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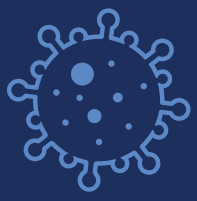
S T U  W

X Y Z

SCIENCE AROUND **THE IMMUNE SYSTEM FROM A TO Z**

Immune responses, Immune cells & organs, Life evolution & Lifestyle choices, Balance, Memory, Tolerance, Pathogens...

Danone Nutricia Research

DANONE
ONE PLANET. ONE HEALTH

RESEARCH & INNOVATION

SCIENCE AROUND **THE IMMUNE SYSTEM FROM A TO Z**

The immune system is one of the most important organ systems in the body, right at the forefront of our health!

With more than 30 years of expertise in immunology, Danone Nutricia Research has been conducting pioneering research and innovation in that field, with a specific interest in the interplay between nutrition and the immune system.

This alphabetical book has been designed as a comprehensive and accessible guide to the remarkable science that governs our body's defense system. Each letter represents a unique facet of its complex mechanisms and can be read and used independently.

Understanding the science behind the immune system is not just a matter of knowledge. It empowers us to make informed decisions about our health, which is at the core of Danone's mission.

Thus, whether you are a seasoned immunologist, a science enthusiast, or simply someone looking to demystify the workings of their own body, this collection offers knowledge for all.

What is the immune system?

How does it function and adapt to countless challenges?

Where in the body is it located?

How can we measure it?

How do life stages and choices impact the immune system?

What do concepts such as herd immunity, immune memory or tolerance mean?

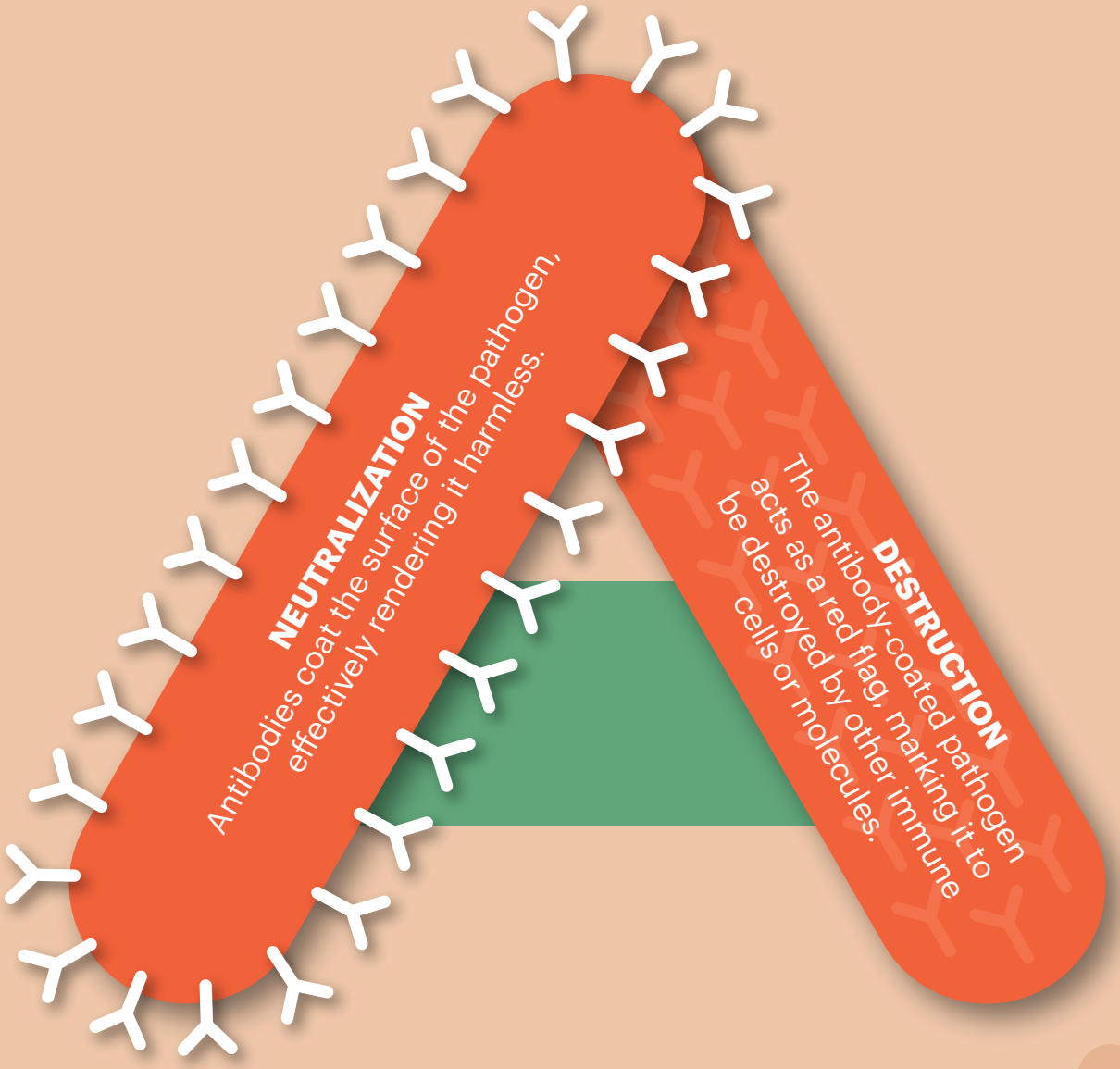
Discover the answers to all these question, and much more!

CONTENTS

ANTIBODIES

Antibodies are our invaluable allies, the special weapons produced by immune cells called B-lymphocytes to fight intruders.

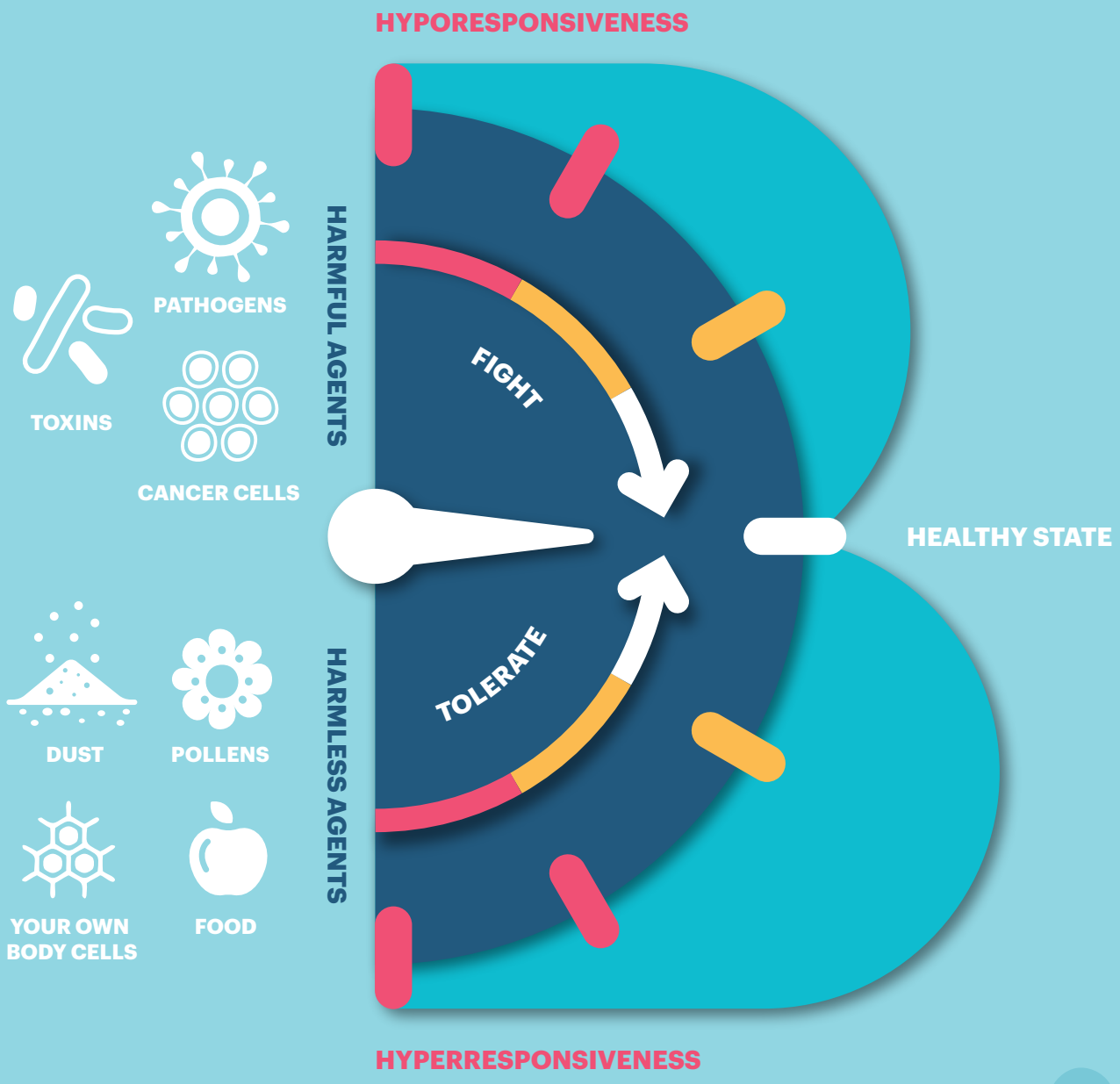
When an intruder like a pathogen attacks, specific antibodies can recognize it and bind to its surface. Two steps then occur:



You may also know antibodies, those incredible allies of ours, under the name **'immunoglobulins'!**

BALANCE

Between fighting off harmful agents & tolerating the harmless ones : immunity is all about balance!



To reach a healthy state, our immune activity **should not be too weak to fight against diseases**, like infections, but **should not loose control either**, to avoid over-reaction against harmless agents, that could provoke allergy, chronic inflammation, or autoimmune disorders.

