's transplant success rates are amongst the best in the world
- Pancreas transplants are the most successful at 94% survival at one year and 87% at five years
- Heart-lung operations have the lowest survival rate of 76% survival at one year and 60% at five years



# Allergy

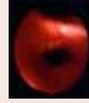


A detrimental immune response to common environmental agents that are otherwise harmless

### Respiratory allergies



Allergic



Asthma

### Food allergy



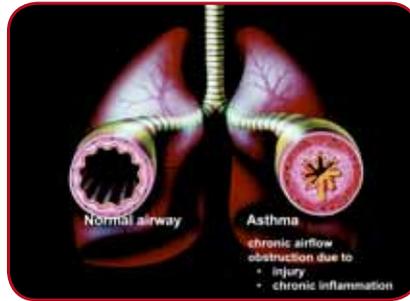
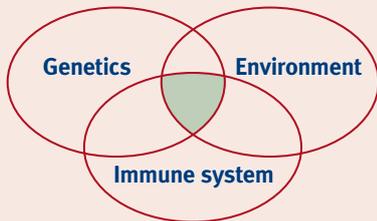
### Bee and Wasp sting allergy



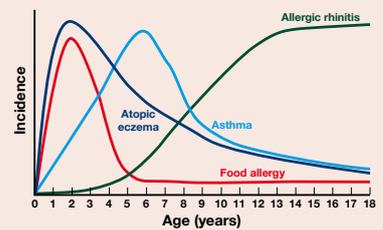
### What are the sources of clinically important allergens?



### What causes allergic disease?



### Allergic diseases



### Detection of allergic antibody

- Skin-prick testing or
- Blood specific IgE testing



### Current treatment for allergic diseases

#### Non-specific

- antihistamines
- $\beta$ -2 agonists
- corticosteroids
- adrenaline

#### Specific

- allergen avoidance
- allergen immunotherapy

### Food allergy

#### Provoking substances in children:

- egg )
- milk )
- peanut )
- soya ) 90% of reactions
- fish )
- wheat )

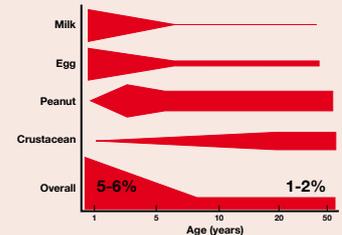
In 80% cases only 1 or 2 foods involved

#### Provoking substances in adults:

- peanut
- tree nuts
- shellfish
- fish

Reactions to egg, milk, soya and wheat usually resolve with increasing age

### Food allergy at different ages



### Mild symptoms

- itching – hand and groin – hives
- flushing, rashes
- vomiting, diarrhoea



### Moderate and severe symptoms



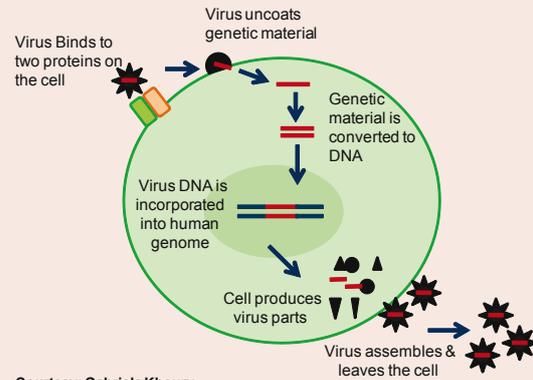
- swelling – lips, tongue – throat
- wheeze (asthma)
- dizziness, loss of consciousness
- death (rarely)



# Human Immunodeficiency Virus (HIV) & Acquired Immunodeficiency Syndrome (AIDS)

## HIV

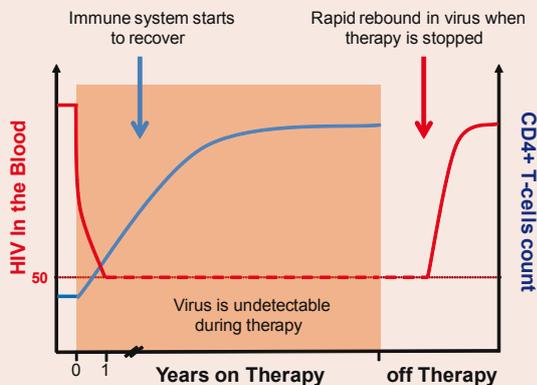
HIV is a retrovirus which is able to infect special cells of the human immune system known as CD4+ T-cells and macrophages. Retroviruses are unique as they are able to insert their genetic material into the human genome and manipulate the cell to allow the virus to hide from the body's defences. Once infected, a cell will produce more HIV which can then infect other cells. This process gradually causes the destruction of the immune system and is referred to as **Acquired Immunodeficiency Syndrome (AIDS)**. Following anti-HIV treatment, virus replication is stopped and in most cases, full health is restored.



