Immunology 7

Ativation of lymphocytes

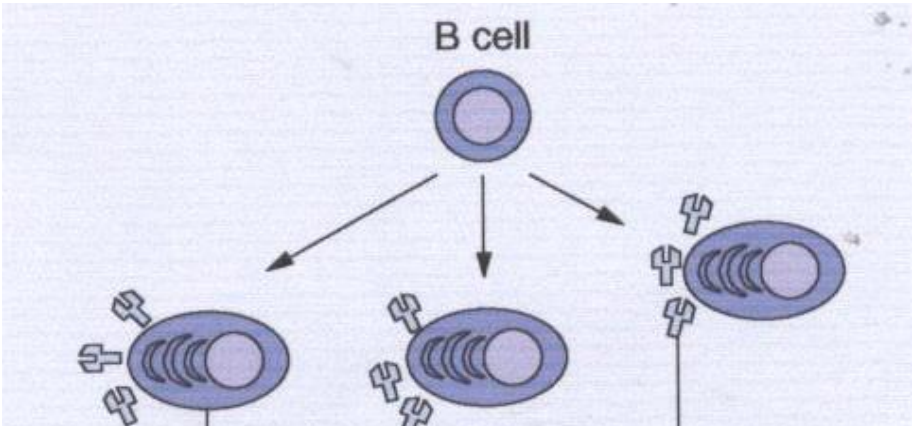
APC

Effector function of lymphocytes

Characterisation of adaptive immunity

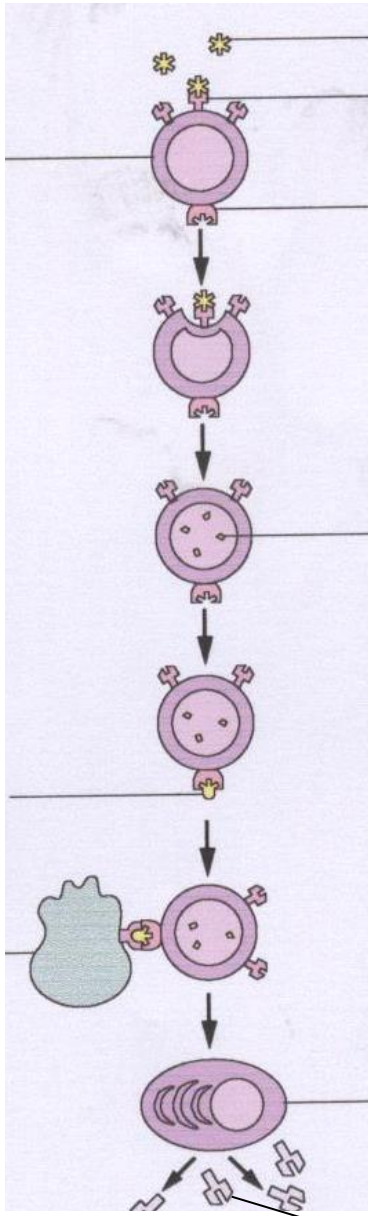
- after 1st exposition to antigen the system reacts slowly and with delay
- even if lymphocytes were screened for self reactiong TCR, they test antigens again to prevent false reactions
- to test and balance reactions is allowed by different cells that – recognise, regulate a effect reactions
- Cooperation with innate mechanisme that prepares antigens for adaptive immunity., adaptive immunity influences innate immunity reactions