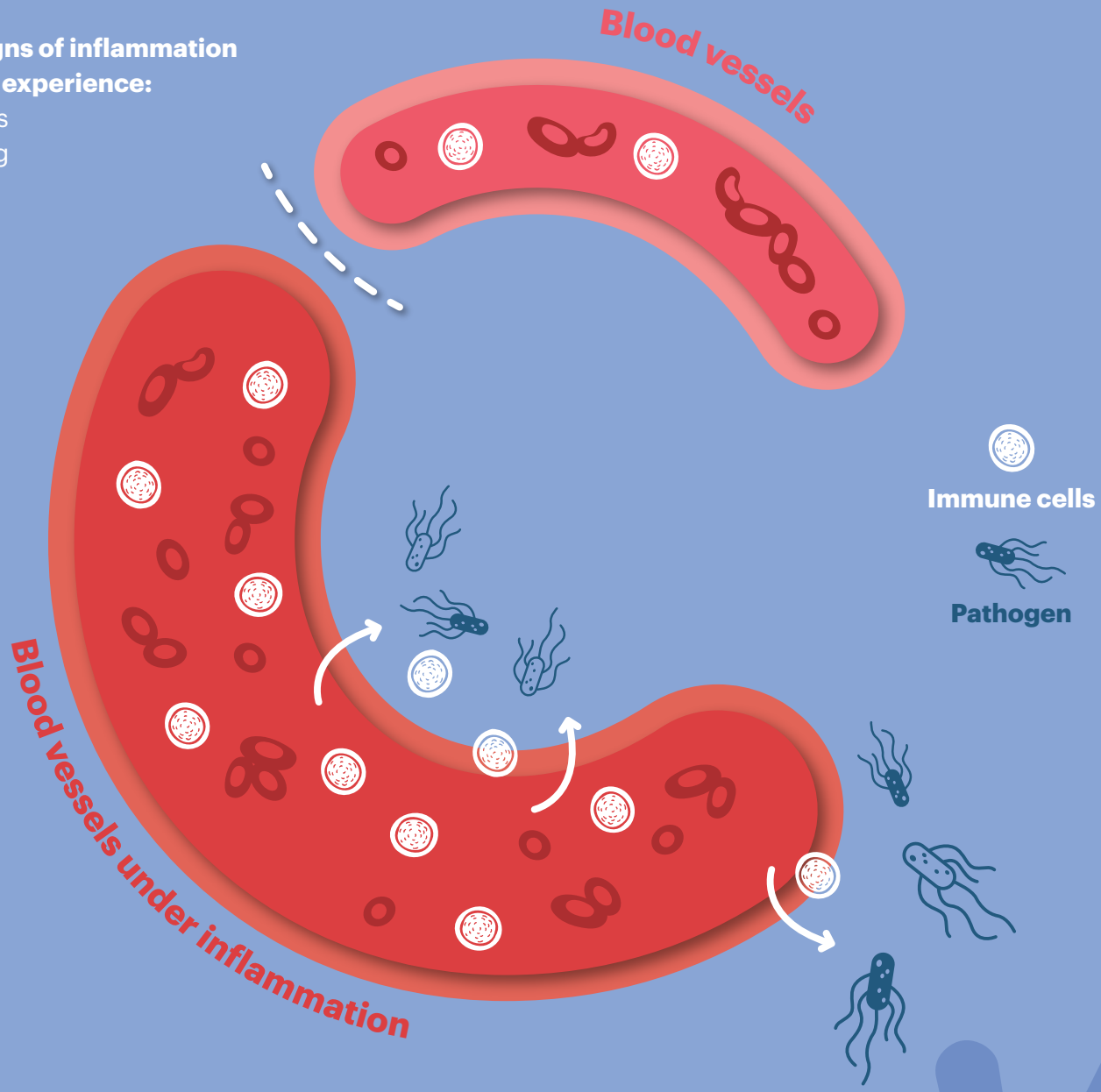
CRISIS CONTROL

Inflammation is an emergency response to an attack. Generally localized and easily observable when you get an infection, it acts as a crisis unit.

But how and why?

The 4 signs of inflammation you may experience:

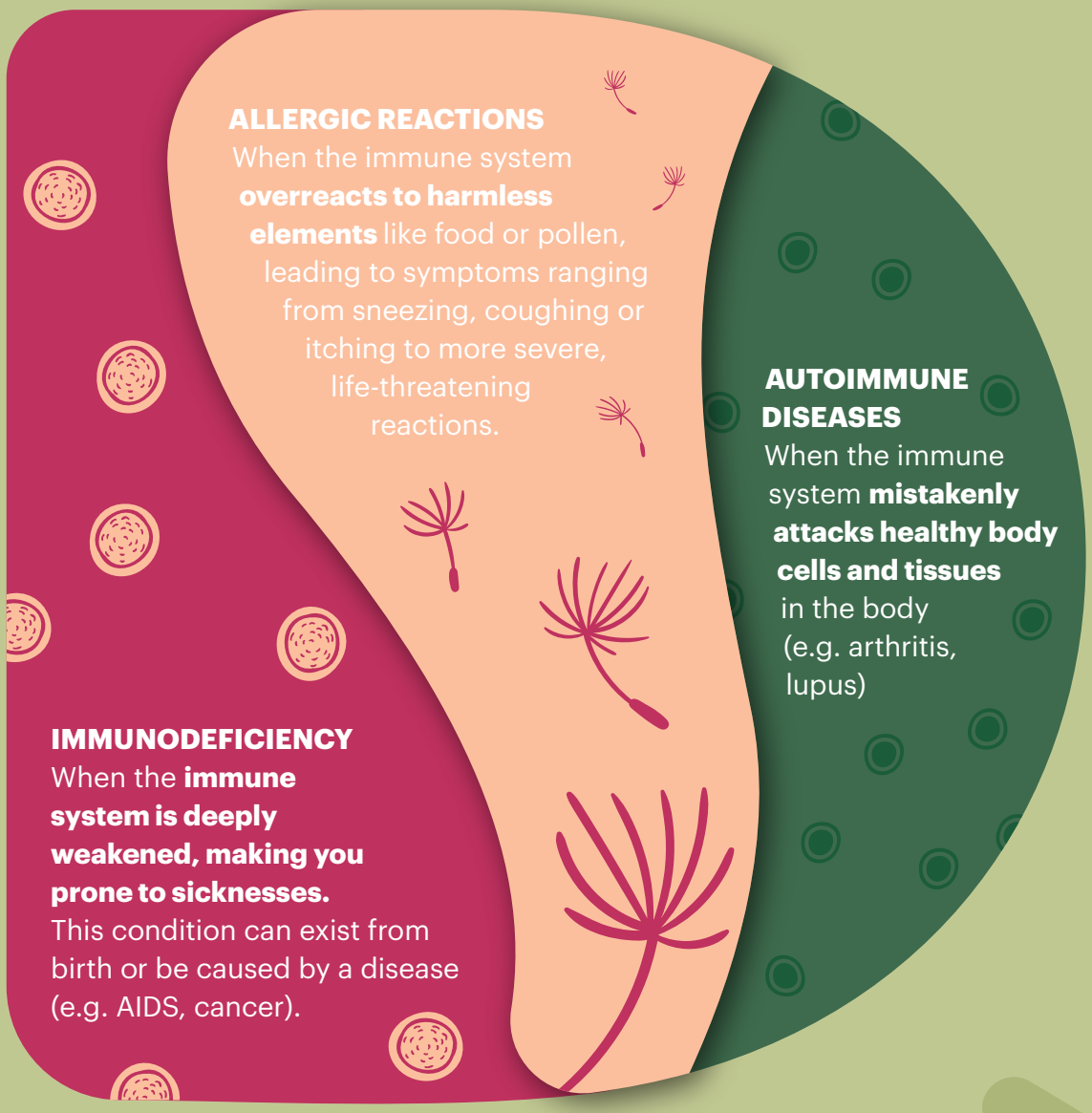
- Redness
- Swelling
- Pain
- Heat



During inflammation, blood vessels get wider to increase the blood flow. They also get more permeable to **allow immune cells and fluids to move quickly from the blood stream to the site of infection, to fight off pathogens.**

DISORDERS

Sometimes, the immune system does not work the way it should. This disruption can lead to disorders.



EFFICACY

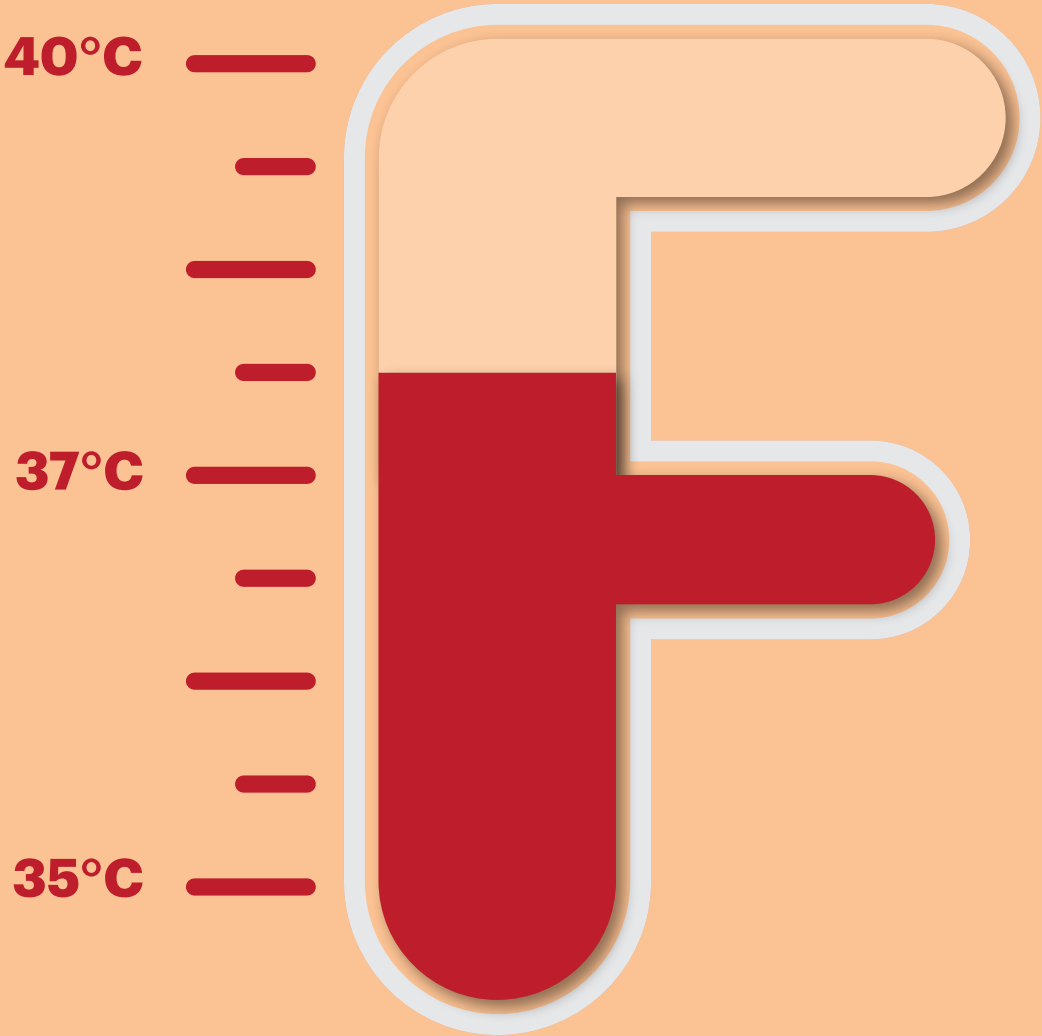
We cannot directly feel our immune system the way we feel sensations in our digestive or respiratory systems. So how do we know that our immune system is healthy and working effectively?