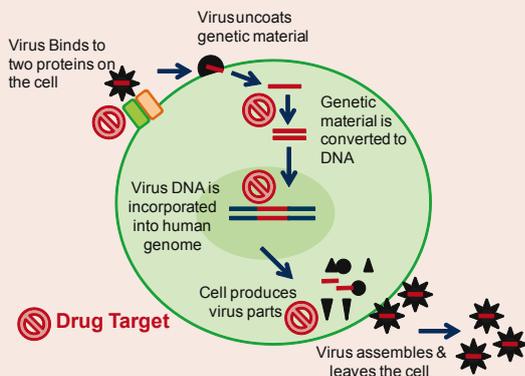
Courtesy: Gabriela Khoury

## Therapy

Currently, there are various drugs available that target different stages of the virus life within a cell. When a patient begins therapy the amount of virus in the blood rapidly declines and the immune system (measured as the level of CD4+ T-cells) recovers. However, current therapy does not eradicate HIV from the body and once therapy is stopped virus rapidly reappears in the blood.



Courtesy: Sharon Lewin



Courtesy: Gabriela Khoury

## Transmission

HIV can be transmitted during unprotected sex with an infected individual, sharing non-sterile injecting equipment, from a blood transfusion with contaminated blood, and from an infected mother to her child during pregnancy, childbirth or breastfeeding.

### World Health Organisation Statistics

- In 2010 estimated that 34 million people are living with HIV around the world.
- There are approximately 2.7 million new infections every year.
- There are 1.8 million AIDS-related deaths every year, 69% of these deaths were in Africa.

## World AIDS Day

Every year many countries host World AIDS Day events on December 1 with the intention of raising awareness of the disease, improve access to treatment, and fighting social stigma that is often experienced by people living with HIV. In solidarity with the cause people often wear a red ribbon.



Red ribbon image courtesy of Wikipedia

## Internet Resources

- UNAIDS** <http://www.unaids.org/en/>
- World Health Organisation** <http://www.who.int/gho/hiv/en/index.html>
- Centers for Disease Control and Prevention** <http://www.cdc.gov/nchhstp/>
- International AIDS Society** <http://www.iasociety.org/>
- World AIDS Day** <http://www.worldaidsday.org.au/>



# Australia, a world leader in immunology



## Medical Research in Melbourne in the 1920s

At the start of the 1920s, there was little focus on medical research in Melbourne, or anywhere in Australia. Most researchers tended to move overseas to pursue their work. The National Health and Medical Research Council, which is now Australia's major funding body for medical research, was not conceived until 1925, and established only in 1936. Only two dedicated medical research institutes existed – the Walter and Eliza Hall Institute of Medical Research, and the Australian Institute for Tropical Medicine



The first site of the Walter and Eliza Hall Institute at the Royal Melbourne Hospital in Lonsdale Street Melbourne.

## Frank Macfarlane Burnet

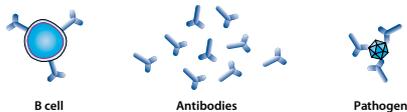
Frank Macfarlane ("Mac") Burnet was a Victorian medical scientist at a period in which most medical researchers left Australia to work overseas. In his early years, Burnet conducted groundbreaking research into viruses at the Walter and Eliza Hall Institute of Medical Research. Later, while director of the Hall Institute, he developed the clonal selection theory, which explained the way vaccines work, and described the process by which the immune system learns not to attack itself. For the latter, Burnet, along with Peter Medawar, was awarded the 1960 Nobel Prize for Physiology or Medicine.

In addition to his science, Burnet was active in public policy. He was a founding member of the Australian Academy of Science, and the first Australian of the Year in 1960. His decision to remain in Australia has left a lasting legacy on medical research in Australia, and particularly Melbourne.



Vaccination was first formally demonstrated by Edward Jenner, who used exposure to cowpox to protect people against smallpox. Since then, vaccination has been used to eradicate smallpox, and reduce the impact of many diseases, including deadly infections such as polio and influenza.

