

Chapter 1: Overview of The Immune System

Anita Spanjer – van Dijk (SPAI)
a.i.r.spanjer-van.dijk@pl.hanze.nl



Waar denken jullie aan bij het afweersysteem?



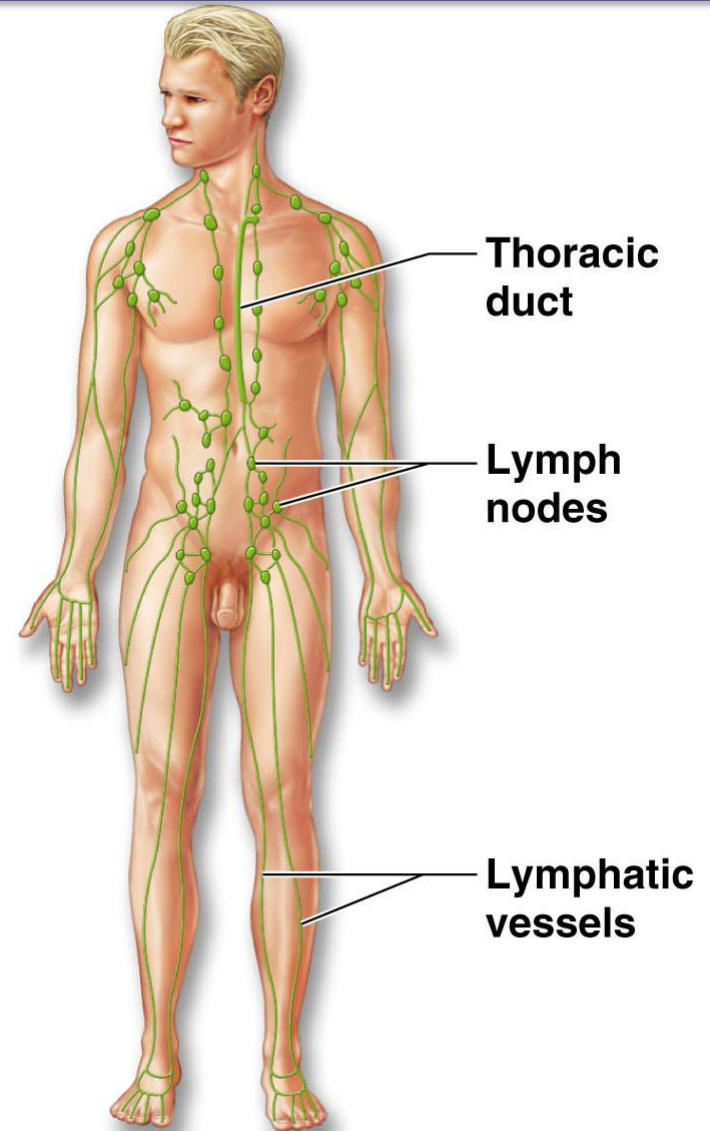
The lymphatic system

Composed of:

- Lymphatic vessels,
- Lymphoid organs: lymph nodes, spleen, tonsils,

Function:

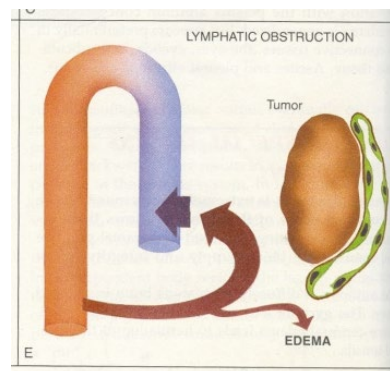
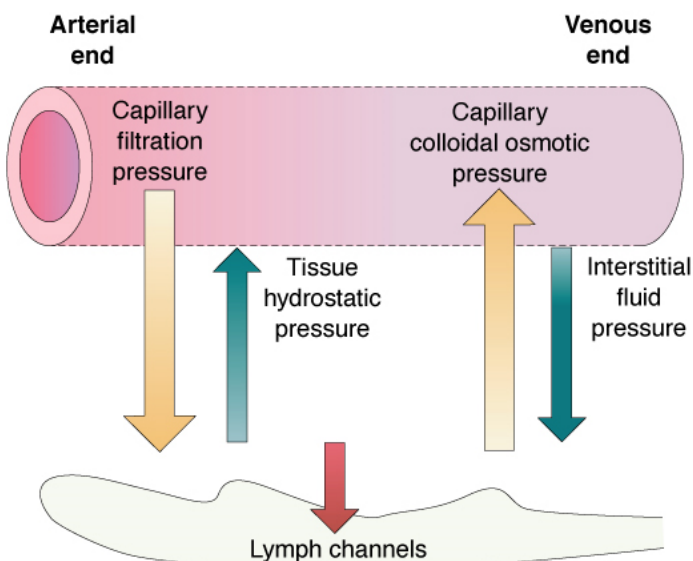
- Returns fluids from tissue back to blood vessels
- Disposes of debris
- Protects from infection



(g) Lymphatic System

The lymphatic vessels

- Returns excess fluid from the tissues back to the bloodstream as lymph (heldere vloeistof)
 - ~3L/day
- One-way system (only from tissue to the heart)
- Lymphatic blockage leads to edema

