Lymphoid Organs and Lymphocyte Trafficking

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Invader recognition

Where does invader recognition take place??

Secondary lymphoid organs:

Lymph nodes

Spleen

Mucosal-associated lymphoid tissue (MALT): (Peyer's patches, tonsils, appendix)

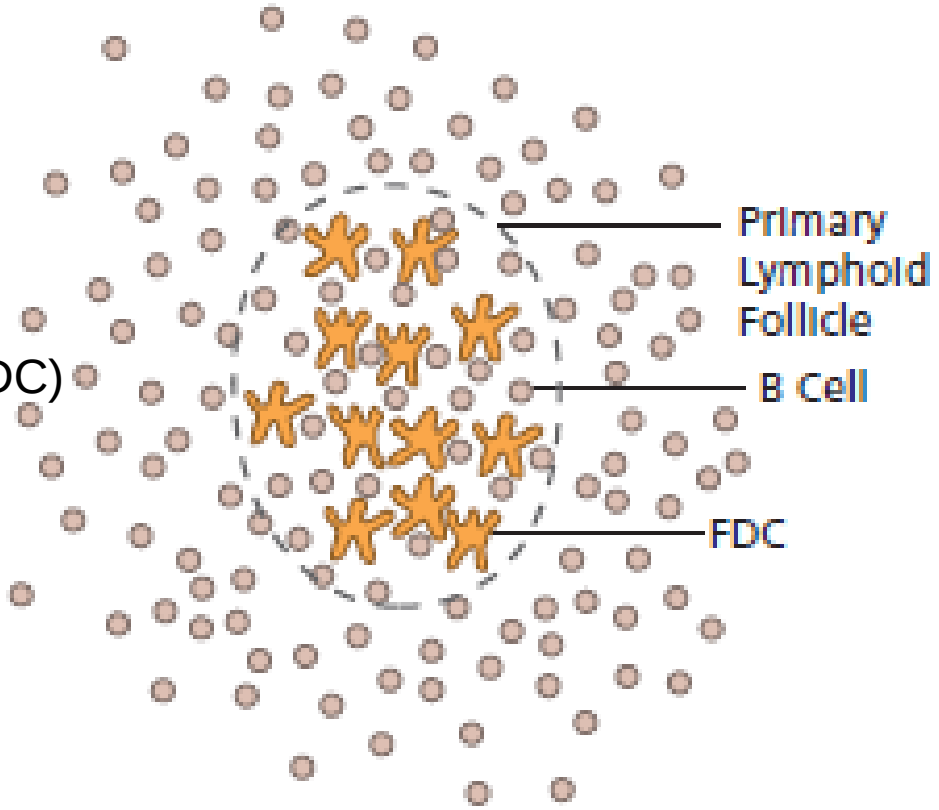
Which are the primary Lymphoid organs?

Lymphoid follicles

Common feature of all secondary lymphoid organs.

Contain follicular dendritic cells (FDC) surrounded by lots of B cells.

FDC vs. antigen-presenting DC?



FDC is an old cell (skin, liver,etc.), takes its position during embryonic development. Capture opsonised (complement or ab) Ag and present it to B cells.

AP DC is produced by the bone marrow, localises to tissue. Presents Ag to T cells.

Primary Lymphoid Follicle

FDC activates B cells upon recognizing opsonised antigen

B cell proliferation (Provided Th co-stimulation is present CD40L-CD40)