When you've been sick with something that causes disease – a bacteria or virus – once, your immune system remembers that disease, and protects you the next time you see that bacteria or virus. Vaccination takes advantage of this strategy, without making you sick in the first place. Reports of vaccination have been found as far back as 200 BC - but for a long time, no-one knew how it worked!

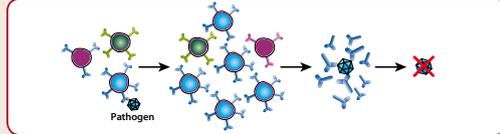


When you're sick, or have been vaccinated, a white blood cell called a B-cell produces antibodies, which specifically recognise the pathogen they've just seen. These antibodies react to the disease, and stop it re-infecting you.

Your immune system can produce antibodies to almost anything – including many things that are not found in nature! How does it do this?

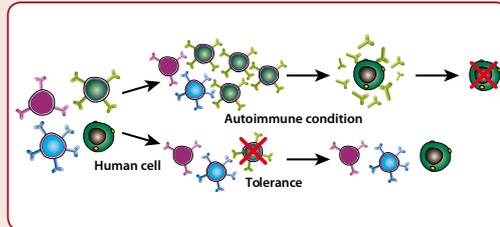
## Burnet's answer – the Clonal Selection Theory

Burnet's idea, which he and his team at the Walter and Eliza Hall Institute demonstrated, was that there are many B-cells, all of which recognise different parts of bacteria or viruses by using antibodies on their surface. According to the theory, B-cells develop their antibodies entirely randomly. It's just a matter of chance that there is an antibody that will recognise the pathogen. But since there are so many different B-cells in our immune systems, there's bound to be one that recognises the pathogen! When you're vaccinated against something, the B-cell that recognises that pathogen starts producing lots of antibodies. So, if you ever see the pathogen again, the antibodies will protect you from it and will stop you becoming sick.



## But if B-cells randomly generate antibodies, shouldn't some react to us?

Yes – and sometimes they do! This results in autoimmune disease, where the immune system unfortunately destroys body tissues. But most of the time, this doesn't happen. To explain why, Burnet proposed that B-cells were taught to be tolerant to the body's own tissues during early development, and those that couldn't were removed from the immune system. So even though what a B-cell reacts to is randomly determined, in most people, the immune system makes sure there aren't any dangerous B-cells left that will attack you. For this idea, Burnet was a co-recipient of the 1960 Nobel Prize for Physiology or Medicine, along with Peter Medawar, who formally demonstrated its truth.



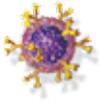
## Immunology research in Melbourne now

Melbourne is now a leading centre for immunology research in Australia, and the world. Researchers in Melbourne are working on a diverse range of medical challenges, including fighting autoimmune disorders, fighting diseases such as malaria, and harnessing the power and intelligence of the immune system to fight cancer.

### Research in Melbourne includes:

- Walter and Eliza Hall Institute of Medical Research
- University of Melbourne
- Burnet Institute
- Peter MacCallum Cancer Centre
- Monash University
- Ludwig Institute for Cancer Research





# Monocyte/macrophage



## General features

Monocytes and macrophages are main players of the innate immune system. They derive from blood stem cells in the bone marrow. Monocytes circulate in the blood and then migrate to the tissue where they differentiate into macrophages.

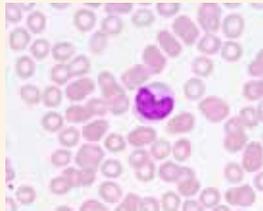
Once mature, macrophages play a very important role in the immune system. They "vacuum" up pathogens by a process called phagocytosis. Once inside the cell, the pathogens are broken up and parts of them are presented on the surface of the cell. This acts to signal other immune cells and alert them to an invading pathogen. Monocytes therefore act as messengers and interact with other cells such as lymphocytes.

Monocytes contain a large single nucleus which gives them their name meaning mononuclear phagocyte.

Macrophages can also phagocytose damaged tissues and are important in wound repair.

Fragments of killed pathogens are displayed on the surface of monocytes to signal to other immune cells

Large single nucleus



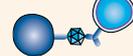
Approximately 3–8% of white blood cells

## Modes of action:

Phagocytosis



Present antigens to activate B and T lymphocytes



Release of cytokines / chemical signals to induce inflammation



Activate complement and antibody secretion

## Pathologies

Over-activation of macrophages can lead to atherosclerosis (a heart disease) and autoimmune diseases such as arthritis.

Reduced function of these cells can lead to increased susceptibility to infection.