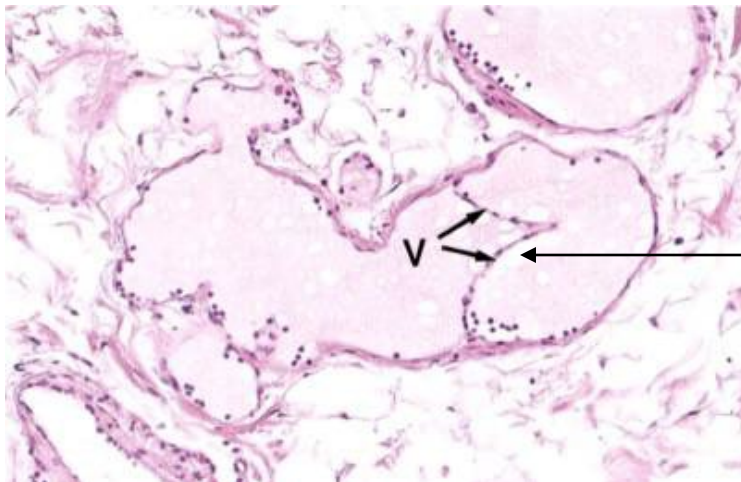


Blocked lymph drainage

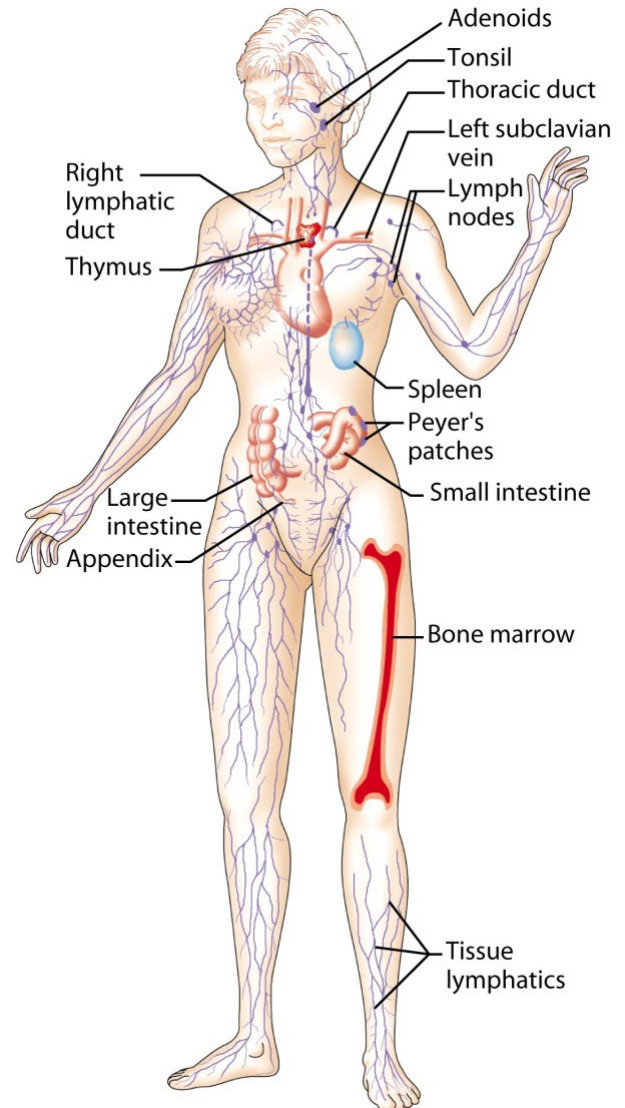


The lymphatic vessels

- One-way system from tissues to the heart
- Skeletal muscles contraction “pumps” the lymph to the heart (similar to veins)
- Larger lymph vessels contain valves (similar to veins)

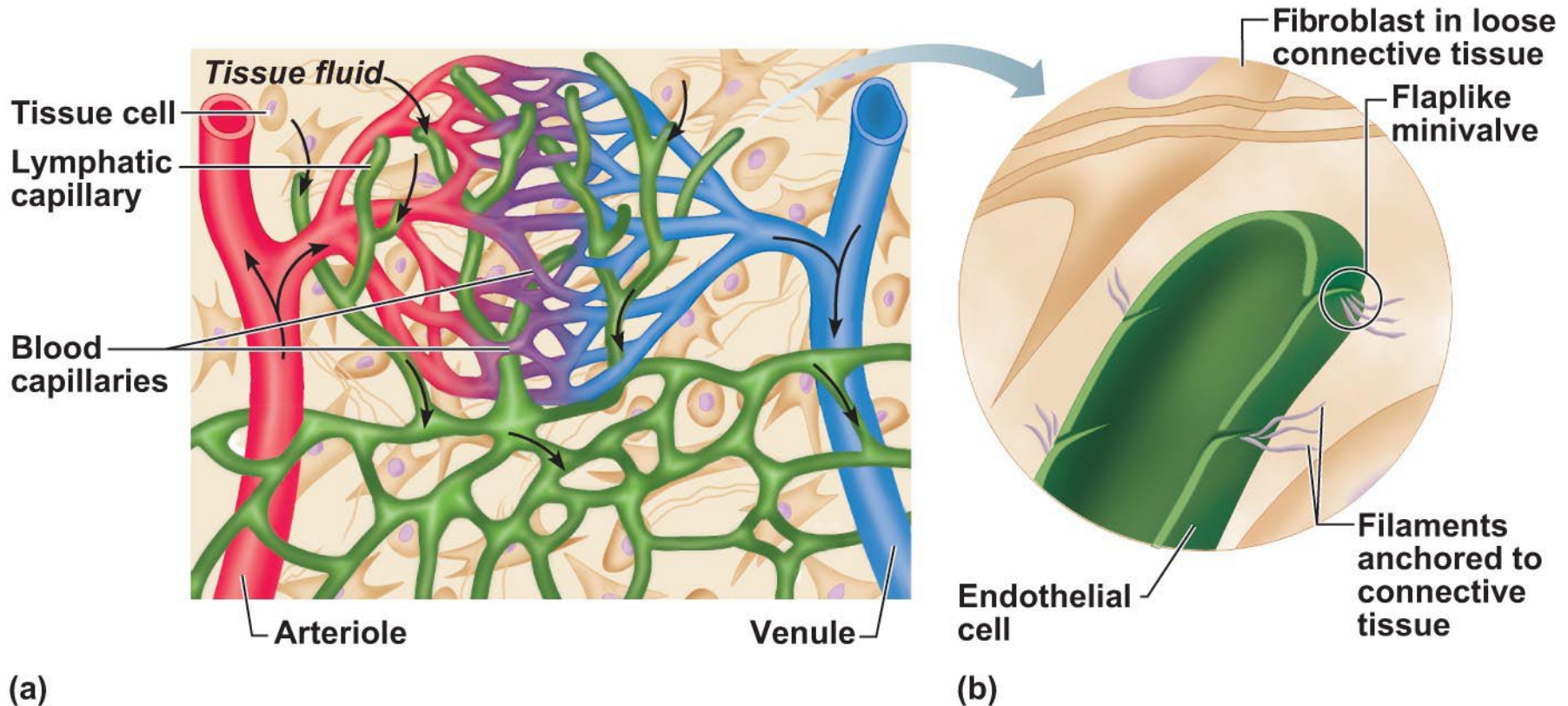


V: valves



- Verschillen lymfevaten met venen?

The lymphatic capillaries

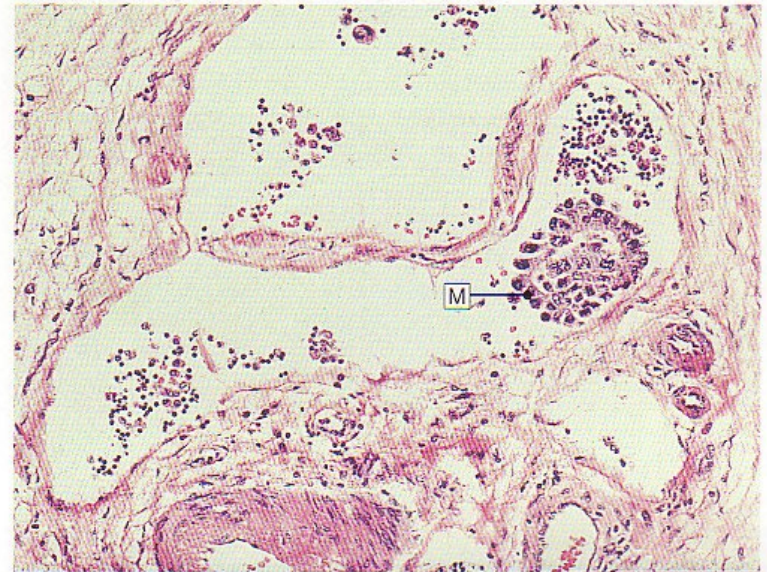


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Endothelial cells in lymphatic capillaries are imbricated (*dakpansgewijs georandiseerd*) and function as one-way swinging doors

What travels through these lymphatic vessels?