B bunka

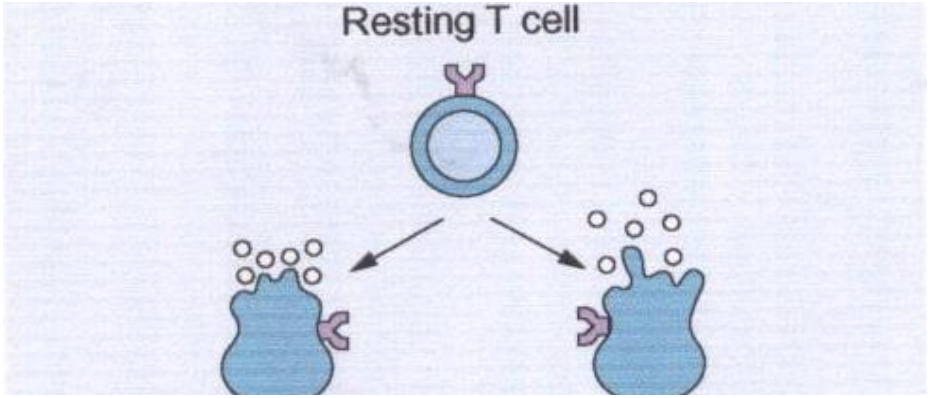


Plazmatická bunka

Protilátky

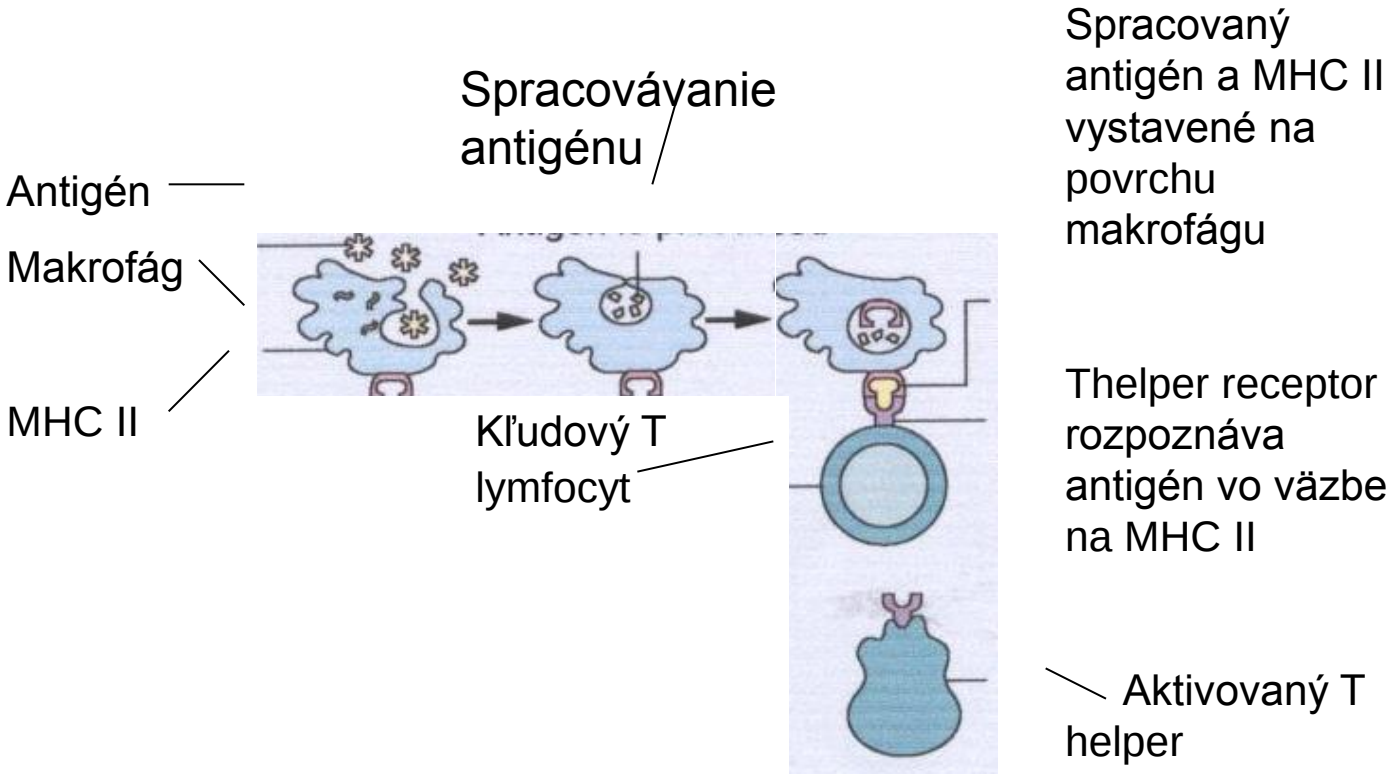

Antigén
Antigén špecifický receptor na B bunke
B bunka
MHC II
Antigén je spracovávaný
MHC II a spracovaný antigén sú vyložené na povrchu B bunky
Aktivovaná T bunka
Plazmatická bunka
Protilátky