Symptoms like fever, inflammation or swollen lymph nodes are not signs of an unhealthy immune system. On the contrary, they precisely show that it is currently working hard to protect you!

The efficacy of your immune system can be perceived through: the frequency of illnesses, their duration and how quickly you recover, the severity of symptoms and even the impact those sicknesses have on your daily life and activities.

FEVER

**The human body temperature is usually set around 37°C.
But when faced with an infection, our immune system can send signals to our brain's thermostat (the hypothalamus) to raise our body temperature.**



Increasing our body temperature has two benefits:

- **It creates a hostile environment that inhibits pathogen growth**
- **It stimulates the activity of both innate and adaptive immunecells to fight the infection**

Once the threat is under control, our body temperature is brought down to normal.

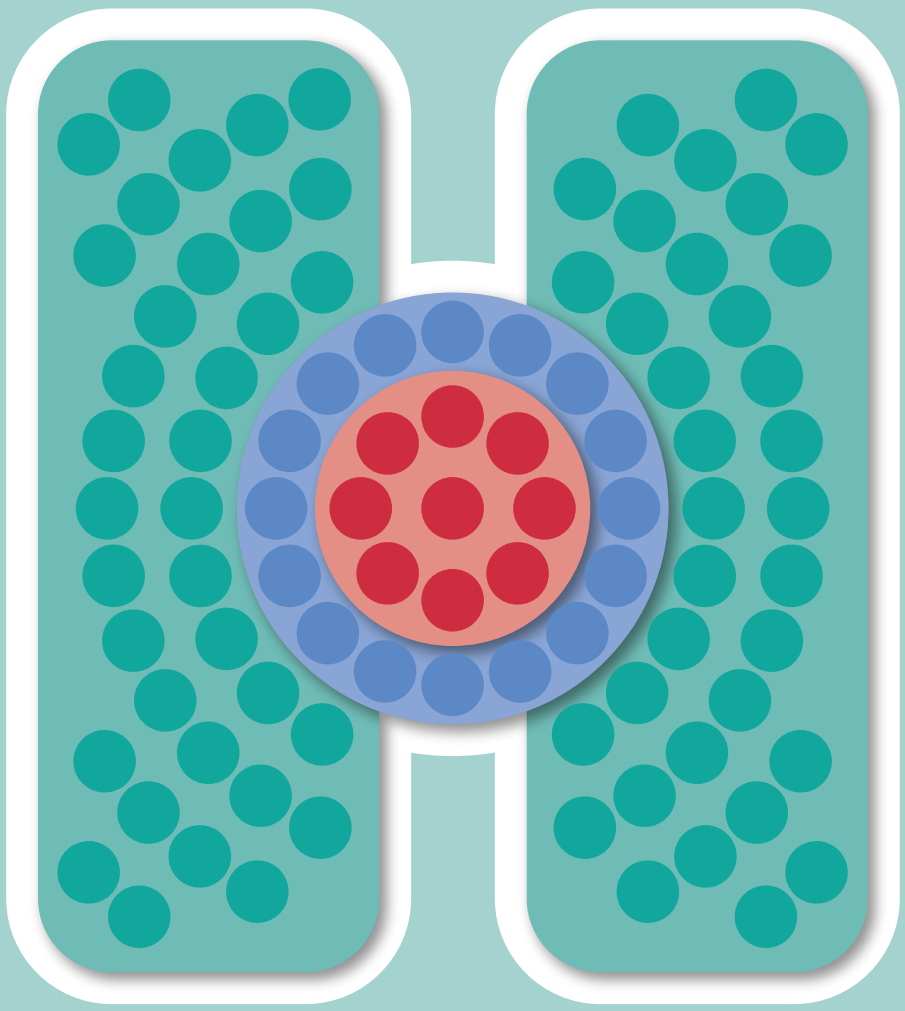
GUTKEEPER

A well functioning immune defense in the gut is an essential gatekeeper to keep intruders at bay.

Our gut is a window to the outer world.
The intestinal wall presents a large surface for nutrient absorption, which also means considerable **exposure to external pathogens getting in our body through food ingestion.**
Lucky enough, **70% of the body's immune cells are located in the gut**, within a structure called **gut-associated lymphoid tissue** (GALT).

HERD IMMUNITY

Being immune to a contagious disease can help others stay healthy. But how?



CONTAGIOUS INDIVIDUALS

IMMUNE INDIVIDUALS

SUSCEPTIBLE INDIVIDUALS

Contagious diseases (like the flu or covid) spread from person to person through pathogen transmission. But **when enough people become immune, the disease spreads less easily in the community.** The immune status is acquired either through vaccination or natural immunity after healing from the disease.

Ultimately, those who are not immune and cannot get vaccinated become less exposed.
This is called Community Immunity or Herd Immunity!

IMMUNE RESPONSE [2]

To fight a pathogen, the immune system has two levels of defense!

The INNATE IMMUNE SYSTEM

ROLE
1st immune reaction against the pathogen

TARGETING
Non-specific identification of the pathogen

TIMING
Quick
(hours after pathogen contamination)

INNATE
Memory **Non-specific** and **short/mid-term** (months/year)

ACTORS
Immune cells & active anti-pathogens molecules

The ADAPTIVE IMMUNE SYSTEM

ROLE
2nd immune reaction against the pathogen

TARGETING
Specific identification of the pathogen

TIMING
Slower
(days after pathogen contamination)

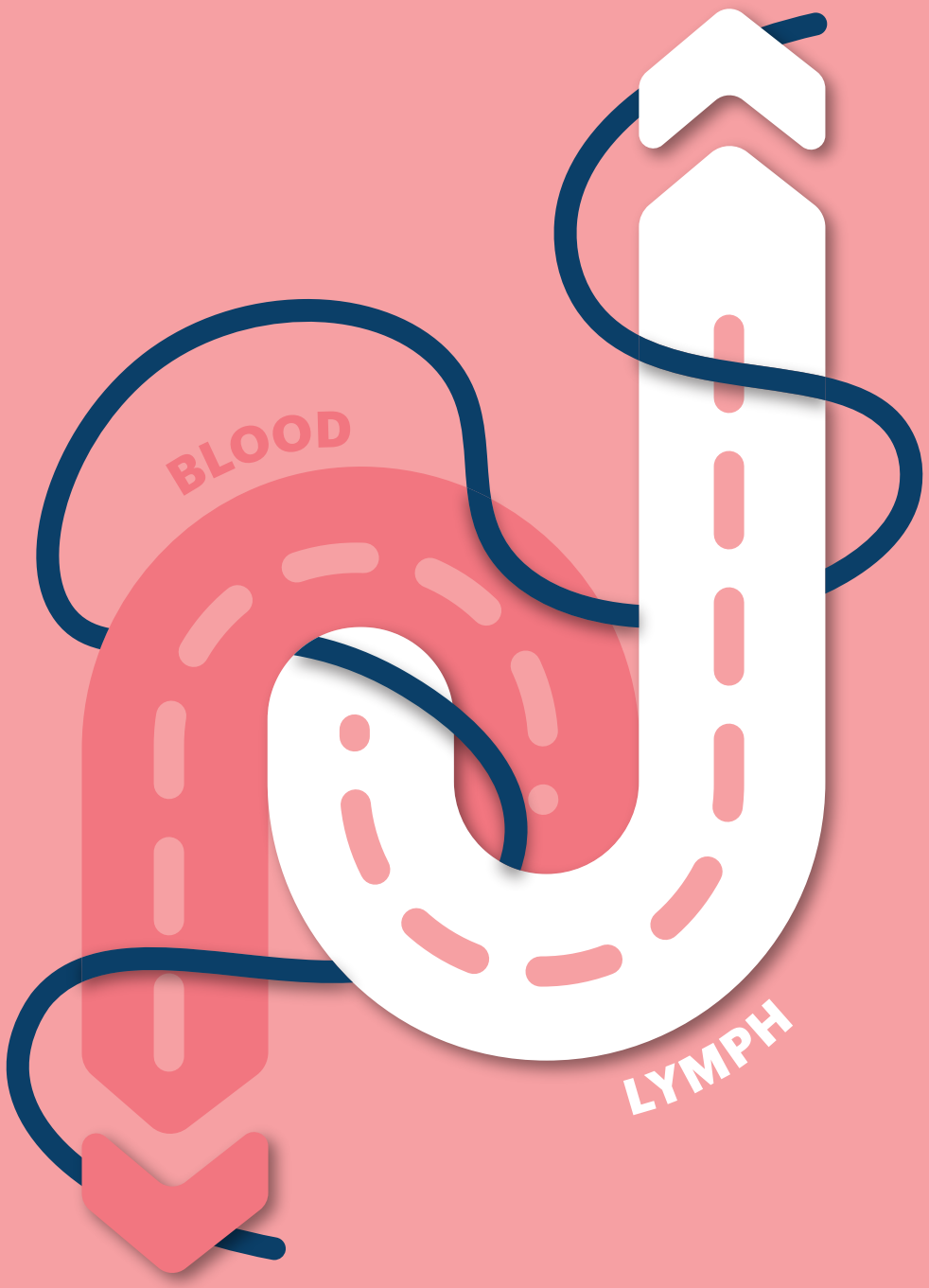
ADAPTATIVE
Memory **Specific** for each encountered pathogen and **long** term (decades)

ACTORS
Neutralizing molecules (Antibodies) & killer cells (Lymphocytes)

Both subsystems are closely linked and work together when an immune response is required to protect us against infection!