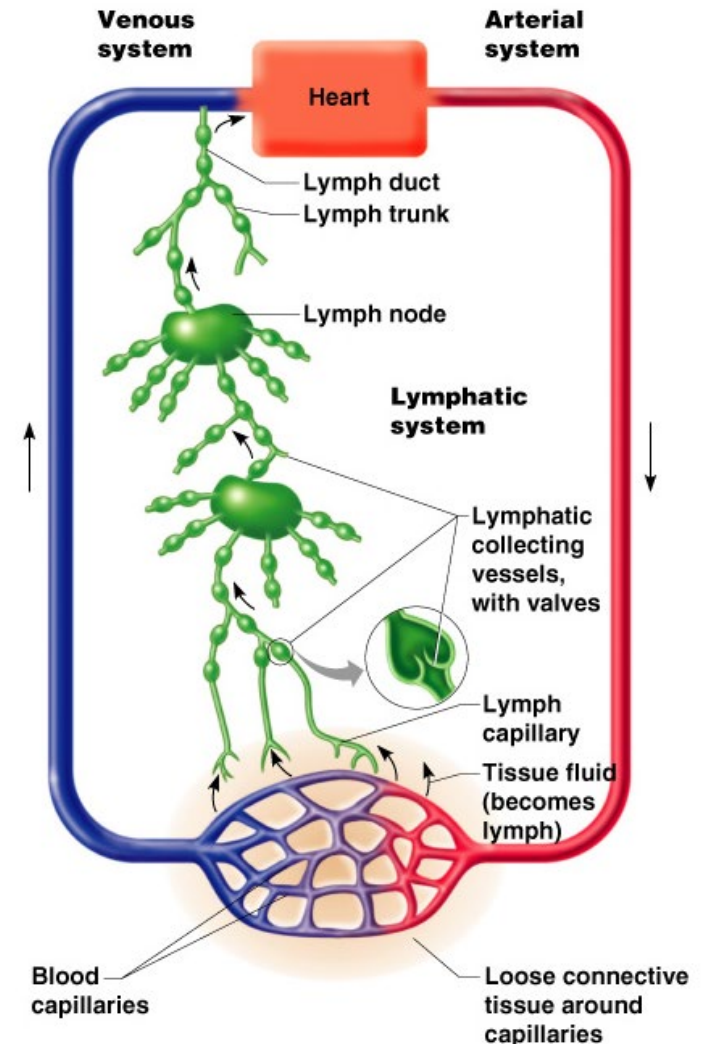
- Substances that need to be returned to the bloodstream
 - (Excess) fluid
 - Blood cells:
 - Red blood cells? Ja/nee
 - White blood cells? Ja/nee
 - (Small) proteins
- But also larger particles such as:
 - Bacteria
 - Virusses
 - Cancer cells



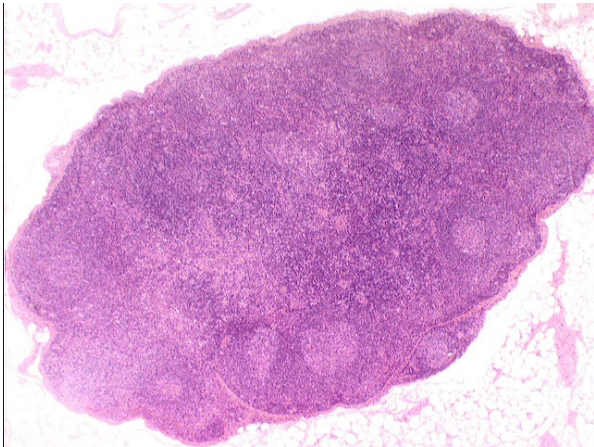
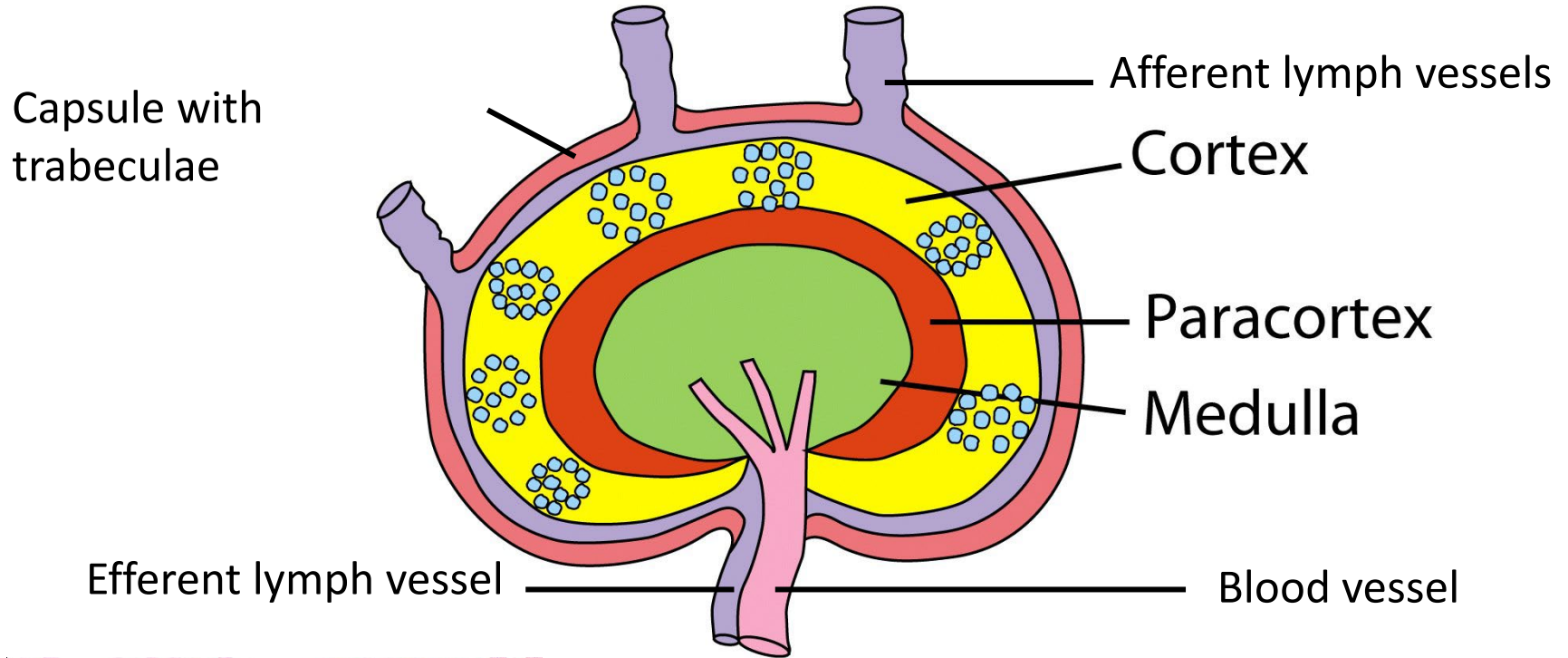
M: metastasis in lymph vessel

Lymph nodes are lymphoid organs

- Lymph nodes are scattered throughout the body, connected to the lymph vessels (and blood vessels)
- Filter harmful substances from the lymph
- Immune cells (white blood cells, or leukocytes) in the lymph nodes filter and destroy these harmful substances
 - Macrophages
 - Lymphocytes
- Lymph passes multiple lymph nodes before being returned to the bloodstream