Kľudová T bunka

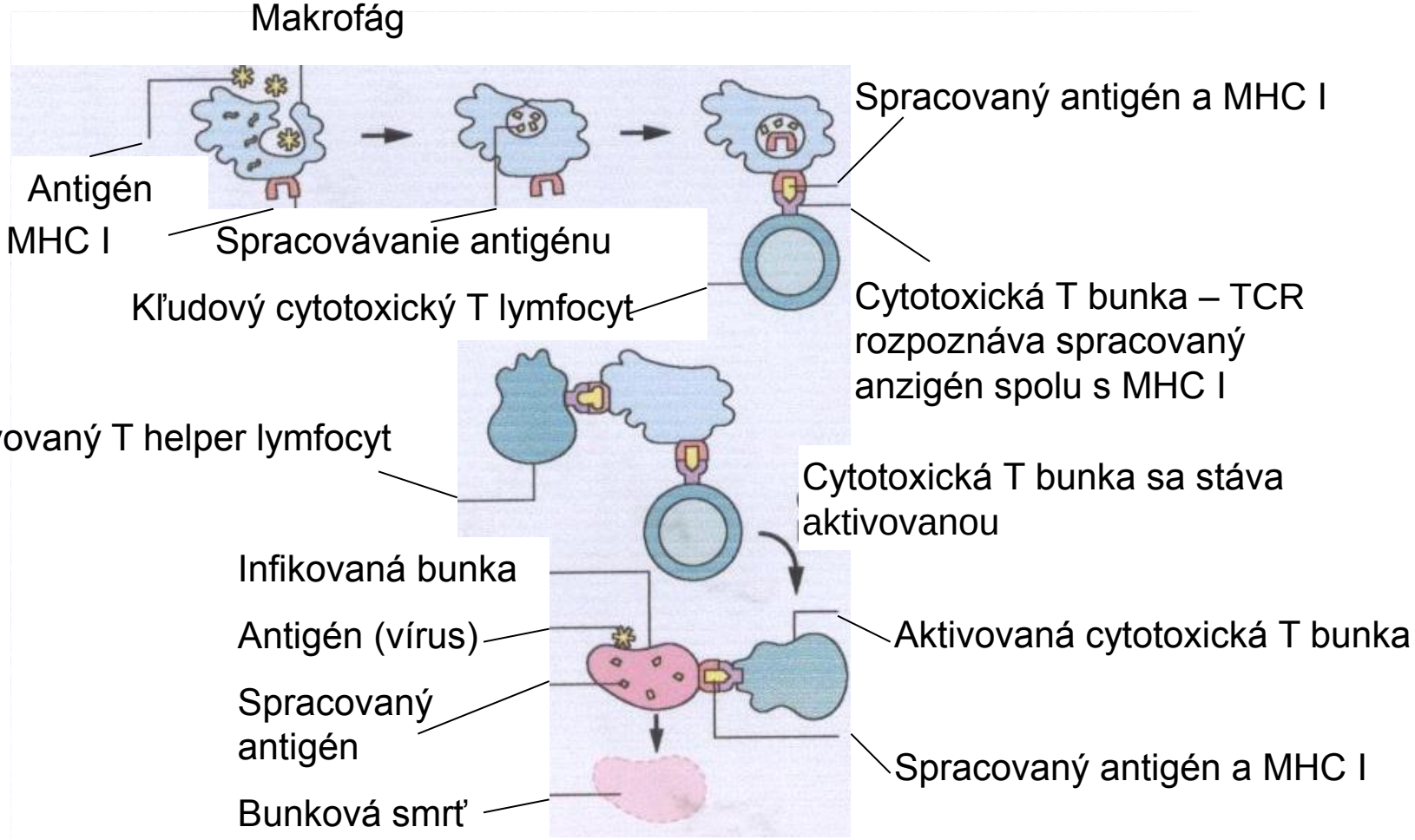


Aktivovaná T helper bunka

Aktivovaná T cytotoxická bunka



Aktivácia T helper buniek

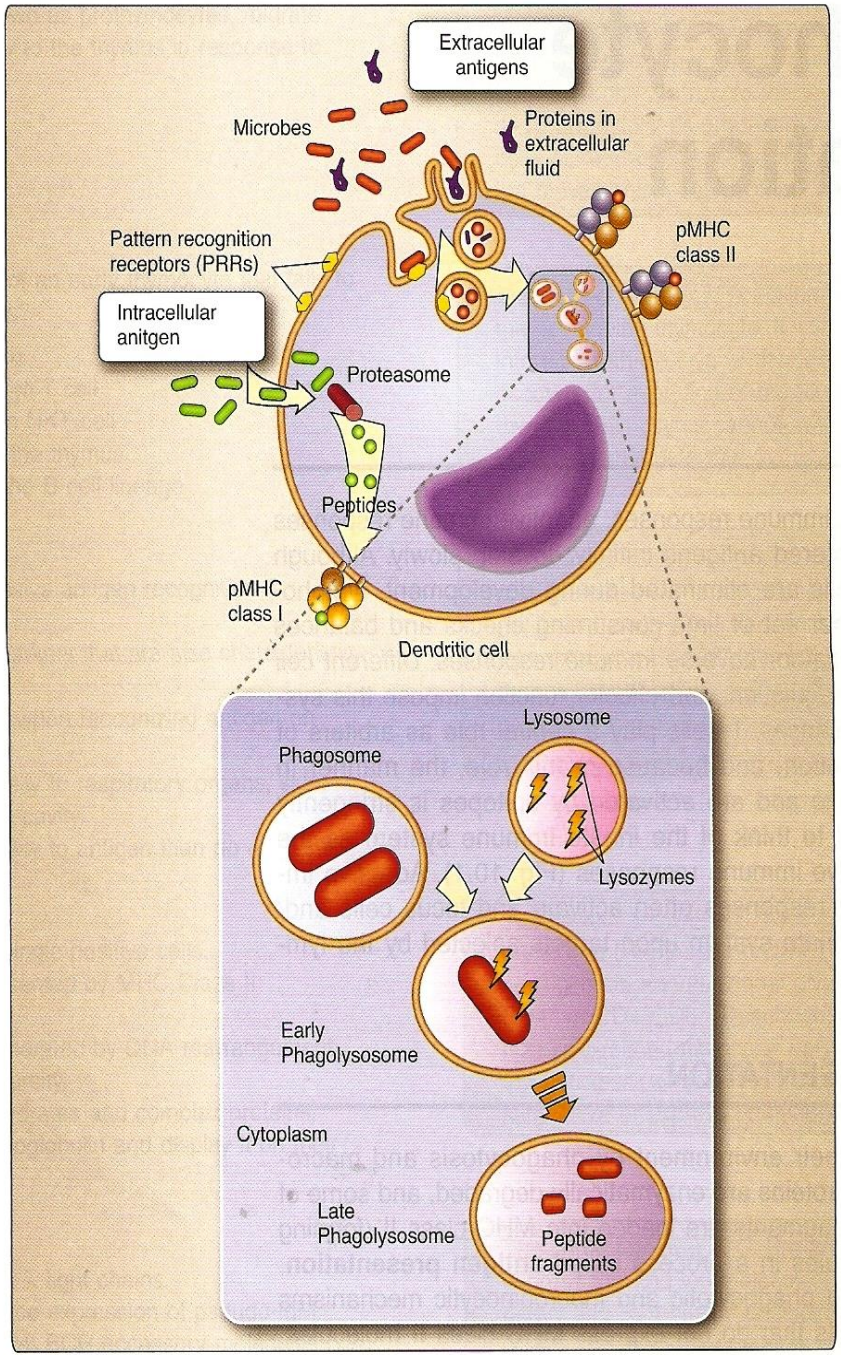


Aktivácia cytotoxických T buniek

Antigen processing and presentation

- Phagocyting cells screen (patrol) environment – phagocytosis, macropinocytosis
- ensymatically split engulfed proteins - degradation
- some fragments of proteins are caught and presented by MHC II – **presentation of antigens**
- some microbes are not phagocyted, or degraded and are processed and presented by MHC I molecules

- i.c.pathogens
- degraded
- MHC I



extracelular

processed

MHC II

Presentation via MHC II

- Dendritic cells – in sites of gate of entry of antigens
- Not mature cell engulf free and bound molecules / antigens – phagocytosis and degradation
- Recognition via PRR receptors – directly (non specific) or
  indirectly via antibodies(specific)