JOURNEY

Our immune cells are traveling, embarked on a continuous journey around our body, through BLOOD & LYMPH, two parallel and connected routes!



Immune cells are distributed to the entire body through the blood vessels, before moving to the lymph vessels where they can circulate and spread in closer contact with our body tissues.
Together, these two fluids transport all the elements composing our immune system, so they can do their jobs deeply in any part of our body.

KILLERS

The immune system possesses a large arsenal of immune cells, each with its own function. Among them are the killer cells!
They are crucial in destroying pathogen-infected cells or cancer cells.

Our body's **2 star executioners**: the Natural Killer cell & the Killer T cell.

KILLER T CELL
ALSO CALLED
CYTOTOXIC T CELL

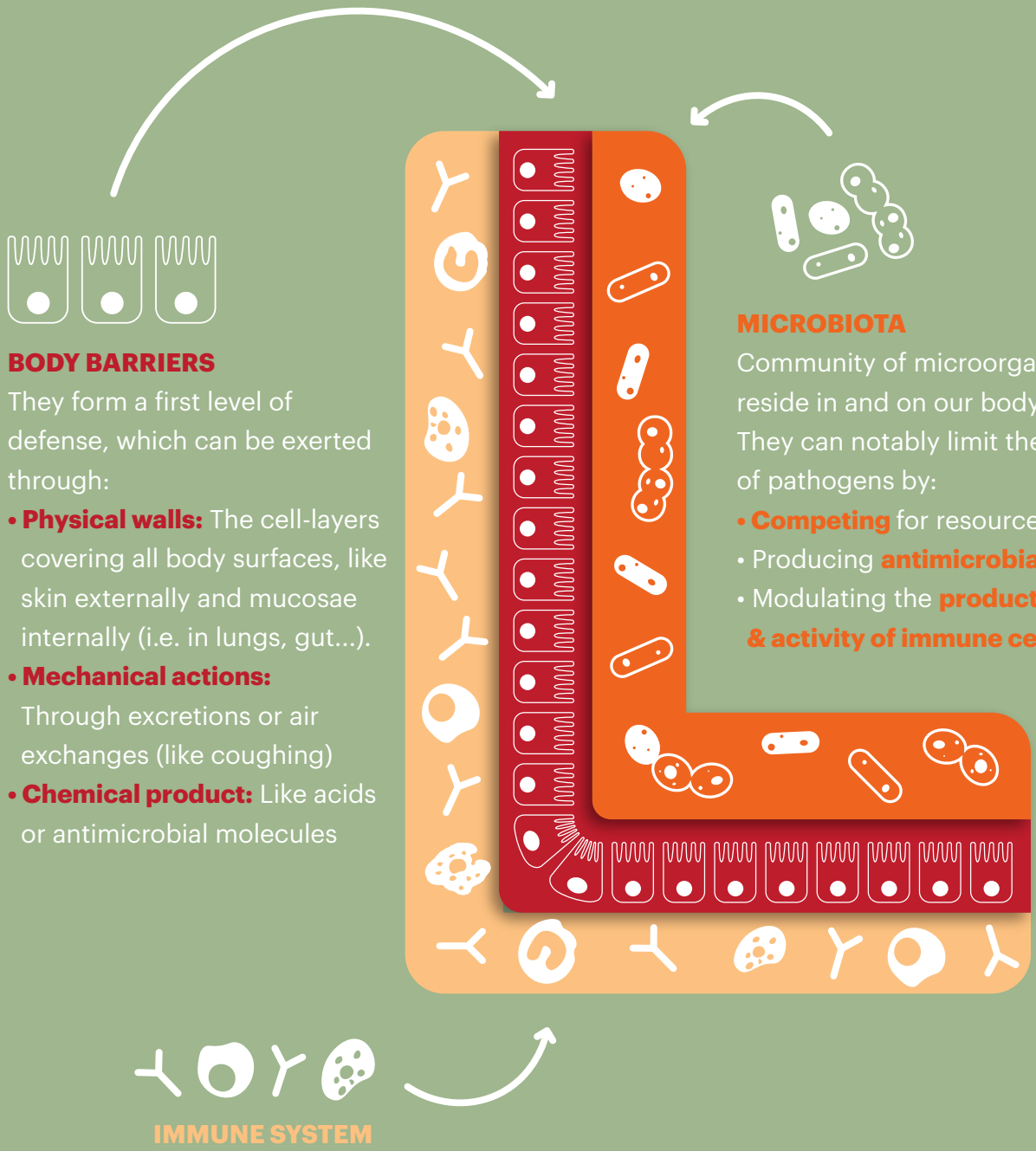
NATURAL KILLER CELL
ALSO CALLED
NK CELL

Both hold reserves of chemicals that they release on their target.
These chemicals can poke tiny holes in infected or cancer cells, causing them to leak, burst open and eventually die!

There are other types of cells which role is to eliminate intruders. For instance, phagocytes can directly ingest and destroy pathogenic bacteria & viruses.

LINES OF DEFENSE

**The immune system is the cornerstone of health.
But it does not work alone to ward off pathogens.
In fact, our body possesses 2 other lines of defense!**



BODY BARRIERS

They form a first level of defense, which can be exerted through:

- **Physical walls:** The cell-layers covering all body surfaces, like skin externally and mucosae internally (i.e. in lungs, gut...).
- **Mechanical actions:** Through excretions or air exchanges (like coughing)
- **Chemical product:** Like acids or antimicrobial molecules

MICROBIOTA

Community of microorganisms that reside in and on our body.
They can notably limit the overgrowth of pathogens by:

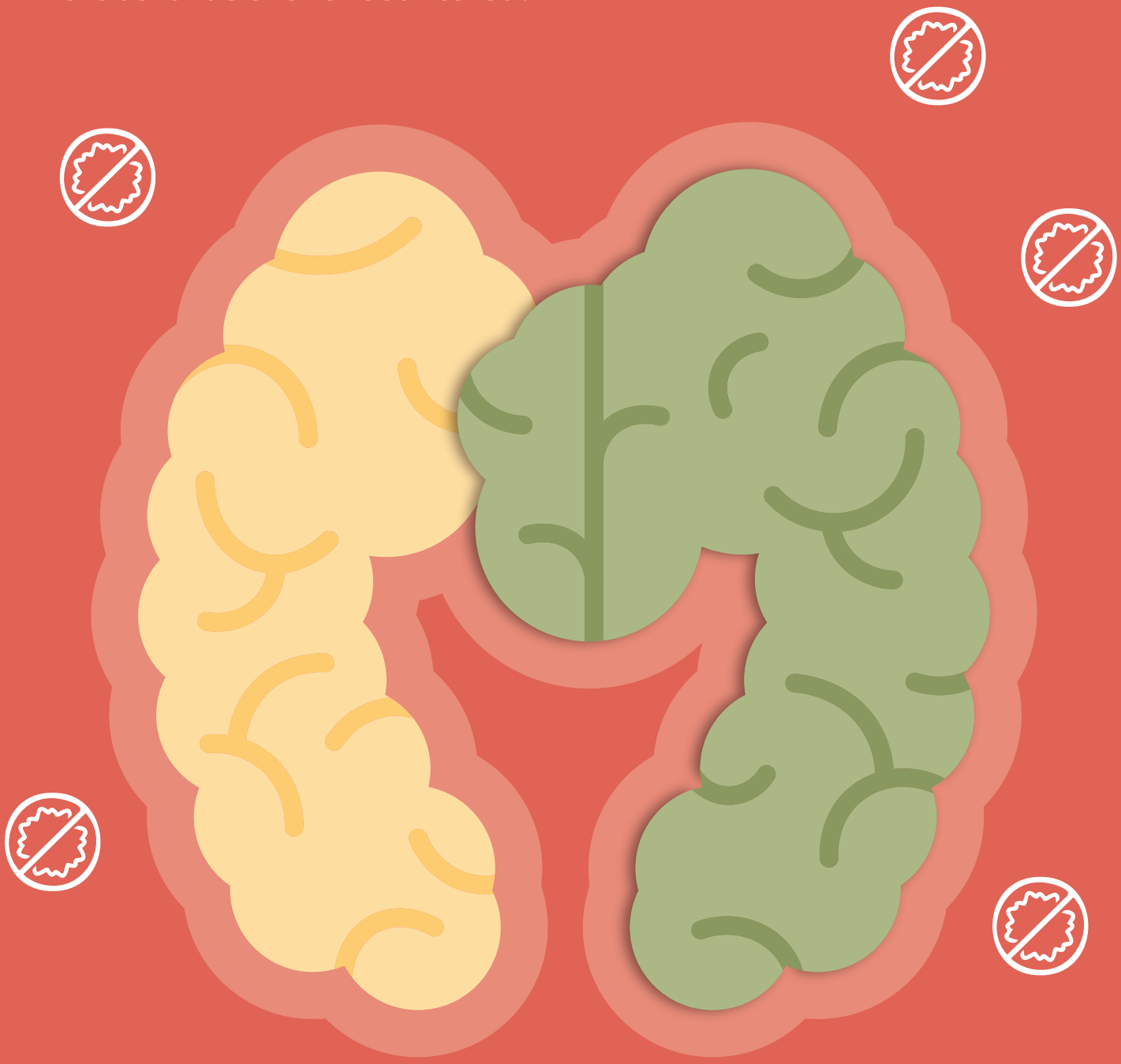
- **Competing** for resources
- Producing **antimicrobial molecules**
- Modulating the **production & activity of immune cells**

IMMUNE SYSTEM

The immune system, body barriers and microbiota are our 3 lines of defense against intruders!