Macrophages also represent a reservoir of viral replication, for instance in the case of HIV infection.

# Neutrophil

## General features

Neutrophils are derived from blood stem cells in the bone marrow and then circulate in the blood. They are relatively short lived, lasting for only a few days. They belong to the innate immune system.

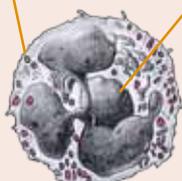
Neutrophils are one of the first immune cells to act against invading pathogens such as bacteria. They contain thousands of tiny granules - small sacks that contain chemicals which help kill pathogens. The neutrophil will engulf the bacteria in a process known as phagocytosis and once the pathogen is inside, it uses the chemicals in its granules to kill the cell.

The neutrophils' toxic activity often results in their own death. Dead neutrophils and their debris are the main constituents of pus at the site of infection.

A defining characteristic of neutrophils is their "multi lobed nucleus".

Granules containing enzymes to help kill pathogens

Multi-lobed nucleus



Approximately 65% of white blood cells

## Modes of action:

Phagocytosis



Degranulation



Cytokine secretion



Neutrophil extracellular trap (NET), consisting of DNA and enzymes to form an extracellular web.



## Pathologies

People with low levels of neutrophils are particularly susceptible to bacterial infection and may die if they are not treated. This can occur as a result of a genetic disorder, cancer, or as a side effect from drug treatment eg. chemotherapy.

Over-activation of neutrophils can result in autoimmune conditions such as arthritis.



# Eosinophil



## General features

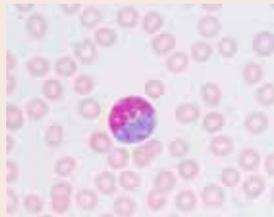
Eosinophils are derived from blood stem cells in the bone marrow and then circulate in the blood. They belong to the innate immune system.

Eosinophils help defend the body against attacks by large invading pathogens. They contain thousands of tiny sacks called granules that contain toxic molecules. Once stimulated, eosinophils release these granules to kill pathogens, that are too big for cells of the immune system to engulf.

Eosinophils are especially important in defence against parasitic infections, eg: parasitic worms in the intestines.

Eosinophils turn a characteristic brick red after staining with the acidic dye eosin.

Once released, the content of granules act to kill parasites, but can also cause asthma



Approximately 4% of white blood cells

## Modes of action:

Degranulation



Cytokines secretion



Phagocytosis



## Pathologies

When eosinophils are wrongly stimulated, they release toxic molecules contained in their granules. This results in damage to the lining of airways causing asthma and/or damage other tissues in allergic reactions.

# Basophil/mast cell

## General features

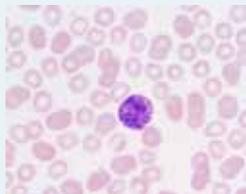
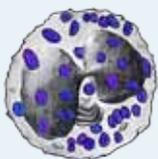
Basophils and Mast cells derive from the blood stem cells in the bone marrow.

Basophils are the rarest of the white blood cells. They contain huge numbers of granules that are used to store chemicals that cause inflammation. The main chemical within these granules is called histamine.

Mast cells are very similar to basophils but reside in tissues. They also contain huge numbers of granules. They are important in wound healing.

After activation, basophils and mast cells degranulate to release different molecules important to eliminate the pathogen. However, this reaction may also lead to allergic reactions.

Basophils are so named as they are "basic loving" ie they can be stained by basic dyes. Staining by Hematoxylin & Eosin will show those cells as blue. Basophils generally have a two lobed nucleus which is often obscured by granules after staining.



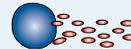
Approximately less than 1% of white blood cells

## Modes of action:

Release of toxic molecules



Release of signalling molecules

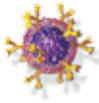


## Pathologies

One important pathology associated with basophils and mast cells is anaphylactic shock, which is a severe, whole body allergic reaction that can lead to death. This may be triggered by food (eg peanut), venom (eg bee sting), or medication.

After a first encounter with such a substance, your body may develop a special type of antibody called IgE against it. On a subsequent exposure, these IgE will recognise the substance immediately and will activate the mast cells inducing degranulation and release of large quantities of histamine.

An increased level of basophils can lead to cancer.