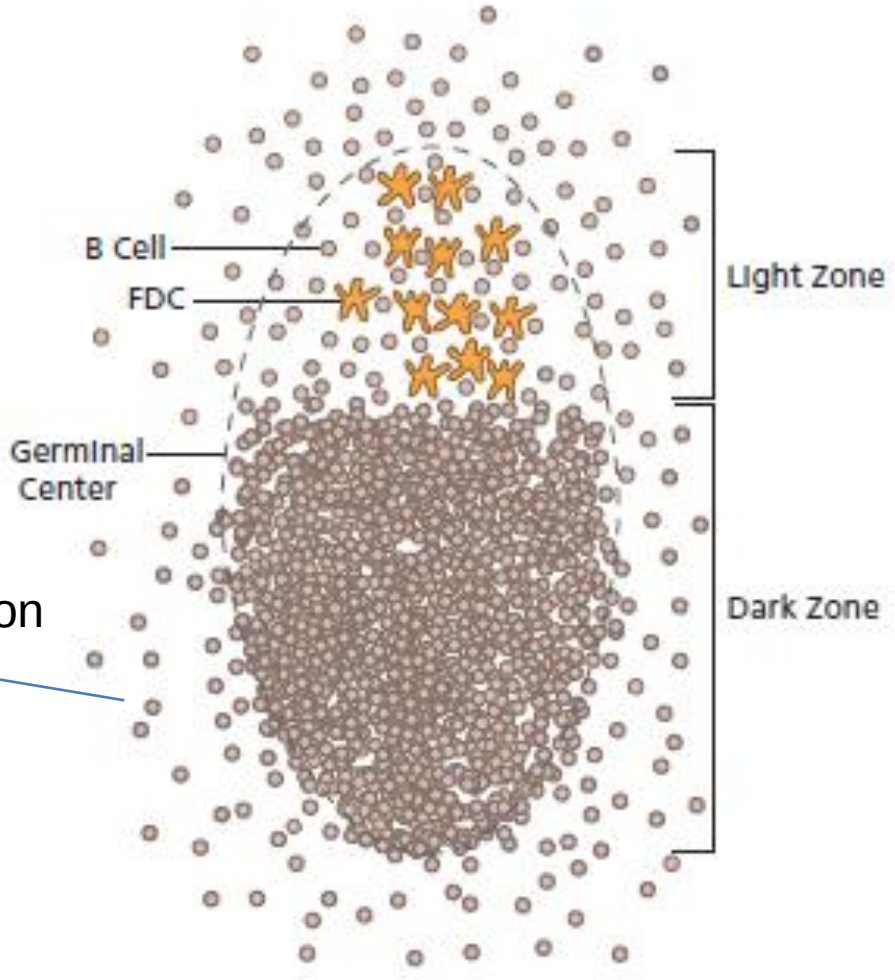
Secondary lymphoid follicle (Germinal Center)

Secondary Lymphoid follicle

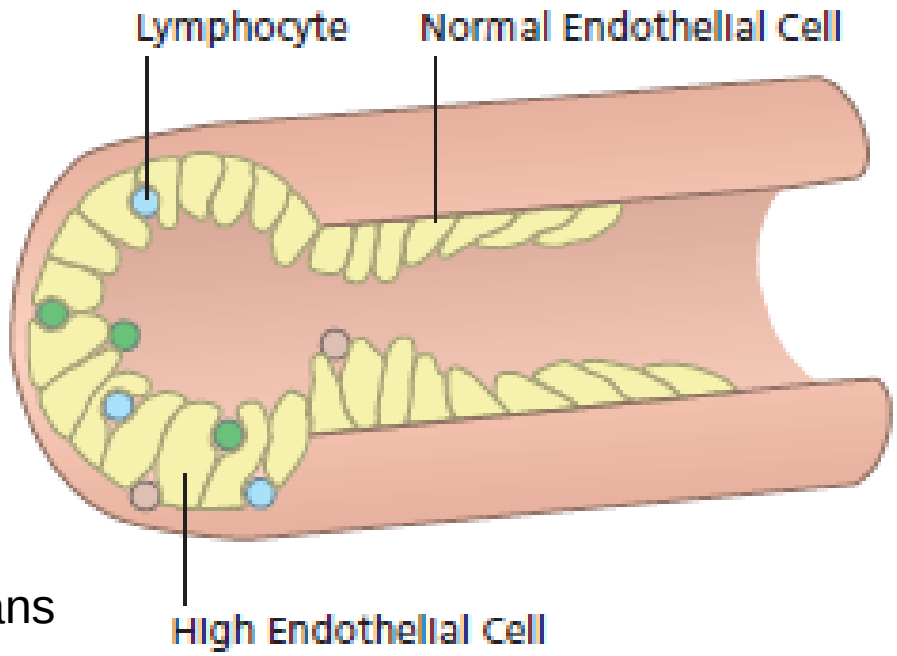
Some B cells will become plasma cell and leave the germinal center.