MEMORY

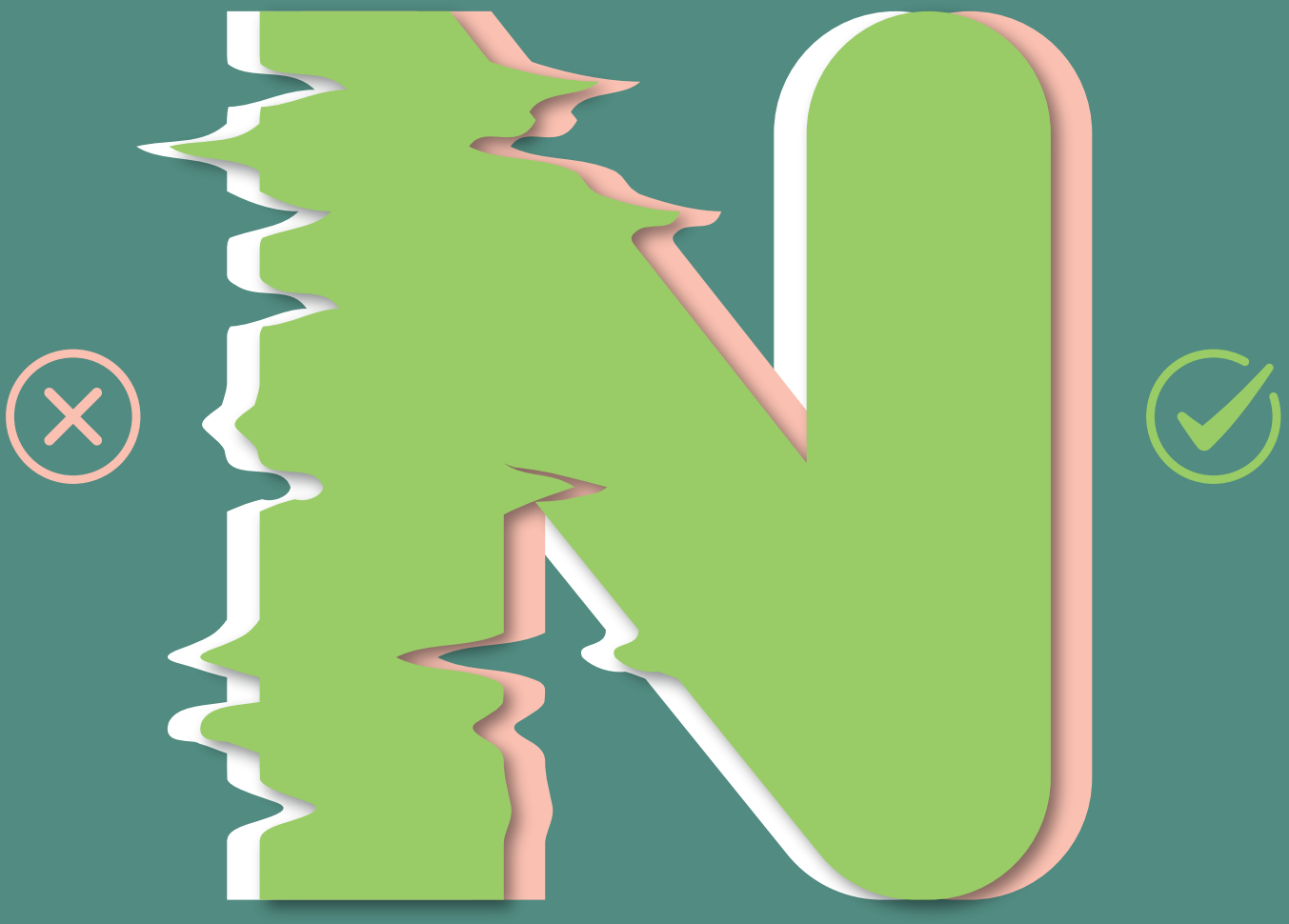
The immune system keeps a record of every microbe it has ever encountered!



When a microbe first infects our body, it is identified by specific immune cells called lymphocytes. After this initial encounter, some of those lymphocytes will become memory cells! **When exposed to the same microbe for the second time, our immune system will recognize it instantly thanks to these memory cells and will fight it off more quickly & more efficiently.**

NON-SELF VS SELF

All cells are coated with protein molecules that act as a sort of ID card. Thanks to them, our immune cells can recognize friend from foe, meaning the self from the non-self!



This cells' ID card is different for each individual. Indeed, in each of us, our immune system has been educated to identify our own body's cells as friends (i.e. self). **But this ID card can be altered.** Such is the case with cancer cells or cells infected by pathogens. **The alteration betrays their 'trespasser' status as non-self, allowing the immune system to identify them as foes to be eliminated.**

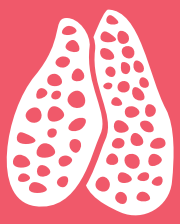
ORGANS

The immune system is an organ system.
It depends on a whole network of cells, tissues and organs.

PRIMARY ORGANS
Where all immune **cells originate**

BONE MARROW
Where all immune cells are **produced**

THYMUS
Where specific immune cells, the "T lymphocytes", **mature**

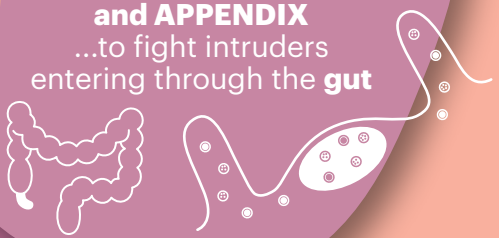


SECONDARY ORGANS
Where immune **cells go into action...**

SPLEEN
...to fight intruders travelling in the **blood**

LYMPH NODES
...to fight intruders travelling in the **lymph**

PEYER'S PATCHES and APPENDIX
...to fight intruders entering through the **gut**



TONSILS
...to fight intruders entering through the **mouth** and the **nose**

These are called the lymphoid organs.
Together with a large circuit of lymphatic vessels, they form the lymphatic system!

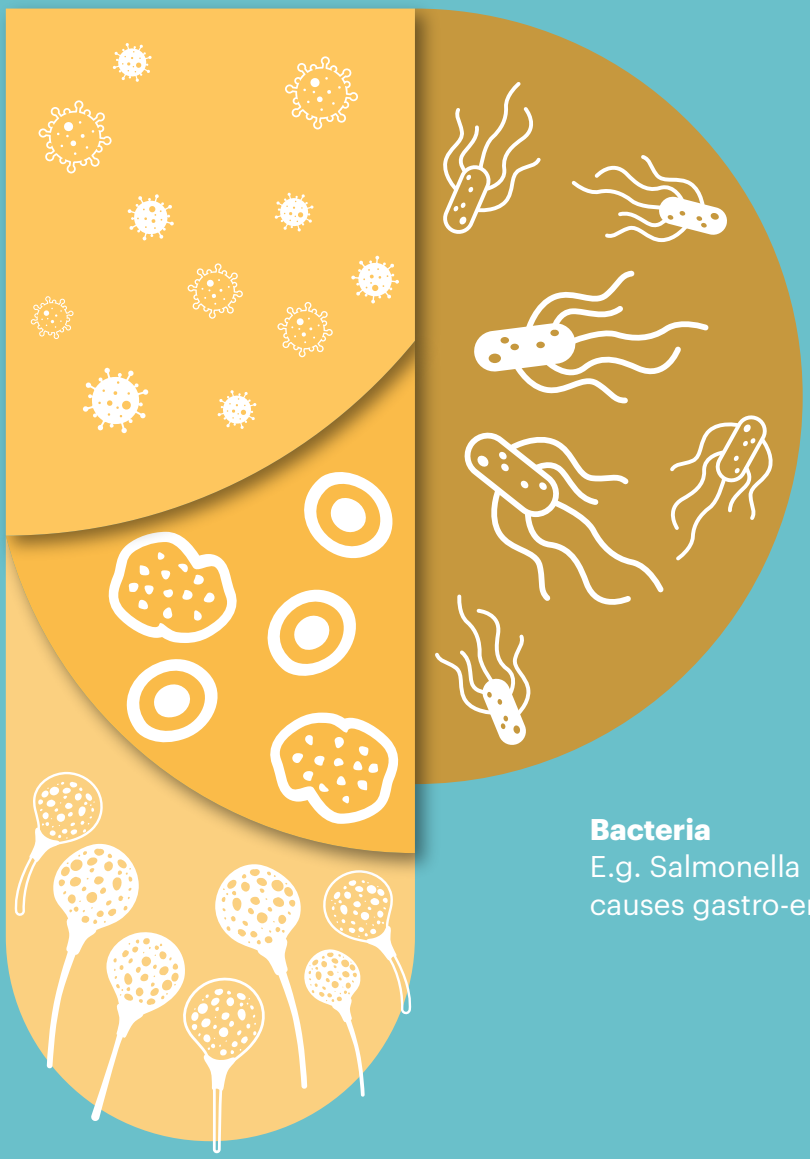
PATHOGENS

One of the immune system's main mission is fighting pathogens. But who are they?