Recognition of threat leads to maturation of dendritic cells

- migration closly to lymphatic nodes
- decrease phagocyting activity
- increase synthesis of MHC II
- transport of MHC II with bound peptid = pMHC II to the surface of dendritic cell and presentation of antigen to CD4

Presentation via MHC I

- Not all antigens enter the cell by phagocytosis.
- Some are bound on the surface of target cells that infects
- The cell degrades them by proteasomes and binds them to MHC I – to produce pMHC I, that is exposed and cooperates with CD8

Activation of T lymphocytes
a) immunological synapsis

- T lymphocytes – direct reactions of adaptive immunity
- TCR does not recognise free molecules
- recognise only peptids presented via MHC I or MHC II
- Specific immunity is influenced by the way how the epitopes are presented by Antigen Presenting Cells

Immunological synapsis:

- TCR recognises pMHC
- pMHC + TCR of CD4 or CD8 – stabilisation is done by constant part of TCR =
  TCR:pMHC:CD4(8) = 1st signal via CD3 to Tcell
- 2nd signal – c**ostimulating molecules**
- 1st and 2nd signal = transmission of signal and i.c. activation of transcription of genes for production of cytokines
- Without costimulation the lymphocytes will be selectively non-respondint **(anergy**) or will be submitted for apapotosis

CD4 maturation

- T cell + antigen = **priming.**
- Primed CD4 **= T helper**
- **Thp** are precursors of Th **=** stimulated and secretes cytokines
- **Th0 –** developes further by one of 2 functional ways accordinig to the character of contact with APC
- **Th1:** microbial LPS + cytokine from APC(IL12) = activation of phagocytosis and CTL
- **Th2 -** IL 4 leads to Th0 development to Th2 that stimulates B ly to change to plasmatic cells and memory cells

CD8 - maturation

- Recognition of pMHC I on the surface of (APC, infected or other) cells by CD8 – formation of **IL-2 receptor**
- IL 2 is produced by CD4, that communicated with the same antigen in MHC II on APC (phagocyted fragments of microbe body)
- IL 2 **stimulates CD8** to differenciate to CTL – cytotoxic T cells – containing cytolytical granules (perforins and granzymes), that kill cell with specific pMHC I

Memory cells

- TCR + pMHC II (**first signal**)
- CD 28 + APC (CD80/86) **2nd signal** that leads to
  - production of IL 2 by CD4
  - to formation of IL 2 receptor on CD8 and
  - to proliferation (negative stimulation – selfregulation to stop if prolifer too much)
- Some CD4 become memory cells – have more CD 28 – react much faster to APC and migrate to the place of infection (do not stay at LNodes)

Activation of B cells

- BCR recognise and process free and bound antigens
- BCR has the shape of monomer of IgD and/or IgM
- Cytoplasmatic part of Ig – play the role of CD3 of Tcells
- Binding of epitop on Ig leads to transmission of signal and to transsduction and transcription and activation of genes, endocytosis, ensymatic degradation amd exposition of fragments by pMHC II and to production of costimulationg molecules
- B cells can act as APC

T independent antigens
T independent activation

TI activates B lymphocytes without T cell

- TI-1 antigens – polyclonal activators of proliferation and Ig production = **mitogens of B cells**
- T1-2 antigens – contain repeated epitopes (polysacharides), activate mature B cells (transmission of signals) – in minimal quantity activates also T cells

2nd signal – other bindings of B cell – coreceptors on B cells (C3b, CD 21= CR2, CR1...)