Others, will undergo somatic hypermutation and class-switching.

Affinity testing and restimulation is done with FDC and Th in light zone.



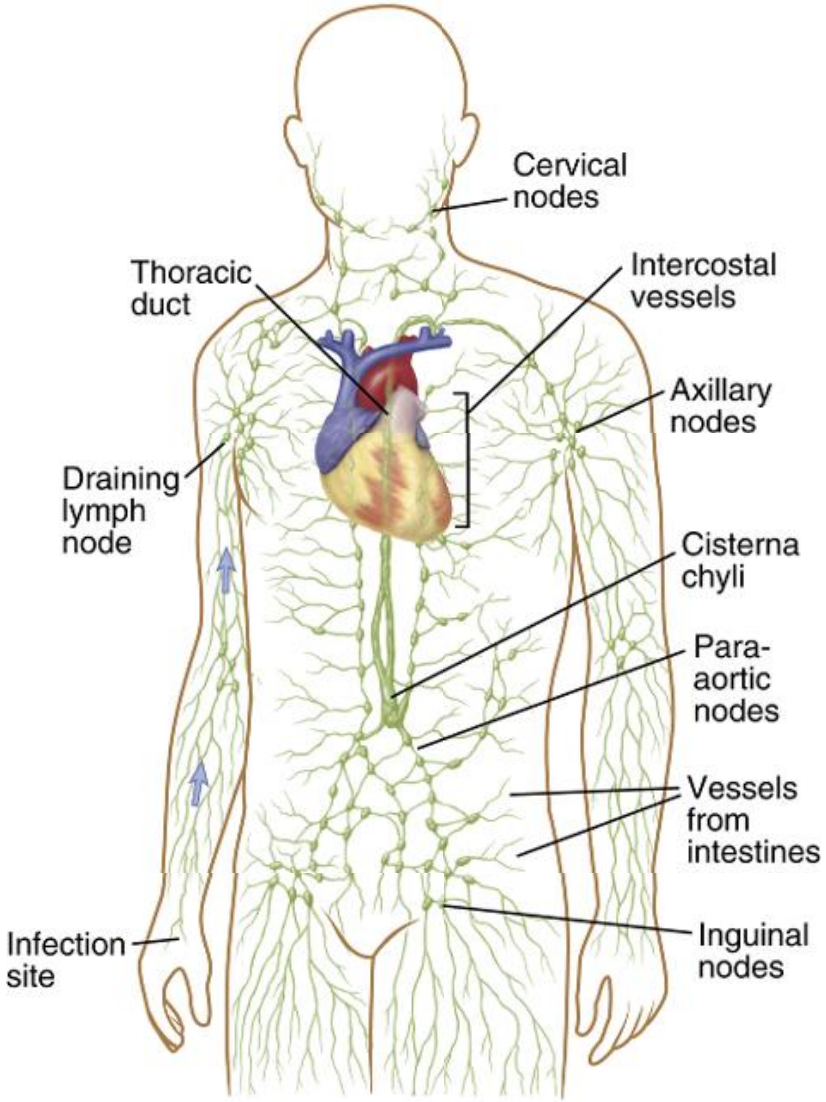
High Endothelial Venules



Common to all secondary lymphoid organs except the spleen.

Doorways through which B and T cells enter secondary lymphoid organs from blood.