Viruses
E.g. Coronavirus causes COVID

Parasites
E.g. Plasmodium falciparum causes Malaria

Fungi
E.g. Candida causes mycosis



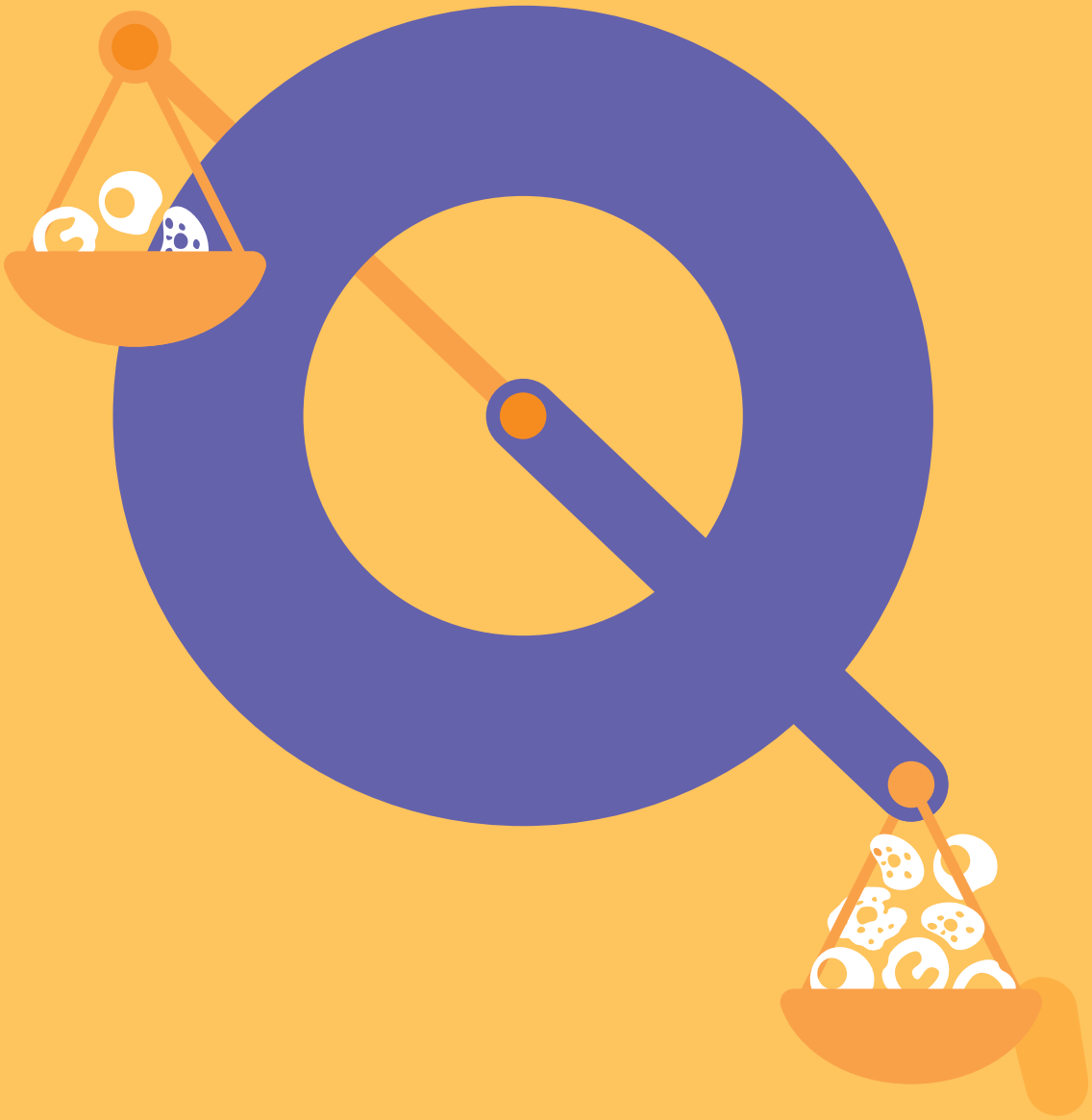
Bacteria
E.g. Salmonella causes gastro-enteritis

Pathogens are microscopic organisms that cause infectious diseases.
They can spread from one person to another through contact, body fluids or aerosol transmission.

The small world of pathogens is incredibly diverse, and includes many types of viruses, bacteria, fungi and parasites.

QUANTIFYING IMMUNITY

While it is difficult to quantify immunity as a whole, it is possible to quantify some immune parameters through biological tests!
It is notably the case when a doctor prescribes us a blood analysis called **hemogram.**

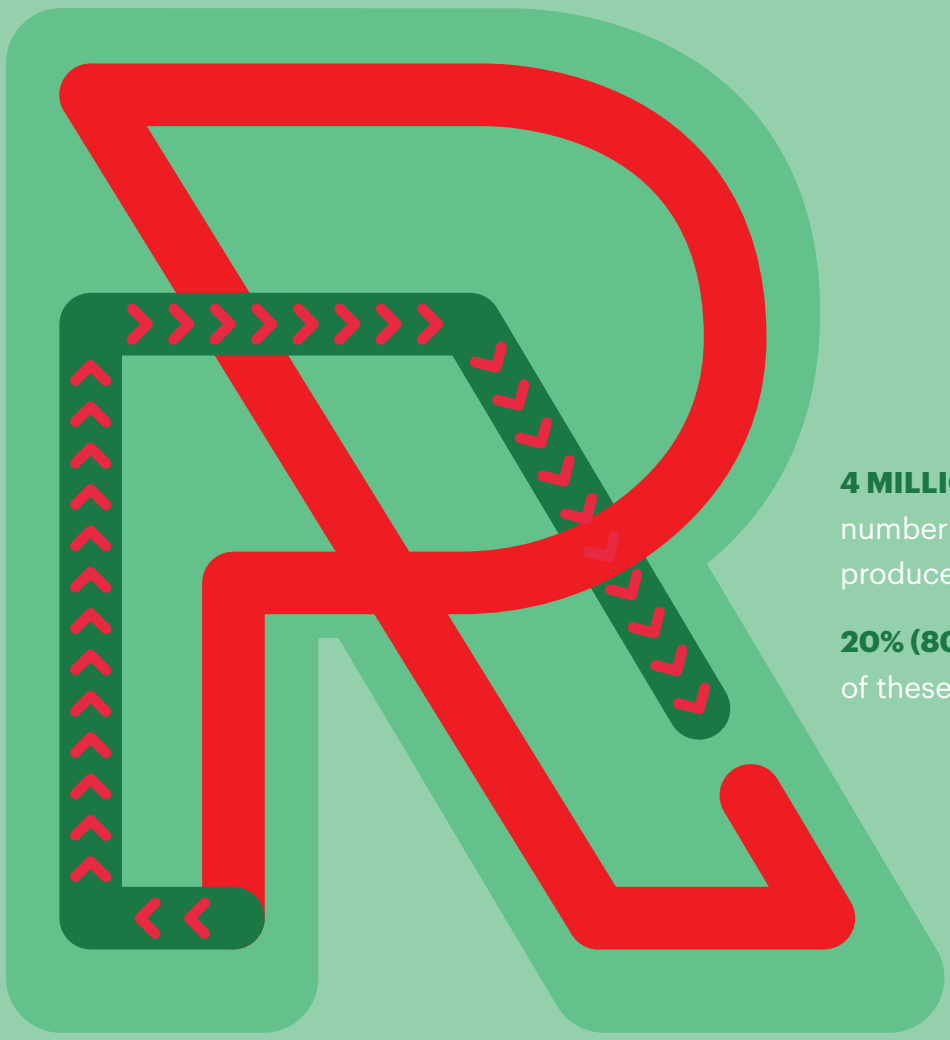


It includes **counts of the different types of immune cells present in our body at a given moment, which provides essential insights into our health!**
When counts are out of normal range, either higher or lower, this can signal diseases such as infections, inflammations or even underlying immune disorders.

In that sense, **blood cells counts work as a sort of 'quality control' of our body's immune system.**

REGENERATION

The immune system's cells are continuously regenerated by our body in order to replenish and replace the ones that are damaged, aged or dead.



4 MILLION/SECOND
number of newly produced body cells.

20% (800 000)
of these are immune cells!

The cells that need to be eliminated are scavenged by the immune system itself by specific immune cells called phagocytes.
Regeneration takes place in the bone marrow, where new cells are born.
They later differentiate into various types of immune cells, each having a specific function.

So you see, **a functional immune system is a delicate balance between the production and the loss of immune cells.**

SENTINEL

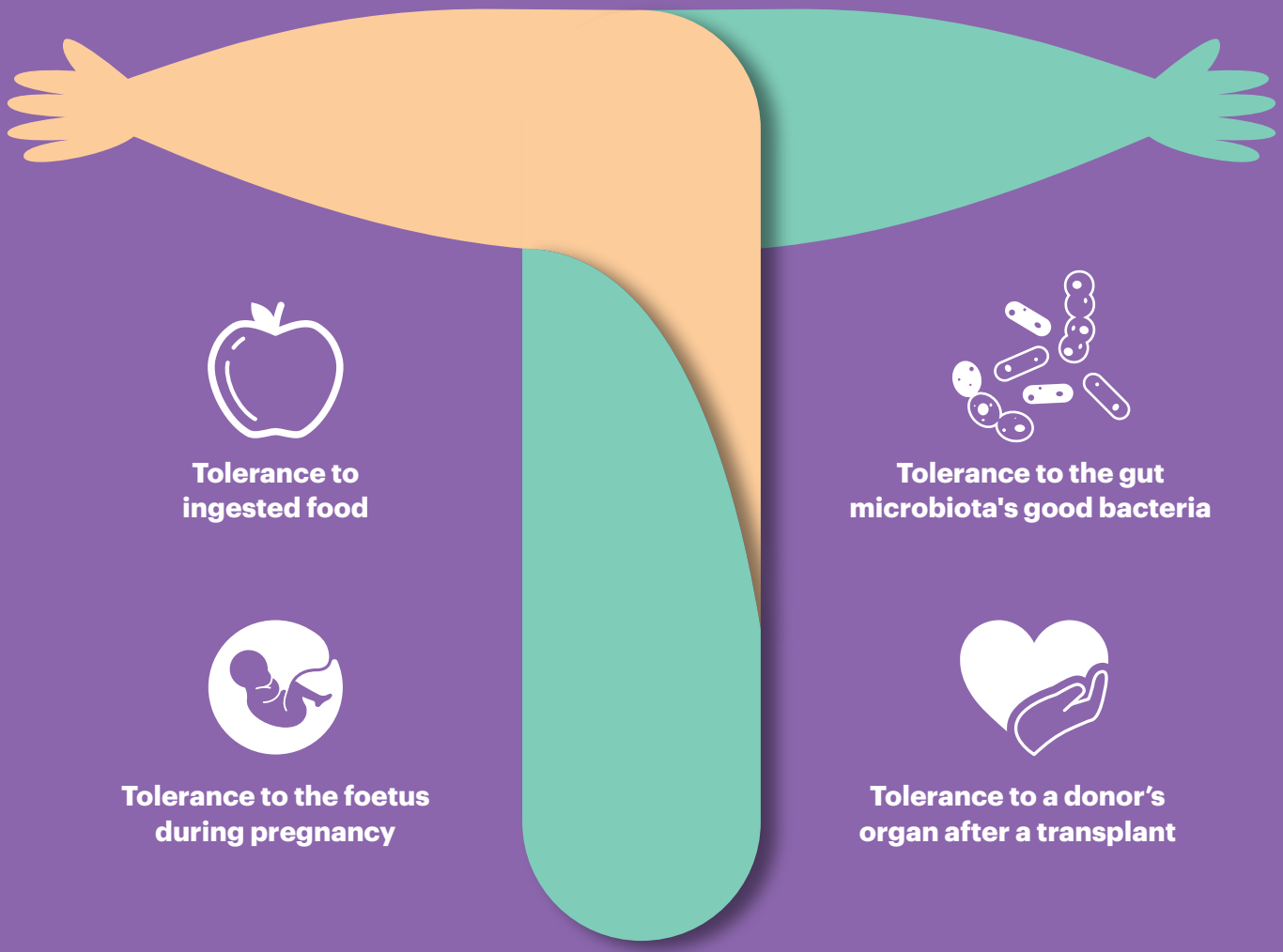
Can you believe that the inside of our body is in permanent contact with the outside environment?