T dependent antigens and activation

- Antigens bound via MHC II (on APC or B cells) – first signal
- 2nd signal to B lymphocyte is given by CD4 helper cell
- MHC II + TCR CD4 cells = production of cytokines (IL4) and formation of IL4 receptore on B cells – proliferation of B cells, differenciation to plasmatic cell

Plasmatic cells and memory B cells

- Plasmatic cells – terminally differenciated B cells
- the same epitope on BCR as on secreted Ig

- Not all B cells differentiate to plasma cells
- Some stay for B memory cells

Effector function of lymphocytes

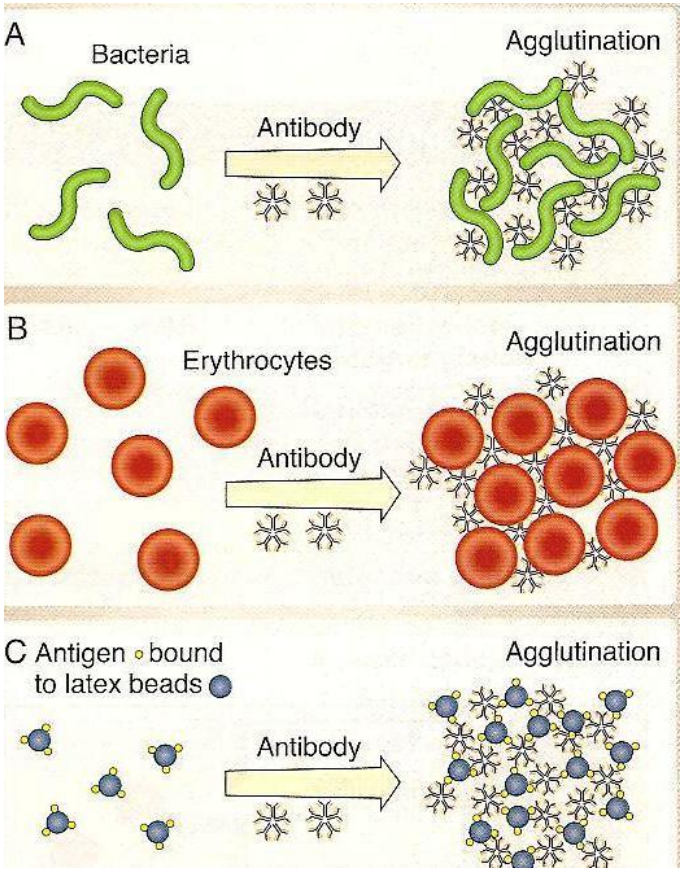
- Innate immunity – cell and humoral
- Adaptive immunity – cell and humoral

- humoral – free molecules in liquid (humors = liquid) – antibodies...
- cellulas – T cells