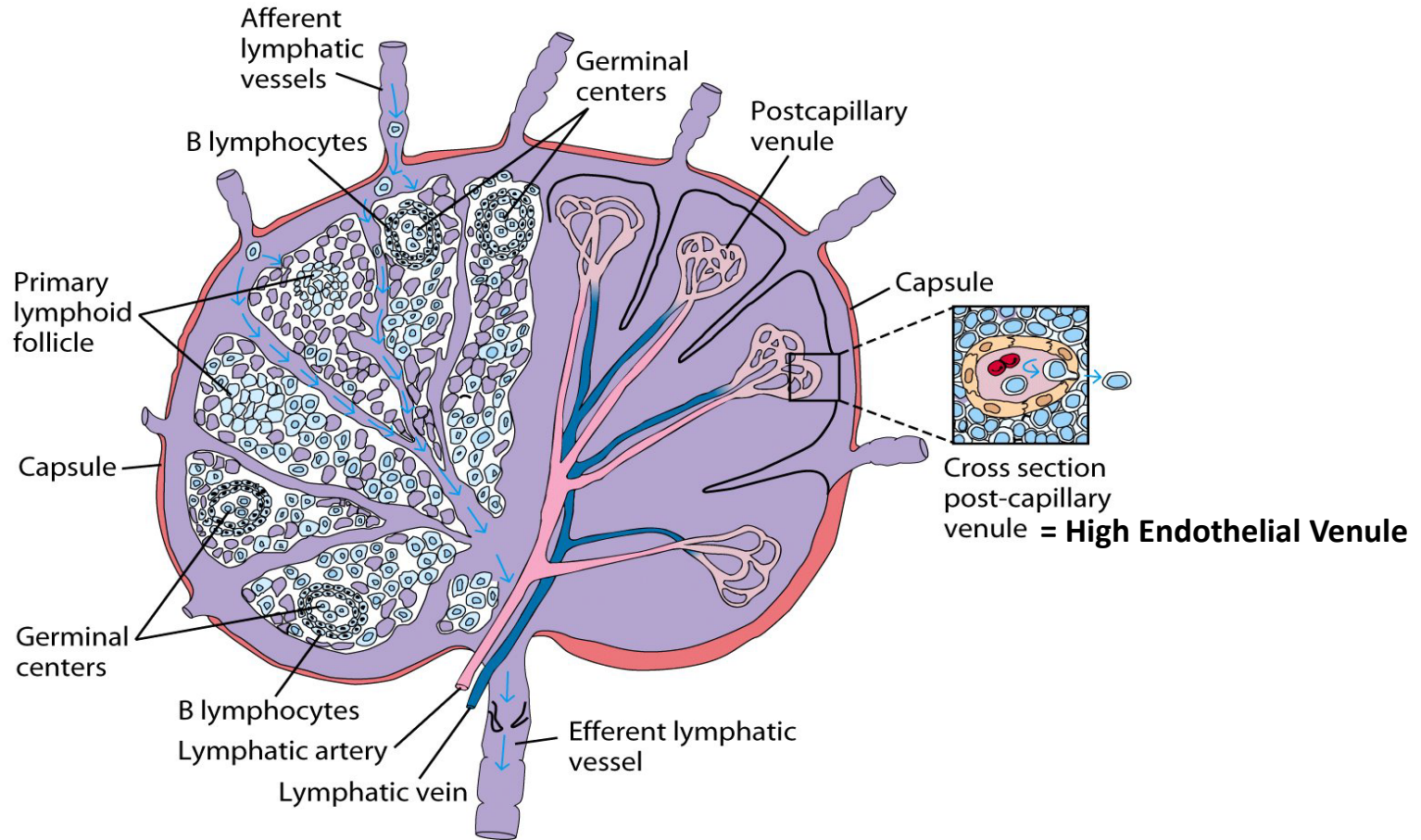


Structure of lymph nodes



Hoe stroomt lymfe door een lymfeknoop en welke structuren en cellen worden er dan gepasseerd?

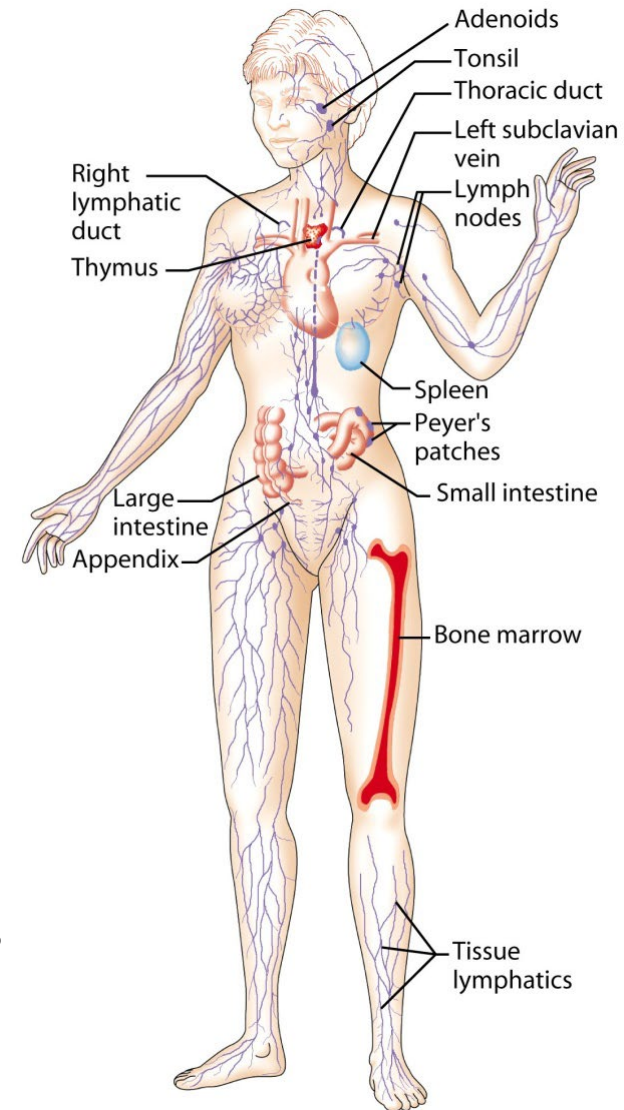
Lymphocytes enter via HEVs



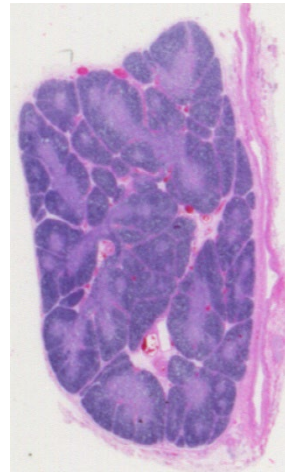
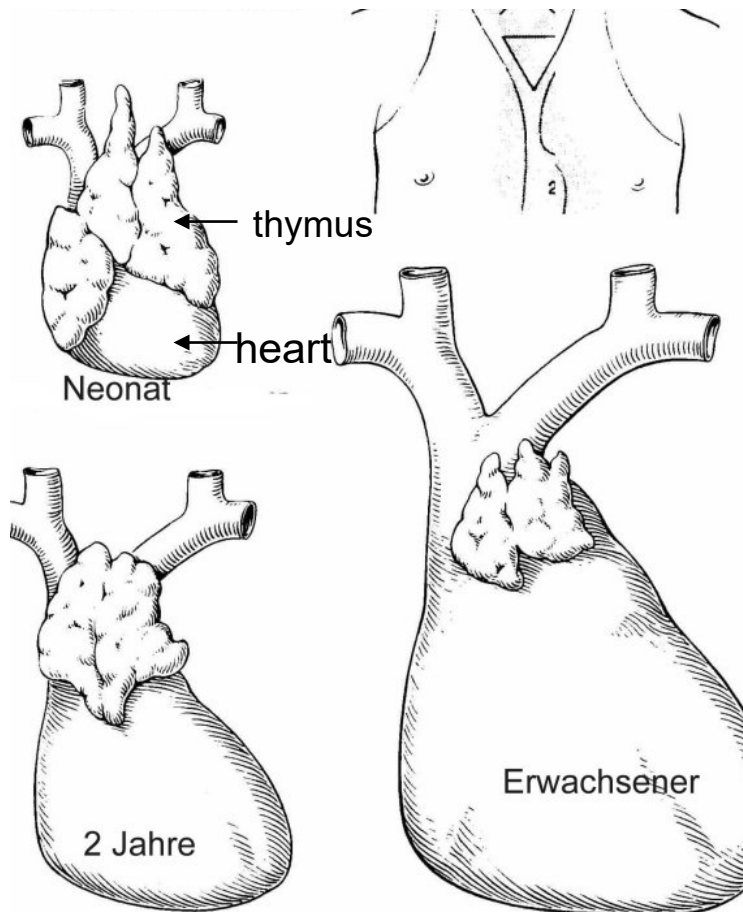
- Lymphocytes enter the lymph node via afferent lymph vessels as well as blood vessels
- Blood vessels are specialized and called 'post-capillary venule' or 'high endothelial venule' (HEV)