The lymphatic system



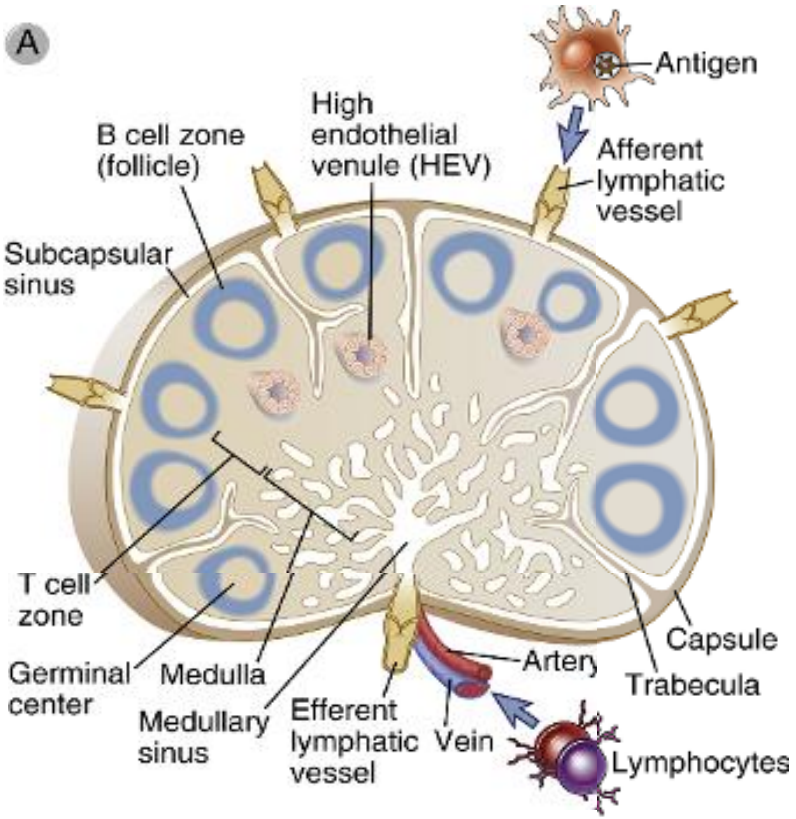
Lymph Node Architecture

Lymphocytes enter node via HEV and lymph.

Antigens are presented to lymphocytes
by DCs migrating from tissue
or by opsonised antigens
coming with lymph and presented
by FDCs.

Mφ in subcapsular sinus help
filter lymph by capturing pathogens.

Lymph nodes are centres of immune activation.



What happens in the lymph node?

Sequence of events:

1- In the T-cell zone, a Th cell will encounter a DC expressing its cognate antigen.

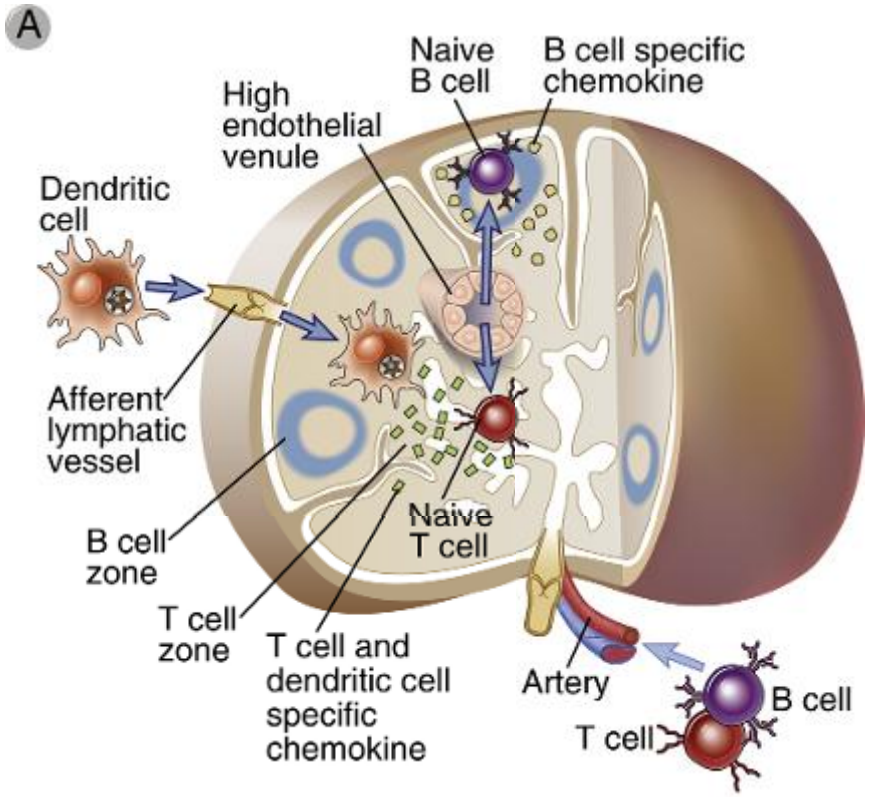
2- Over the following few days, the T cell gets activated and proliferates.