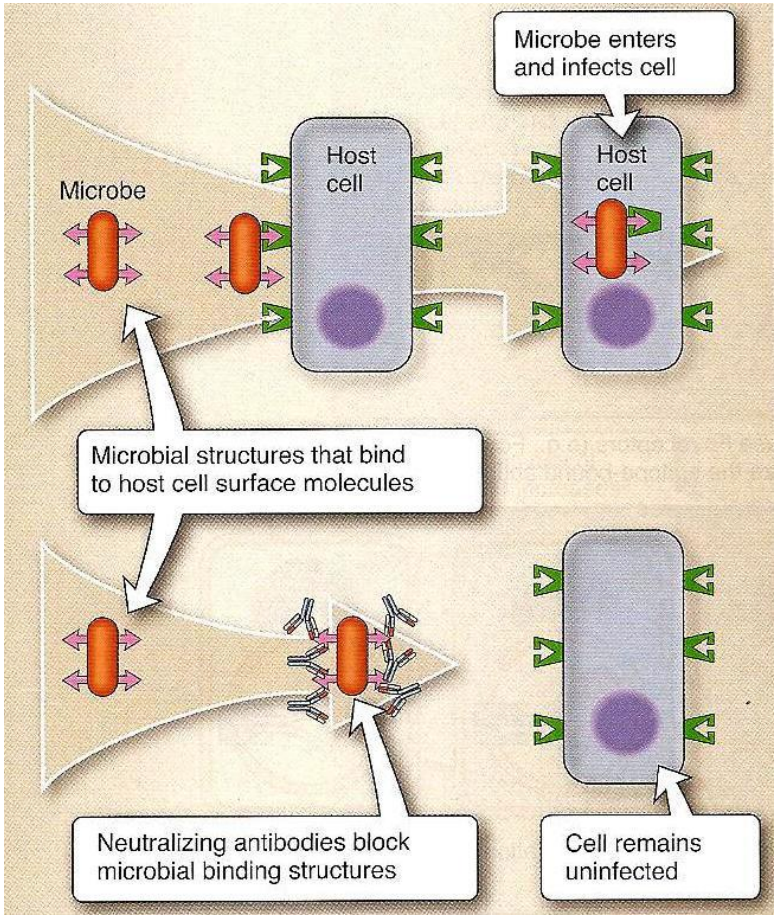
Humoral immunity - adaptive

- Reaction of antigen and antibodyg
- Agglutination, neutralisation, opsonisation
- ADCC – antibody dependent cell cytotoxicity – (NK cells, eosinofils) – antibodies bound on microbes bind by Fc fragment on cytolytical cell (eosinofils), that will then produce the lysis of microbe
- Activation of complement
- Hypersensitivity of the Ist type

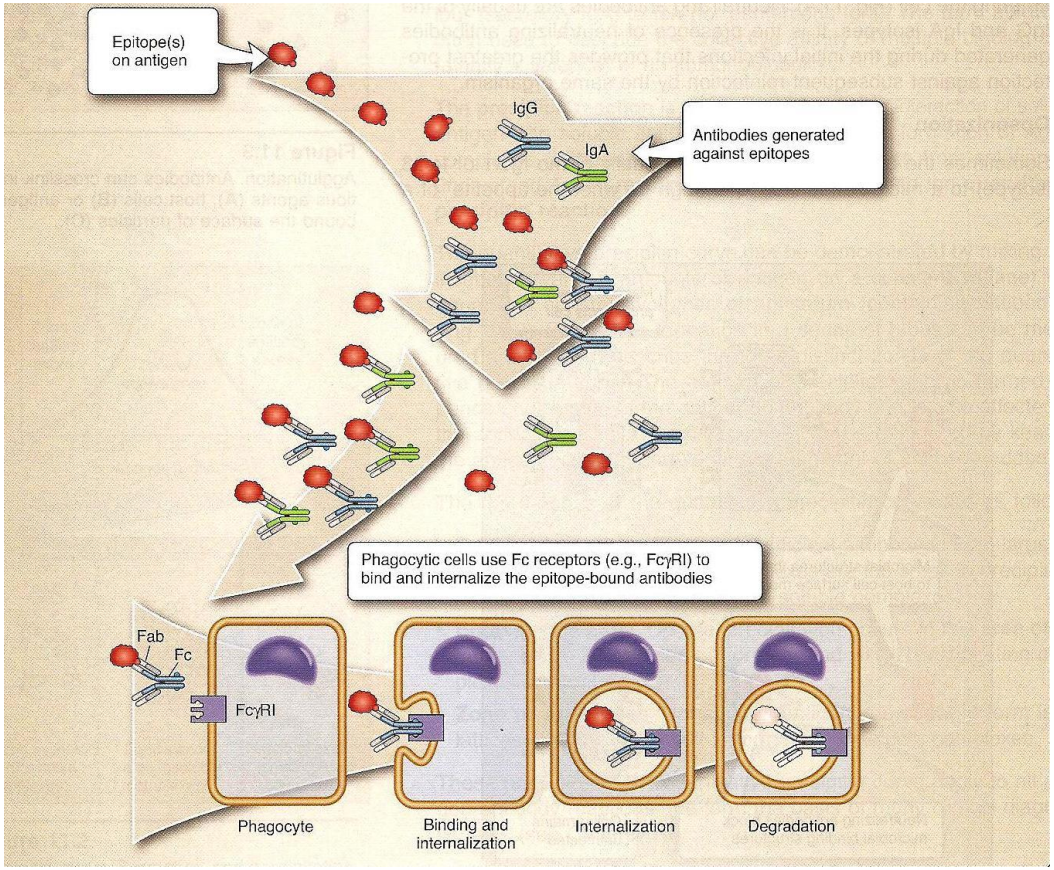
agglutination



neutralisation



Opsonisation



T cell mediated immunity

2 forms to eliminate microbes (antigen)

- DTH –delayed type of hypersensitivity – via CD4 Th1 (activation of macrophages via Th1) *Mycobycterium tbc*
- cell mediated lysis via CD8 Tly - CTL - lysis of infected, changed or foreing cells

Immunological memory

- primary answer to ag
- secondary answer by stimulation of memory cells – faster,isotype switch
- Vaccination