Other lymphoid organs

- Thymus
 - Bone marrow
 - Spleen
 - Tonsils
 - Intestine: peyer's patches and appendix
-
- All lymphoid organs contain reticular connective tissue and many lymphocytes
 - Only the lymph nodes filter lymph!



The thymus



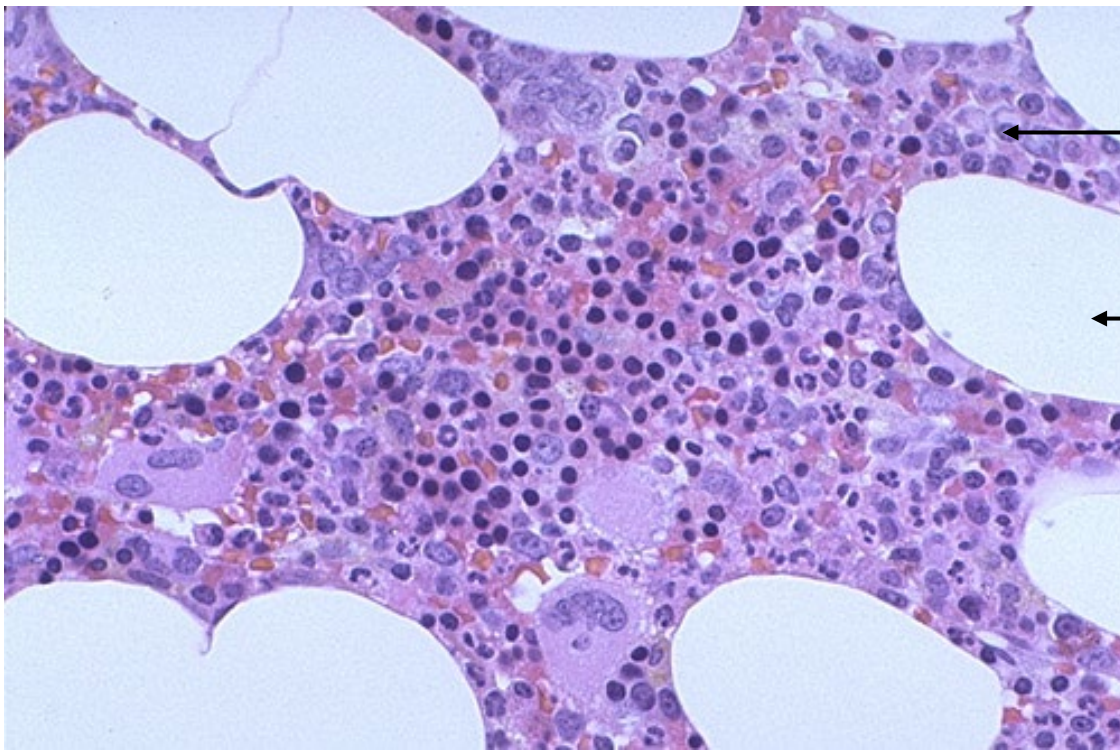
Thymus of a young child



Old thymus (more connective tissue and fat)

- The size of the thymus decreases with age
- The thymus produces thymosin
- In the thymus T-cells develop and are 'educated' to distinguish 'self' from 'non-self'

The Bone Marrow



← Developing blood cells

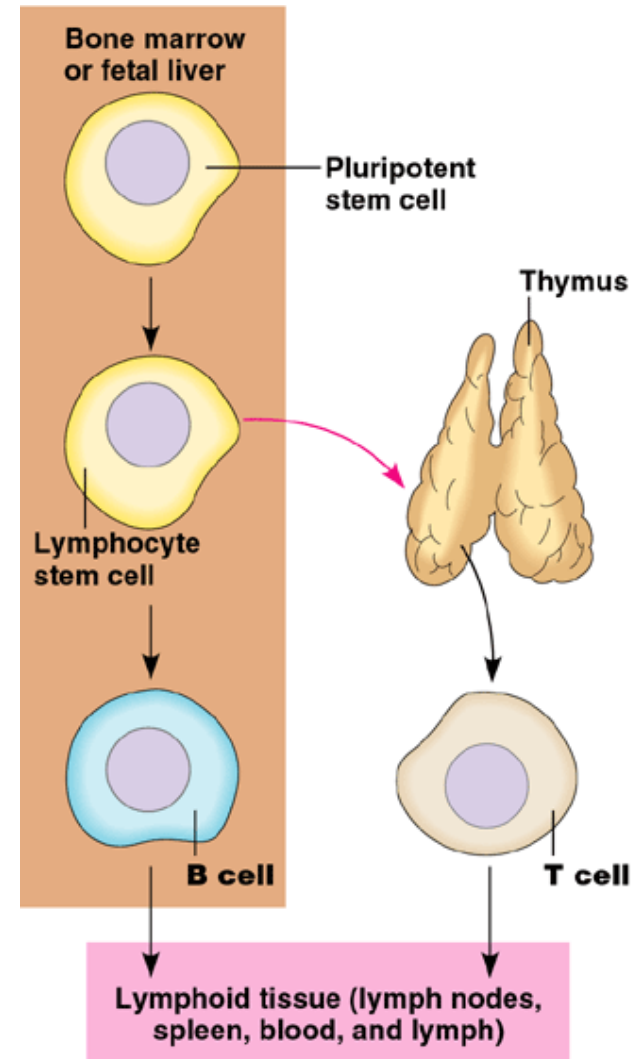
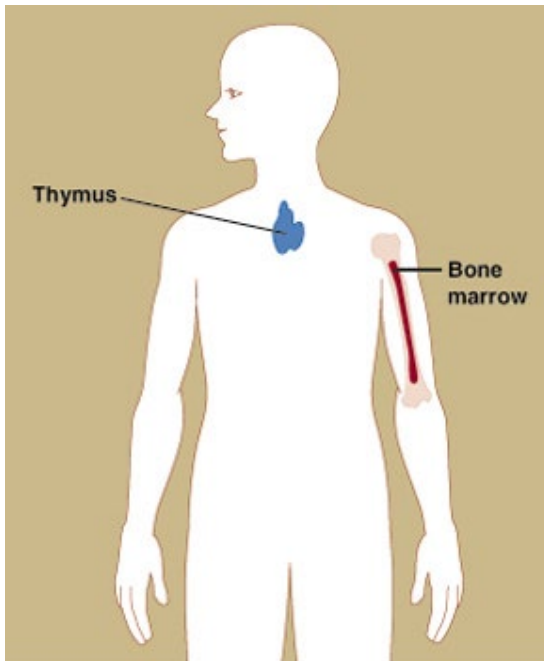
← Fat