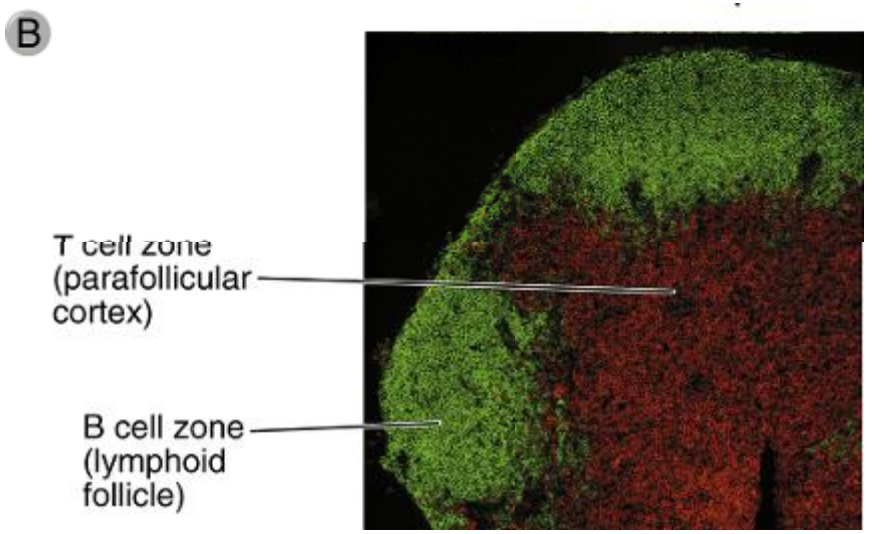
3- T cells then exit lymph node via the lymph, recirculate through the blood, and re-enter lymph nodes via HEV. (Done in less than a day)

4- Proliferation and recirculation are key events that make sure that there are enough of the right T cell in secondary lymphoid organs to meet other immune cells (B cells) and provide them with help.

5- Once T and B cells are activated, some continue to stimulate and be stimulated in lymph nodes, others go to body tissues to do their defensive job.

Segregation of B and T cells in lymph nodes





How do APCs and lymphocytes know where to go within a lymph node?

Chemokines!

FDCs produce the chemokine CXCL13 which attracts B cells that express the receptor to this chemokine (CXCR5).

If a B cell finds its cognate antigen, it downregulates CXCR5 and upregulates CCR7 which mobilizes it to the border between B and T cell areas.

Likewise, T cells that find their DC carrying their antigen migrate to the border of follicle to meet B cells, and later into the follicles to help in class switch and somatic hypermutation.

Swelling of lymph nodes? Clinical significance?