# B lymphocyte



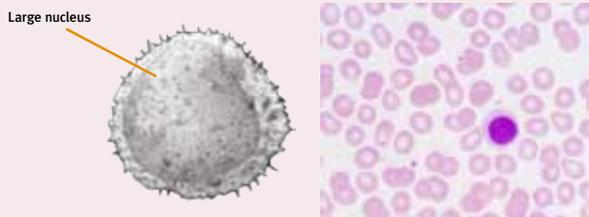
## General features

B lymphocytes belong to the adaptive immune system. They develop in the bone marrow and subsequently reach the peripheral organs such as the spleen and the lymph node where they become activated.

Every B lymphocyte can recognize only one particular antigen. Upon encountering this antigen, the B lymphocyte will proliferate and differentiate into either plasma cells or memory B cells.

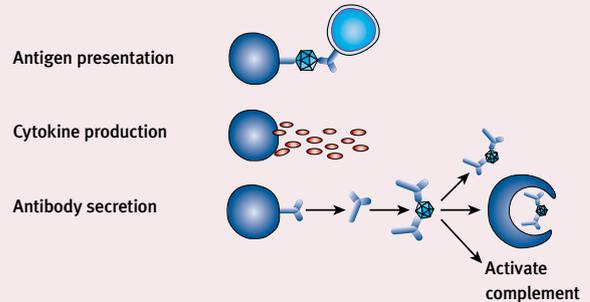
Plasma cells have an enlarged cytoplasmic compartment and secrete large amounts of antibodies. An antibody is a Y-shaped protein that can recognize and bind to a pathogen or an antigen. It can directly block the pathogen or trigger other defence mechanisms such as the complement system or phagocytosis by cells such as neutrophils, monocytes and macrophages.

Memory B cells are able to differentiate very quickly to become plasma cells if the same pathogen infects your body a second time.



Approximately 25% of white blood cells

## Modes of action:



## Pathologies

During their activation process, B cells proliferate at a high rate and can accumulate a lot of mutations which may result in cancer called lymphoma.

When plasma cells become malignant, this is called multiple myeloma.

If B cells produce too many inappropriate antibodies, eg antibodies against a normal human antigen, this can result in autoimmunity. One example of this is lupus where antibodies can be generated against DNA and histones normally present in our own cells.

# T lymphocyte

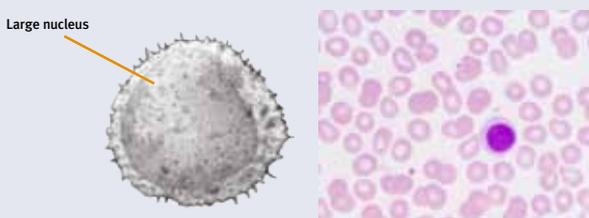
## General features

T lymphocytes derive from blood stem cells in the bone marrow and migrate to the thymus where they mature. Like the B lymphocytes, they belong to the adaptive immune system.

There are two different classes of T cells - helper T cells and cytotoxic T cells. Every T cell of both classes expresses a specific T cell receptor (TCR). The TCR is a surface protein which enables the recognition of a specific antigen presented by antigen presenting cells. This interaction leads to the activation of T cell function. The activated helper T cells are important to activate B cells, and the activated cytotoxic T cells can directly kill cells infected with a virus.

Some T cells also differentiate into memory T cells to generate a more efficient response if your body encounter the same pathogen a second time.

By histology using H & E staining, B & T cells are indistinguishable.



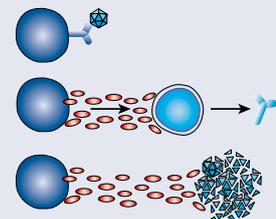
Approximately 25% of white blood cells

## Modes of action:

One T cell recognizes one type of antigen

Helper T cells activate B cells

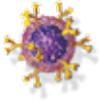
Cytotoxic T cell recognize & lyse (kill) pathogens



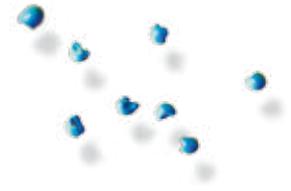
## Pathologies

When the activation and the proliferation of T cells is not perfectly regulated, a type of cancer known as T cell lymphoma may occur. T cell lymphoma accounts for up to 40% of lymphomas in childhood.

In HIV infection the virus destroys helper T cells. As a consequence, the immune system of the infected patient is very weak and the patient may die from infection by another pathogen (eg influenza virus), that they would normally easily fight.



# Dendritic cell



## General features

Dendritic cells (DC) derive from blood stem cells in the bone marrow. They help to the innate immune system.