- In the bone marrow platelets, red and white blood cells (leukocytes) develop
- T-cells go to the thymus for further development and 'education'
- B-cells are 'educated' to distinguish 'self' from 'non-self' in the bone marrow (will be discussed later)
- Other leukocytes do not need education! (will be discussed later)

Education of T- and B-cells

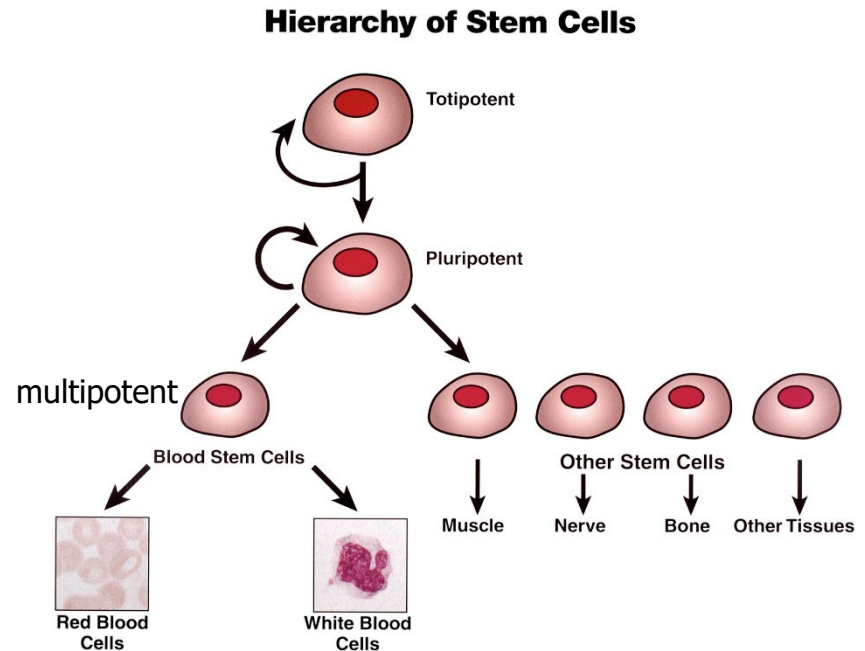
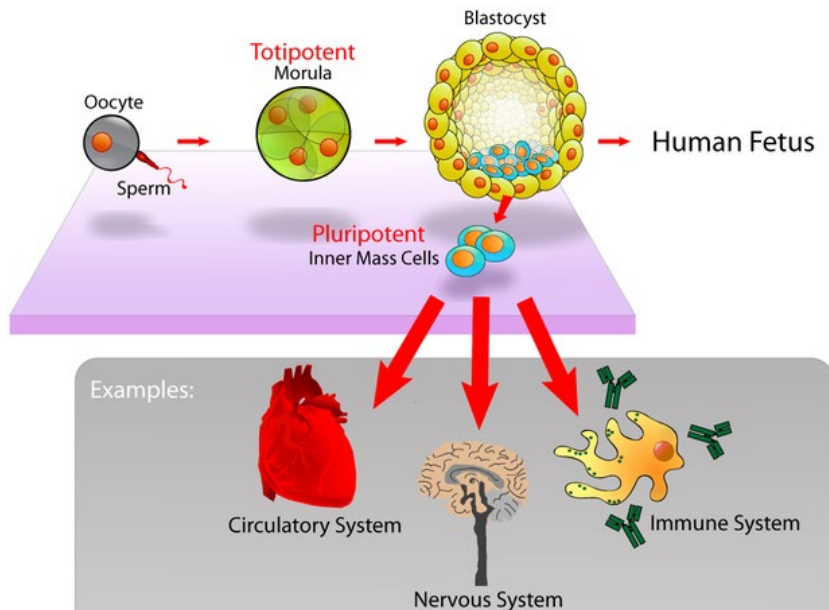
Where do T- and B-cell learn the difference between SELF and NON-SELF?

- T-cells in the Thymus
- B-cells in the Bone Marrow (*but named after the Bursa of Fabricius in chickens*)



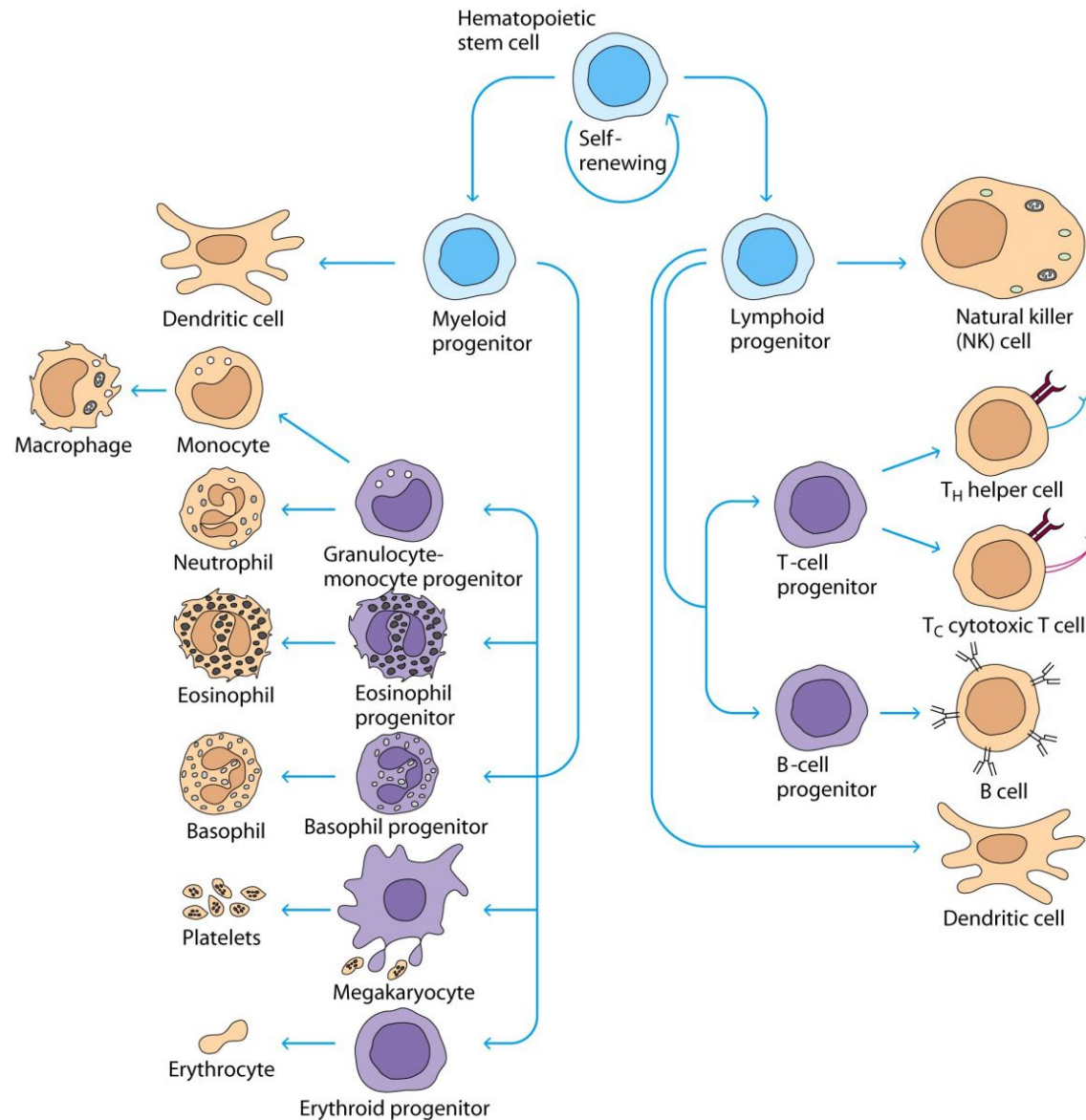
T- and B-cell development

Totipotente stamcel → pluripotente stamcel → multipotente stamcel = Hemopoïetische stamcel (HSC)