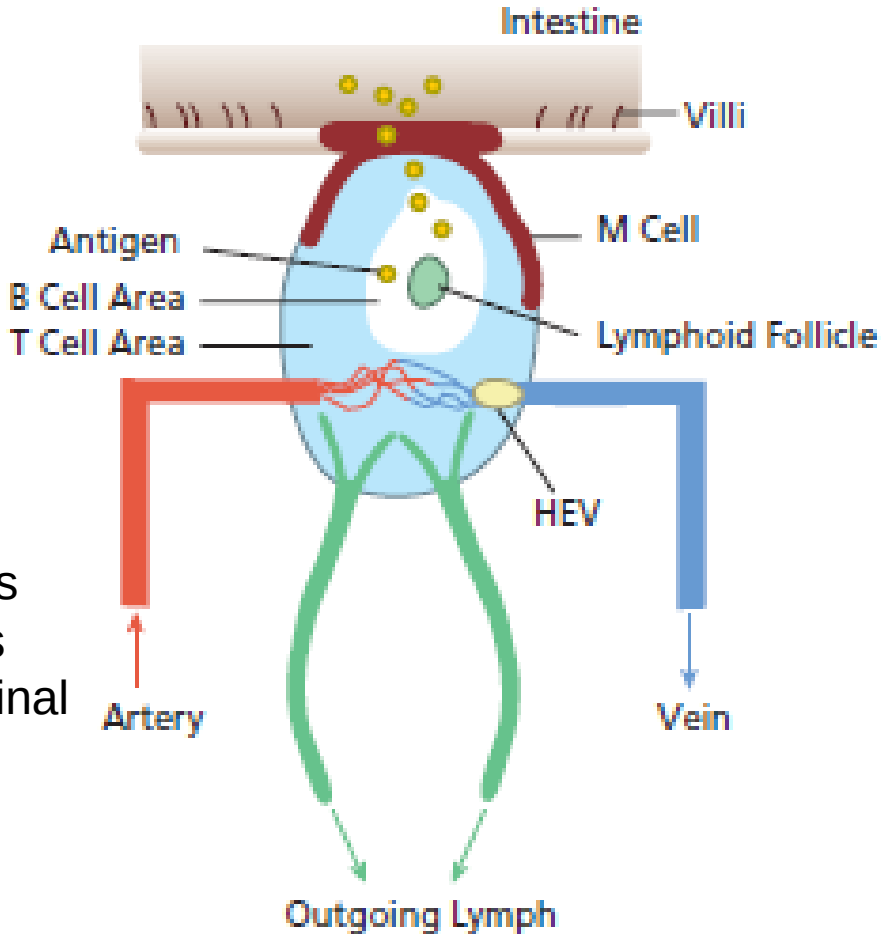
Peyer's Patches

An example of MALT.

No incoming lymphatics.

M cells enclose intestinal antigens in vesicles and transports them across.

Similar to a lymph node except that it does not sample lymph but rather intestinal Ags that are able to BIND the surface of intestinal cells