Simple and sometimes vital acts like breathing, eating, touching are bringing in outside elements into our respiratory, digestive, urinary or sexual tracts every day!

It is the **immune system's job to act as a sentinel to check all elements coming in from the outside**, in order to identify the harmful ones and react appropriately. To do so, immune cells are standing guard at multiple checkpoints all along each of our body's tract.

TOLERANCE

TOLERANCE is a state of unresponsiveness of the immune system that suppresses immune reactions. This feature, set up by the immune system itself proves essential in many situations.



Tolerance to ingested food

Tolerance to the gut microbiota's good bacteria

Tolerance to the foetus during pregnancy

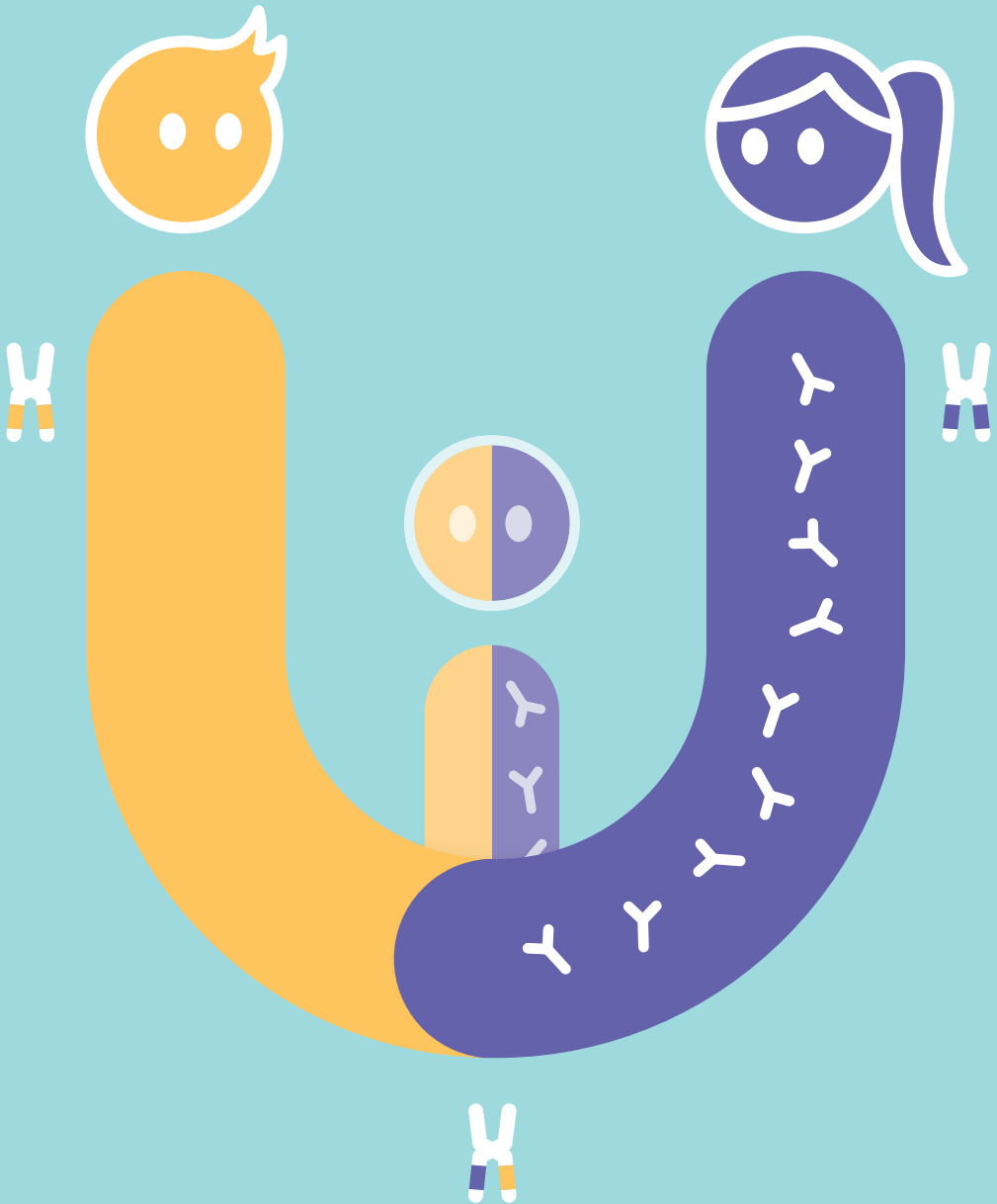
Tolerance to a donor's organ after a transplant

Tolerance to the body's own cells

In these cases, **when tolerance is lost, it can lead to disorders** like autoimmune disease against one's own body tissues, food allergy, inflammatory bowel disease, miscarriage or transplant rejection.

UNVALUABLE LEGACY

When it comes to our immune system, we may owe some of it to our parents !

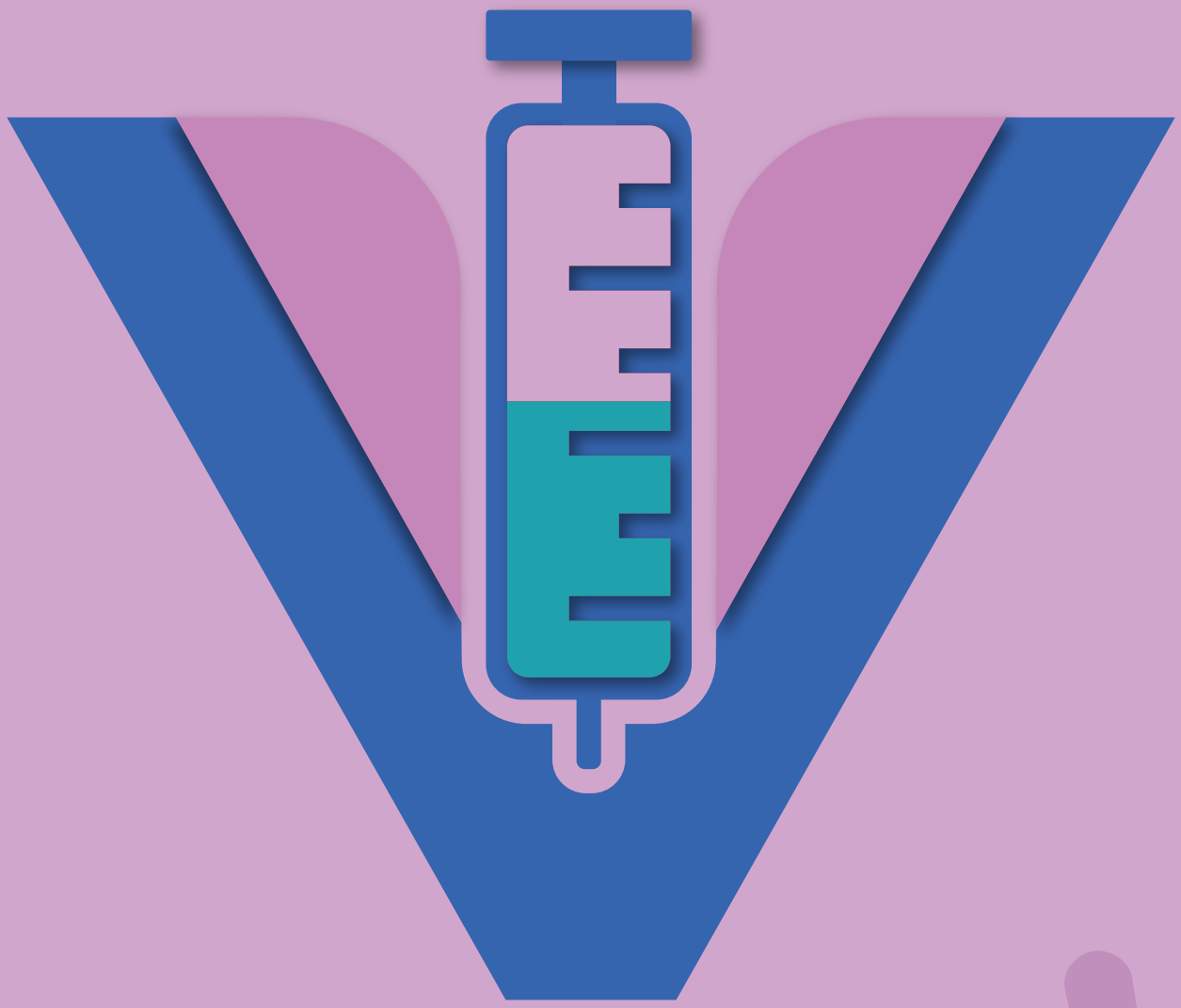


Babies inherit a number of IMMUNE-RELATED GENES from their parents, that allow them to build their own immunity. Sometimes, heredity can also anchor genetic predispositions to immune disorders like immunodeficiency, allergies or autoimmune diseases.

But it does not stop here! **Mothers can transfer elements like antibodies to their babies through the placenta and breastfeeding** to protect them when their immune system is still immature. This form of immunity is called **PASSIVE IMMUNITY!**

VACCINATION

Vaccination is an effective strategy to protect against infectious diseases based on the adaptive immune system's memory.



A vaccine contains a weakened pathogen or some fragments of it. It is meant to stimulate the immune system to memorize the pathogen without provoking a disease. **If the real pathogen enters the body, the immune system is already trained to recognize it and can counterattack** immediately by producing antibodies to neutralize it and avoid the disease altogether.