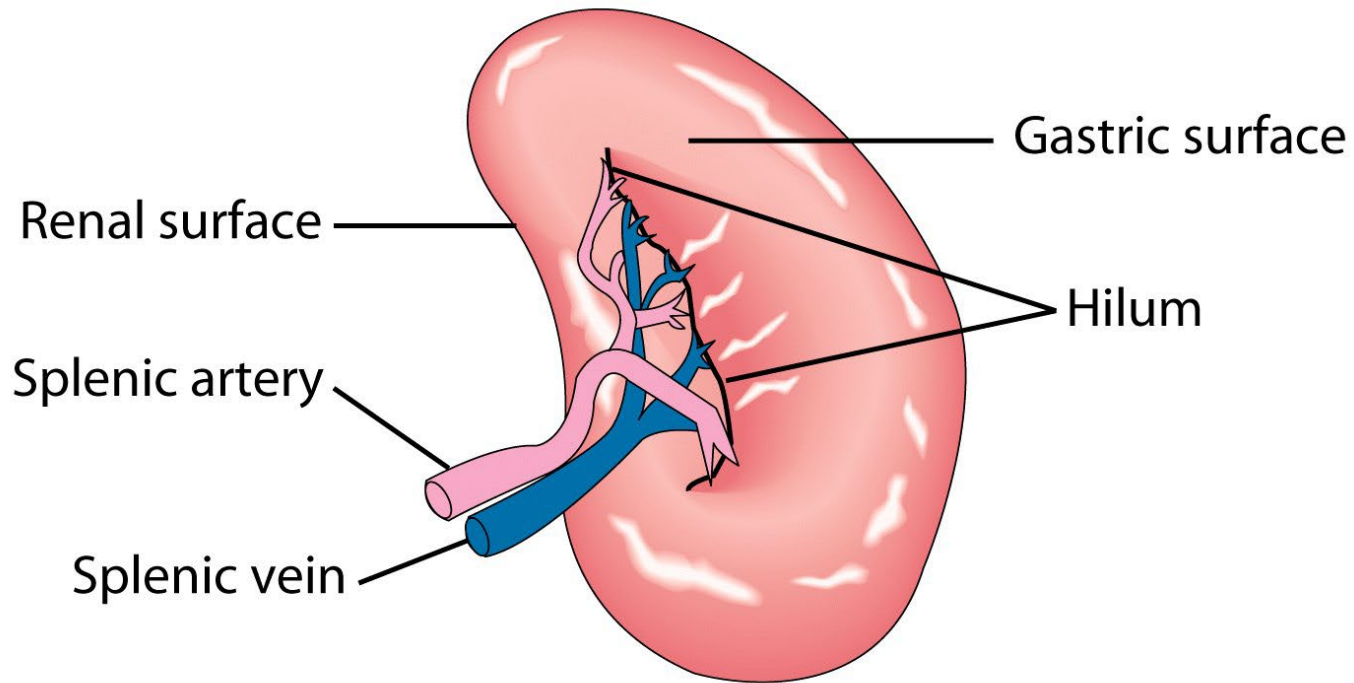


- Een totipotente stamcel kan differentiëren tot **elk** type cel (toti=alles). Komt alleen voor in vroeg embryonaal stadium.
- Een pluripotente stamcel kan **vele** cellen (weefsels) vormen.
- De hemopoïetische (multipotente) stamcel kan alleen de bloedcellen vormen.

All blood cells are derived from the hematopoietic stem cell

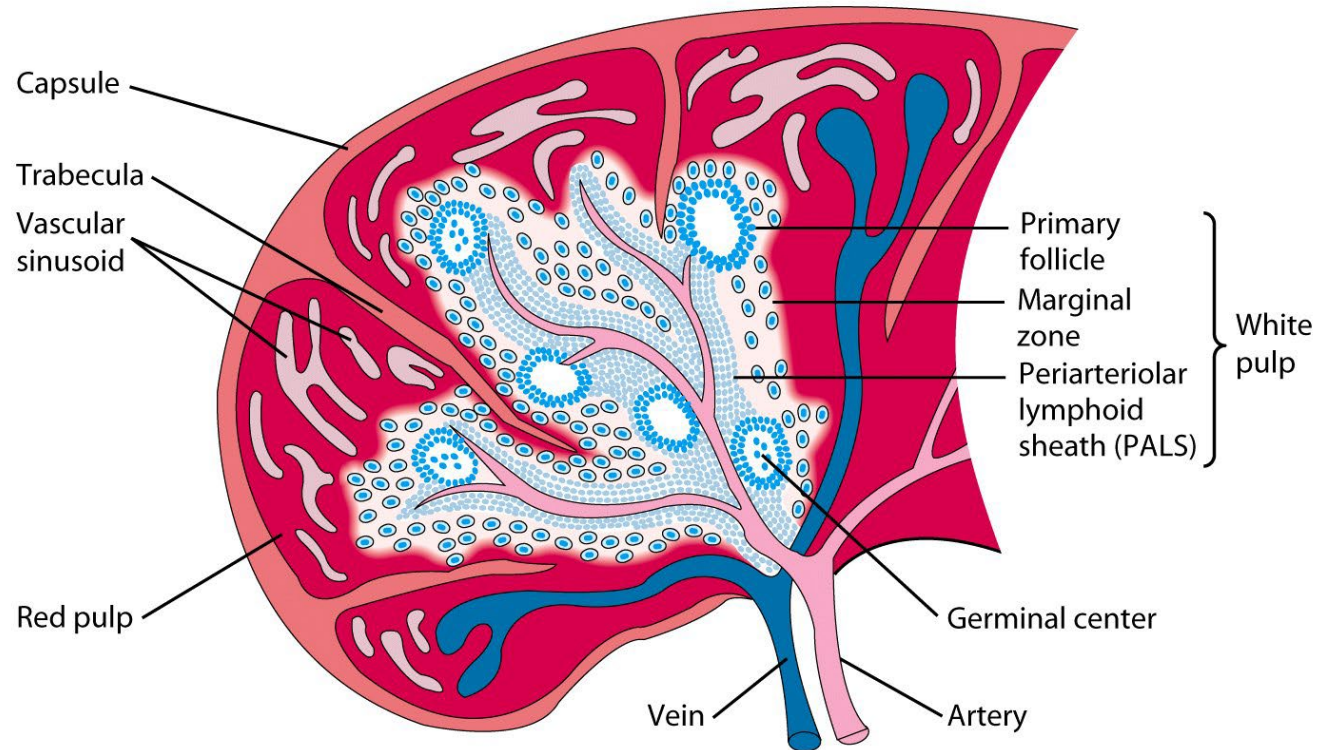


The spleen



- The spleen is part of the vasculature and filters (and stores) the blood
- The spleen has two functions:
 - Removal of old erythrocytes in the red pulpa
 - Activation of the immune system in the white pulpa