Dendritic cells are always patrolling the peripheral tissues in order to find pathogens. At the mature stage, they have a particular morphology with long projections called dendrites. This morphology is particularly helpful to scan the environment efficiently. They are able to phagocytose the pathogen and present antigen at the cell surface.

Once activated, DC migrate to the draining lymph node or the spleen, to present the antigen to B and T cells and activate them. They make a link between the innate and the adaptive immune systems.



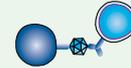
Less than 1 % of white blood cells

## Mode of action:

Phagocytosis



Antigen presentation



Cytokine production



## Pathologies

Abnormal proliferation of certain types of dendritic cells can lead to a form of histiocytosis, a disease very close to cancer.

# Complement system

## General features

A number of small proteins in the blood act following an activation cascade to help or "complement" the ability of antibodies or phagocytic cells to destroy pathogens.

Over 25 proteins or fragments of small proteins form the complement system. These are originally produced mainly in the liver and circulate through the blood in an inactive state. Several triggers set off a cascade of events that act to amplify and activate the complement system. These can include binding of complement precursors to antibody-antigen complexes and direct binding to the pathogen itself. Complement activation leads to the formation of the Membrane Attack Complex (MAC) that forms on the pathogen surface.

Tight regulation of the complement system is necessary as the system has the ability to damage our own tissue.

The following are the basic functions of the complement system: (1) opsonization - complement and antibodies cover the pathogen to enhance phagocytosis, (2) chemotaxis - attracting phagocytes to the pathogen and (3) lysis - rupturing of the pathogen through the MAC.



Complement is a link between innate and adaptive immunity.

## Modes of action:

Complement proteins:

(1) cover the pathogen to enhance phagocytosis (opsonisation),



(2) attract phagocytes to the pathogen (chemotaxis), and



(3) rupture the pathogen (lysis).



## Pathologies

Decreased complement levels may be seen with:

- Recurrent bacterial infections
- Autoimmune diseases
- Various types of kidney disease

Complement protein levels are usually increased during acute or chronic inflammation.

## Internet Resources

- Australasian Society for Immunology, Inc. Basic Immunology information page, with link to an immunology related quiz.  
<http://www.immunology.org.au/immquiz.html>
- British Society for Immunology. A concise and easy to follow description of the immune system, its importance and how it works.  
<http://www.immunologyexplained.co.uk/>
- European Federation of Immunological Societies (EFIS). An entertaining and interesting site designed to inform people about their immune system. Links to downloadable films and books, including "Your Amazing Immune System - How It Protects Your Body".  
<http://www.immunology-info.org/>
- A downloadable game where you must navigate a nanobot through a 3D environment of blood vessels and connective tissue in an attempt to save an ailing patient by retraining her non-functional immune cells. Learn about the biological processes that enable white blood cells to detect and fight infections. Brought to you by the Federation of American Scientists.  
<http://fas.org/immuneattack/>
- Australian government "Immunise Australia Program" website. Includes vaccination program guide and links to publications and references on topics of vaccination.  
<http://www.immunise.health.gov.au/>
- United States (CDC) vaccination information site.  
<http://www.cdc.gov/vaccines/>
- Walter & Eliza Hall Institute for Medical Research – TV. A number of cool biomedical animations, including immunology related.  
<http://www.wehi.edu.au/education/wehi-tv>
- Cells Alive. Look inside and understand the way cells work. Descriptions and animations of various immunological processes including making antibodies, phagocytosis, cytotoxic T cell killing etc. Also includes a quiz and links to other cell biology areas.  
[http://www.cellsalive.com/toc\\_immun.htm](http://www.cellsalive.com/toc_immun.htm)
- Images of antibodies. Webpages on immunoglobulin structure and function prepared by Mike Clark, PhD, Cambridge University, Cambridge UK.  
<http://www.path.cam.ac.uk/~mrc7/mikeimages.html>
- The Biology Project (Arizona University) – Immunology. Basic tutorial on the immune system and antibody structure. HIV and AIDS. Further www resource links.  
<http://www.biology.arizona.edu/immunology/immunology.html>
- A collection of Allergy and Asthma resources on the Internet.  
<http://www.immune.com/allergy/allabc.html>
- Immunology university course materials. Includes flash animations to help students learn immunology. Requires 'Shockwave' plugin.  
<http://www.bio.davidson.edu/courses/immunology/bio307.html>
- A general Science education website by the Howard Hughes Medical Institute (USA). Includes "Cool Science for Curious Kids".  
<http://www.hhmi.org/coolscience/>