

# Immunological tolerance and possibilities of its induction

**Immunological tolerance** is a condition in which the organism does not respond to an antigens stimulus. Immunological tolerance may be specific or nonspecific.

1. **Nonspecific:** The immune system is inactivated and does not react against any antigens (incl. bacteria and viruses). It can be induced, e.g. by irradiation or cytostatics, by which immunocompetent cells are rendered inoperable and immunosuppression is induced.
2. **Specific:** The organism does not respond only to the antigen that was used to induce tolerance, but responds normally to other antigens.

Physiologically, tolerance is induced against the organism's own components (*self tolerance*), thereby protecting it from immune attack.

## Tolerance of the body's own components

The response of effector T and B-lymphocytes is T cell dependent.

**Mechanisms of inducing T cell unresponsiveness:** occur during the development of **T cells from their precursors in the thymus**, rearrangements of genes for T cell receptors occur, which then appear on the cell surface. T cells are then subjected to two types of selection:

- **negative selection:** clones with high affinity for class I or class II molecules with their own antigens die;
- **positive selection:** clones that have very low or no affinity for the complex of MHC and self antigen molecules also die.

Selection results in **clonal deletion** and the survival of clones with low affinity for their own MHC molecules with a peptide fragment. **Matures in CD4+ or CD8+ T cells.**

T cell receptors interact in the thymus with cells that present their own antigens, peptide fragments of cellular proteins, via MHC molecules. Antigens not presented in the thymus can also be tolerated because:

1. they are in so-called *immunologically privileged sites* - due to anatomical barrier these antigens are inaccessible to lymphocytes (e.g. antigens of spermatozoa in testes, eye lens, etc.),
2. encounter cells that cannot present the antigen because they do not express MHC molecules,
3. are present in small quantities and are therefore not detected by T-lymphocytes,
4. there is insufficient contact of TCR and accessory molecules with the antigen.

## Tolerance induced to foreign antigens

- **In an experiment** tolerance can be induced to antigens of allogeneic origin - after inoculation of allogeneic cells or transplantation of tissue into a newborn organism that does not respond because it does not have a mature immune system.
- Tolerance can also be induced in an adult host whose immune system has been suppressed - by radiation, drugs, lymphocyte antibodies, etc.
- In adult animals, tolerance can be induced without suppression of the immune system - it depends on the dose, the route of administration and the nature of the antigen - low and high doses of antigen usually induce tolerance, medium doses induce immunity; very high doses of antigen can cause immune exhaustion (*clonal exhausce*) - caused by stimulation of all cells capable of responding, no memory cells are formed - the organism does not respond to repeated antigen intake.

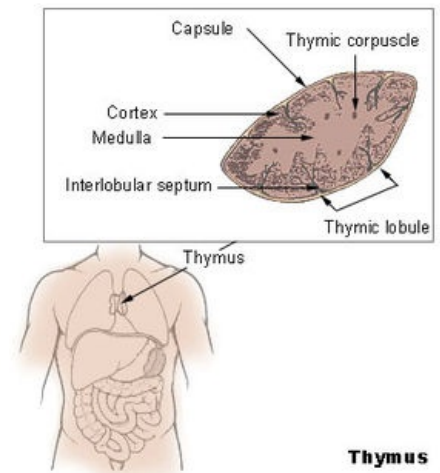
## Links

### Related articles

- Ig, B and T receptor genetics
- Major histocompatibility complex
- Immunocompetent cells

### External links

- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 11. 2. 2010]. <<http://www.stefajir.cz>>.



Central immunological tolerance induction of T-lymphocytes happens in thymus