Organisation of the spleen



- The white pulp consists of a T- and B-cell area
 - B-cells are organized in follicles in the marginal zone
 - T-cells are organized around the arteries in the PALS

Casus: Jeroen heeft geen milt

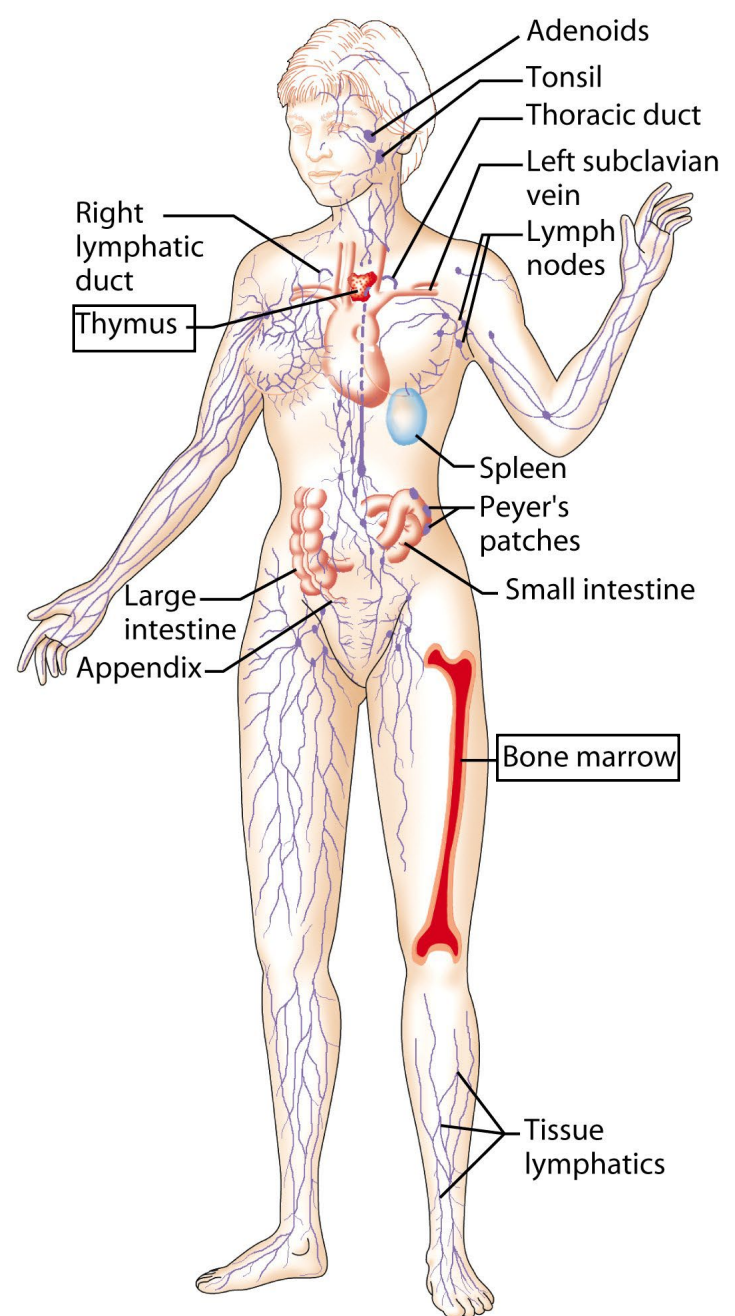
- Jeroen wordt op 7 jarige leeftijd aangereden door een vrachtwagen. Hij zat op de fiets en was op weg naar school. Hij heeft ernstige inwendige bloedingen en zijn milt moet verwijderd worden.
 - Kan Jeroen verder een “normaal” leven leiden?
 - Welk risico loopt Jeroen in zijn verdere leven?
 - Wat voor voorzorgsmaatregelen kunnen genomen worden?

Mucosa Associated Lymphoid Tissue (MALT)

- Most lymphocytes are located in the mucosal surfaces (slijmvliezen) in for instance the tonsils, peyer's patches, or scattered around
- The MALT consists of:
 - The BALT (Bronchus Associated Lymphoid Tissue)
 - The GALT (Gut Associated Lymphoid Tissue),
 - But the bladder wall and the wall of the vagina also contain many lymphocytes

Immunologic organs

- **Primary lymphoid organs:**
 - fetal liver & fetal spleen, bone marrow, thymus.
 - Development and education of T- and B-cells
- **Secondary lymphoid organs:**
 - Lymph nodes, spleen, MALT (Mucosa Associated Lymphoid Tissue) etc.
 - Generation of the immune response



The lymphatic system and body defenses

Innate body defenses

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Immunology

The immune system:

- Protects the body from harmful elements such as bacteria, viruses, parasites, molecules, or foreign cells

The 2 rules by which the immune system plays

1. Recognize and destroy foreign elements (**NON-SELF**)
2. Recognize and spare own body (cells) (**SELF**)

Wat gebeurt er als regel 1 niet goed wordt toegepast?

Wat gebeurt er als regel 2 niet goed wordt toegepast?

Begin van de immunologie

- In 1798 voerde Jenner de eerste vaccinaties uit met koeienpokken. Het was Jenner opgevallen, dat melkmeisjes, die in aanraking waren geweest met koeienpokken “immuun” waren voor mensenpokken.
- Een besmetting met het koepokkenvirus verliep veel milder dan een besmetting met het humane pokkenvirus
- Het woord vaccinatie hangt hiermee samen: vacca = koe
- Het vaccineren van koeien werd al eerder gedaan → **Geert Reinders** (volgende dia)



Geert Reinders

Geert Reinders werd geboren in 1737 te Bedum en overleed in Bellingeweer in 1815. Hij ligt in Winsum begraven.

Hij verloor zelf tot twee maal toe bijna al zijn vee aan runderpest. Hij wordt gezien als de “uitvinder” van het middel tegen de veepest.



Publicatie van Geert Reinders:

“Waarneemingen en proeven meest door inenting op het rundvee gedaan, dienende ten bewyze, dat wy onze kalvers van gebeterde koejen geboren, door inenting, tegen de veepest kunnen beveiligen ...”

door Geert Reinders - Groningen 1776

Regel 1/ Regel 2/ Regels worden wél goed toegepast

Twee regels van het immuunsysteem:

1. Herken en vernietig de vreemde (het **NIET-ZELF**)
2. Herken en spaar het eigen individu (het **ZELF**)

Welke regel/regels van het immuunsysteem wordt/worden NIET goed toegepast bij:

1. Auto-immuunziekten
2. Fatale longontsteking
3. Transplantatie
4. Allergie
5. AIDS
6. Kanker

Organisation of the immune system

- 3 Lines of defense
- 2 of those lines of defense are not specific
 - Non-specific defense: all “foreigners” are removed in a similar fashion
 - Specific defense: immune system adapts the immune response to the “foreigner”

The Immune System		
Innate (nonspecific) defense mechanisms		Adaptive (specific) defense mechanisms
First line of defense	Second line of defense	Third line of defense
<ul style="list-style-type: none">• Skin• Mucous membranes• Secretions of skin and mucous membranes	<ul style="list-style-type: none">• Phagocytic cells• Antimicrobial proteins• The inflammatory response	<ul style="list-style-type: none">• Lymphocytes• Antibodies• Macrophages