Some microbes (e.g. the flu or the COVID viruses) evolve constantly and the immune system has to build its memory with every new version. In this type of cases, seasonal vaccination is used each year.

WAY OF LIFE

You can positively act on your immune system through lifestyle choices!

HEALTHY CHOICES FOR THE IMMUNE SYSTEM

BALANCED DIET

GOOD AND LONG SLEEP

STAYING ACTIVE

SOCIALIZING AMD LAUGHING

MANAGING STRESS

Our immune system's activity can be impacted by different factors, like genetics, age, or the environment, which are elements beyond our control. But thankfully, not everything is out of our hands! **A healthy way of life can make a serious difference**: your immune system will thank you!

(e)XPOSURE OR (e)XTREME HYGENE ?

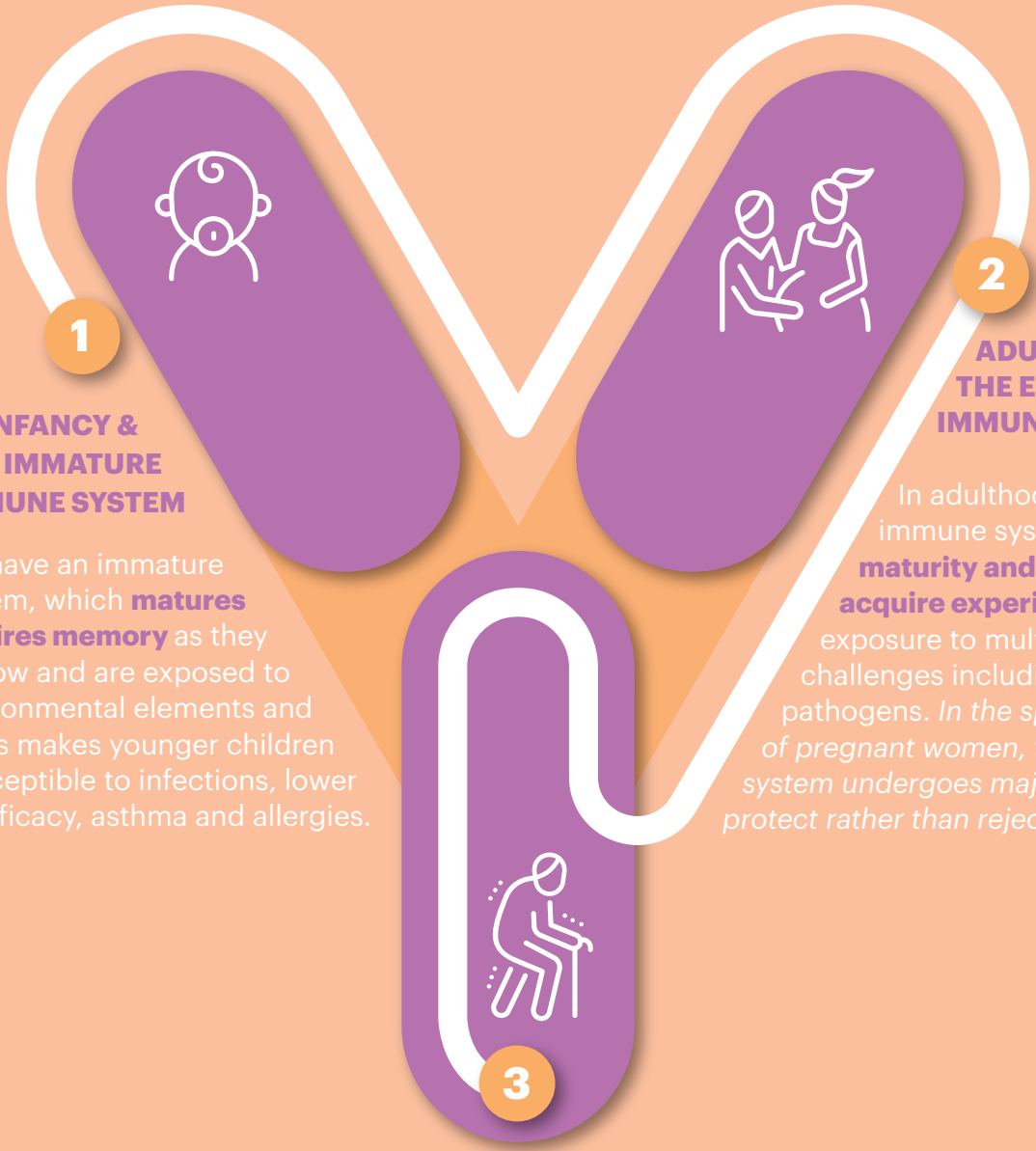
Keeping healthy doesn't necessarily rime with avoiding germs altogether by going overboard with hygiene. Some level of exposure to micro-organisms can actually be beneficial!

Of course, **good hygiene is essential in situations where harmful pathogens are prevalent in order to limit infections** and the spread of contagious diseases in communities.

However, **a controlled exposure to germs can also help, notably to educate the immune system in early life**, teaching it to distinguish between harmful pathogens and harmless micro-organisms. It also helps reduce the risk of allergies and autoimmune diseases and develop tolerance for a well-balanced immune system.

YEARS IN THE MAKING

Our immune system changes over the years!



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INFANCY & THE IMMATURE IMMUNE SYSTEM

Newborns have an immature immune system, which **matures and acquires memory** as they grow and are exposed to environmental elements and microbes. This makes younger children more susceptible to infections, lower vaccine efficacy, asthma and allergies.

2

ADULTHOOD & THE EXPERIENCED IMMUNE SYSTEM

In adulthood, the immune system **reaches maturity and continues to acquire experience** through exposure to multiple foreign challenges including pathogens. *In the specific case of pregnant women, the immune system undergoes major changes to protect rather than reject the foetus.*

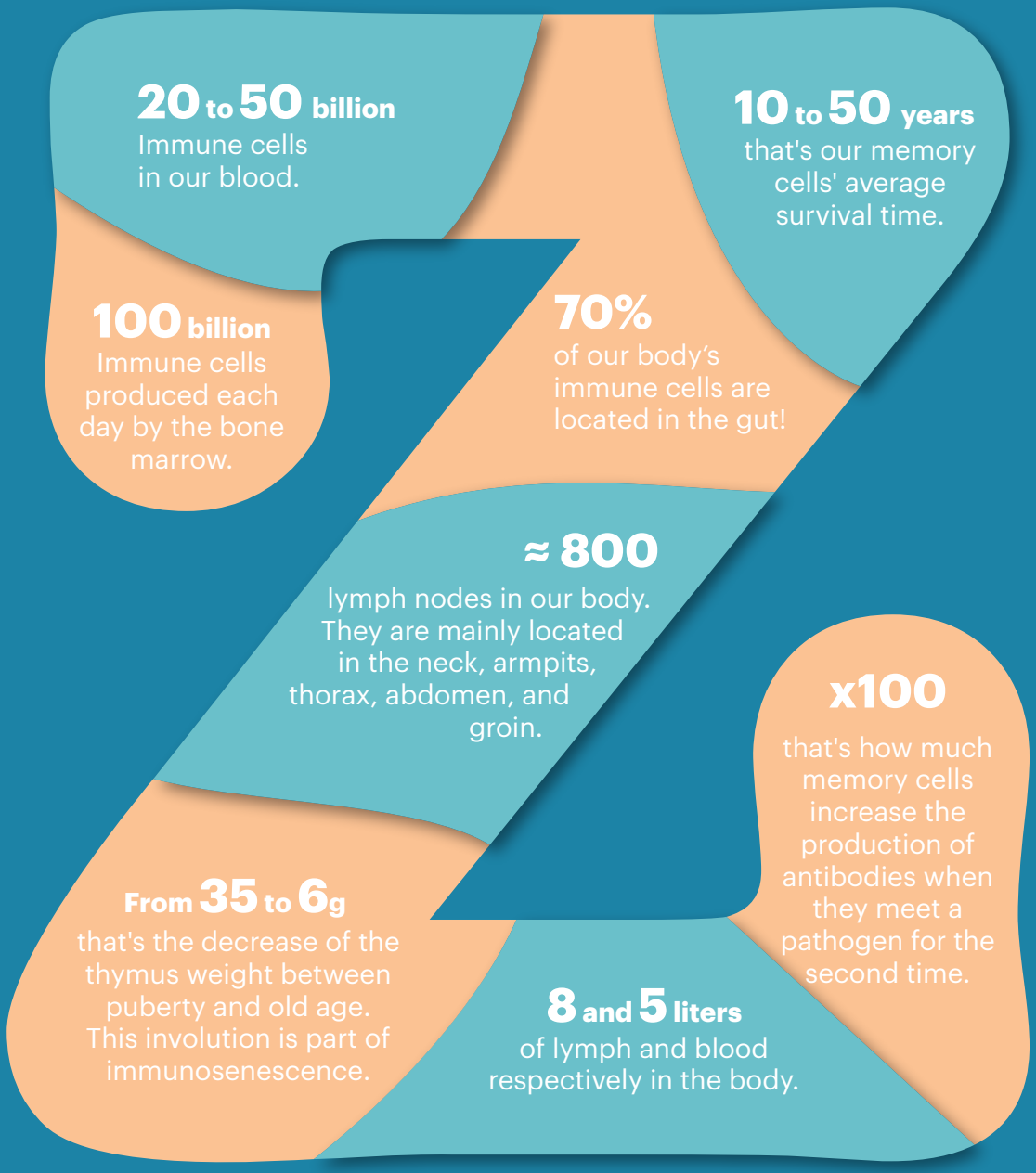
3

OLD-AGE & IMMUNOSENESCENCE

The elderly go through a **natural deterioration** of their immune system called immunosenescence. It results in a decreased number and activity of immune cells, and a gradual atrophy of the immune organs.
This makes older people more prone to diseases like infections, cancer, autoimmune and inflammatory diseases, and poorer vaccine efficacy.

ZILLIONS

Immunity in numbers



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How do life stages and choices impact the immune system?

What do concepts such as herd immunity, immune memory or tolerance mean?

A riveting – and accessible to all - alphabetical journey through the wonders and complex mechanisms of the immune system!

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