The spleen

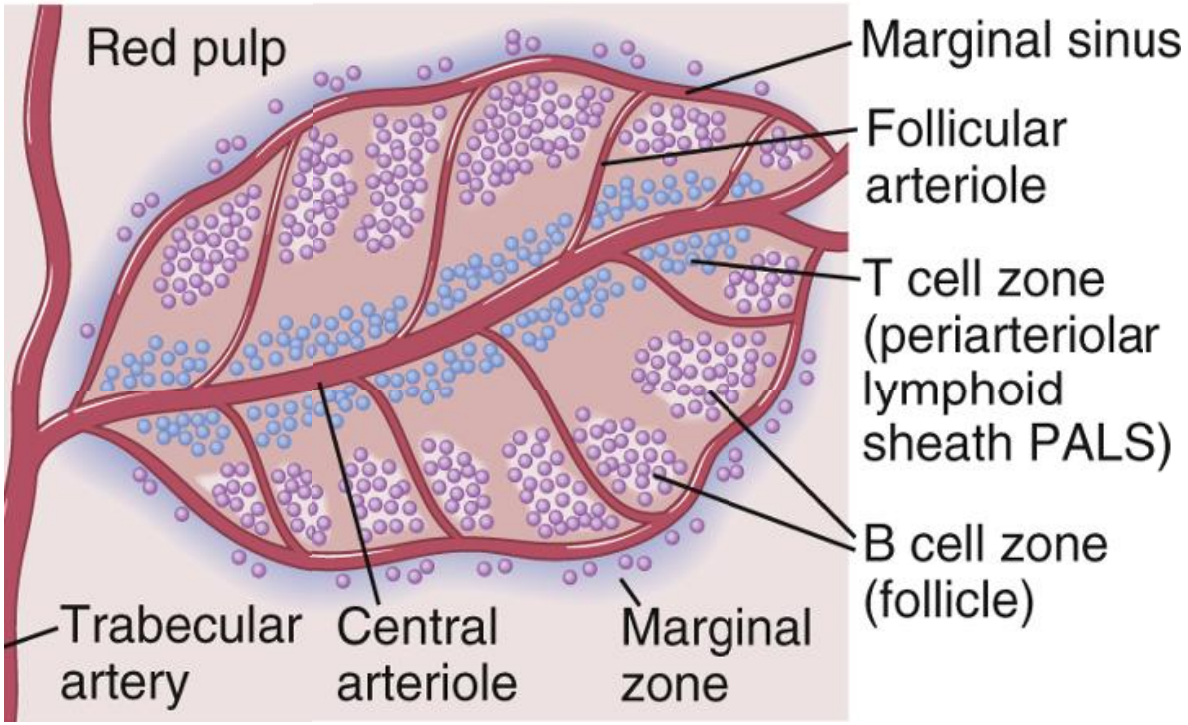
Filters blood in about half an hour!

No HEV but rather all blood can go in.

Marginal sinuses are lined with Mφ
that phagocytose debris and invaders.
They also contain resident DCs
that present Ags to T cells.

T cells are found in Periarteriolar lymphocyte sheath (PALS).

B cells are located between the marginal sinus and PALS.



The Logic of Secondary Lymphoid Organs

Each secondary lymphoid organ is strategically positioned to intercept invaders that enter the body via different routes. (Lymph node vs. MALT vs. Spleen)

Only B and T cells that find their cognate antigens remain in lymph nodes while others go on to circulate.

Once T cells stimulate B cells, they run out of CD40L, how can they be restimulated while away from T cell zones??

B cells do the job by acting as APCs and providing B7 co-stimulation.

Lymphocyte Trafficking

Traffic patterns of naive and experienced lymphocytes are different.

T cells originate in the bone marrow, get educated in the thymus, and then exit to circulation.

Naive T cells express an array of adhesion molecules (L-selectin, α4β7, etc..) that allows them to recognise molecules in HEV and therefore visit the different secondary lymphoid organs.

Once in secondary lymphoid organs, T cells pass through fields of APCs in T cell areas. If no cognate antigen is found, they return to blood whether through lymph or directly (Spleen). (Process continues for about six weeks!)

T cells that encounter their cognate antigen become experienced T cells.

Lymphocyte Trafficking-Cont'd

Experienced T cells will express adhesion molecules depending on **WHERE** these cells were activated.

When activated cells re-circulate, they usually exit the blood and re-enter the same type of secondary lymphoid organ in which they originally encountered antigen.

Experienced T cells also express adhesion molecules which direct them to exit the blood at places where invaders have started an infection.
(Will not go round and round!)

Naive T cells have adhesion molecules that allows them to visit all sec. lymph. org. but NOT sites of inflammation.

Experienced T cells express restricted adhesion molecule to allow them to return to a similar sec. lymph. org. and exit to sites of inflammation to provide help to Tc and other immune cells.

Naive B cells behave similarly to T cells, experienced B cells tend not to migrate too much, they reside in bone marrow or sec. lymph. organs and secrete Abs!

Why mothers kiss their baby??

Baby's immune system is incomplete at birth (no IgG produced)

Mom provides IgG protection via placenta and IgA via breast milk.

How can the mom provide useful protective antibodies to her baby?

an EBV antibody for example will most likely not be needed at this stage?

Kissing....Sampling?

Activation of memory B cells, migration to breasts

Production of useful Abs!

Thank you!

Questions???