

# IMMUNOSENESCENCE AND STROKE

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## Background

- 65+ - 30% of the total population by 2030. (Japan)
- 2050. most of the world – Africa and Middle East 65+
- >20% 65+ = SUPERAGED SOCIETY
- 65+ - 27,4 % of the total population by 2025. Croatia
- 2002 – life expectancy 78,6 yF, 71,0 M
- further increase in the expected life expectancy

Inoue S i sur. Immunosenescence in neurocritical care. *Journal of Intensive Care*.2018;6:65.

<http://croatia.eu>

## Aging and breakdown of BBB

Aging → BBB dysfunction – hypertension, seizure, stroke  
↑ inflammatory cytokines and free radicals  
extravasation of plasma proteins into the brain →  
neuroinflammatory responses

+  
Aging → BBB/blood-cerebrospinal fluid barrier degeneration →  
↑ albumin, fibrinogen, IgG (Alzheimer's disease)

Ryu JK i sur. A leaky blood-brain barrier, fibrinogen infiltration and microglial reactivity in inflamed Alzheimer disease brain. *J Cell Mol Med* 2009.

## Results

12 h after ischemic stroke → several weeks  
*„Stroke – induced immunodeficiency syndrome“*

↓ T cells and other immune cells  
(spleen, thymus and lymph nodes)  
+  
hyperactivity of the sympathetic nervous system (SNS)  
and hypothalamic-pituitary-adrenal axis (HPA)  
=  
↑ apoptosis of immune cells  
=  
→ secondary lymphatic organs atrophy  
+  
shift from the production of cytokine TH1 to Th2  
=  
infectious complications after stroke  
→ worse outcomes

*„SNS-mediated stroke-induced immunodepression“*  
→ post-stroke infections

PANTHERIS (Preventive Antibacterial Treatment in Acute Stroke)  
post hoc analysis – the impact of distinct lesion patterns on SNS activation, immunodepression and frequency of post-stroke infections

impaired immune function / higher susceptibility to post-stroke infections:  
large stroke volume – not independently associated  
regions of the MCA cortex – independent risk factor  
SNS activation (↑ norepinefrin) – independent risk factor

circulating costimulatory cells  
(splenic non-T cells - mice)

proinflammatory cytokine-mediated activation SNS + HPA

vagal cholinergic anti-inflammatory pathway  
(acetylcholine + macrophages)

potential mediators and therapeutic targets of stroke-induced immunodepression

*„SNS-mediated stroke-induced immunodepression“*

IMMUNOMODULATION THERAPY?

Santos Samary C et al. 2016, Aslanyan S i sur. *Eur J Neurol* 2004; Hilker R i sur. *Stroke* 2003., Langhorne P i sur. *Stroke* 2000.

## Conclusion

age-standardized incidence, mortality, prevalence and DALYs/YLDs 1990 - 2015 ↓

the absolute number of people affected by stroke ↑

POPULATION GROWTH AND AGING

THE GLOBAL STROKE BURDEN ↑

geographical (country and regional) differences  
(low- and middle-income countries)

the global burden of neurological disorders ↑

policy makers and health-care providers