

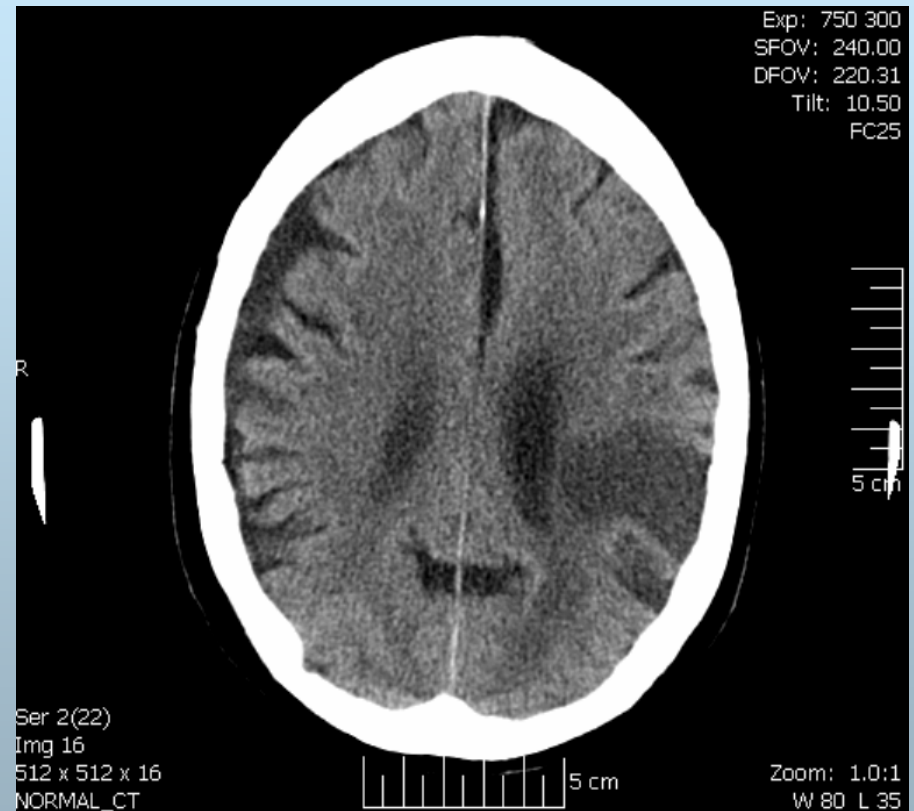
# Role of infection, inflammation and immunity after stroke

Prof. Joseph Kwan  
Consultant Stroke Physician  
Royal Bournemouth Hospital

Visiting Professor  
Chair of Dorset Vascular Research Group  
School Health Social Care  
Bournemouth University

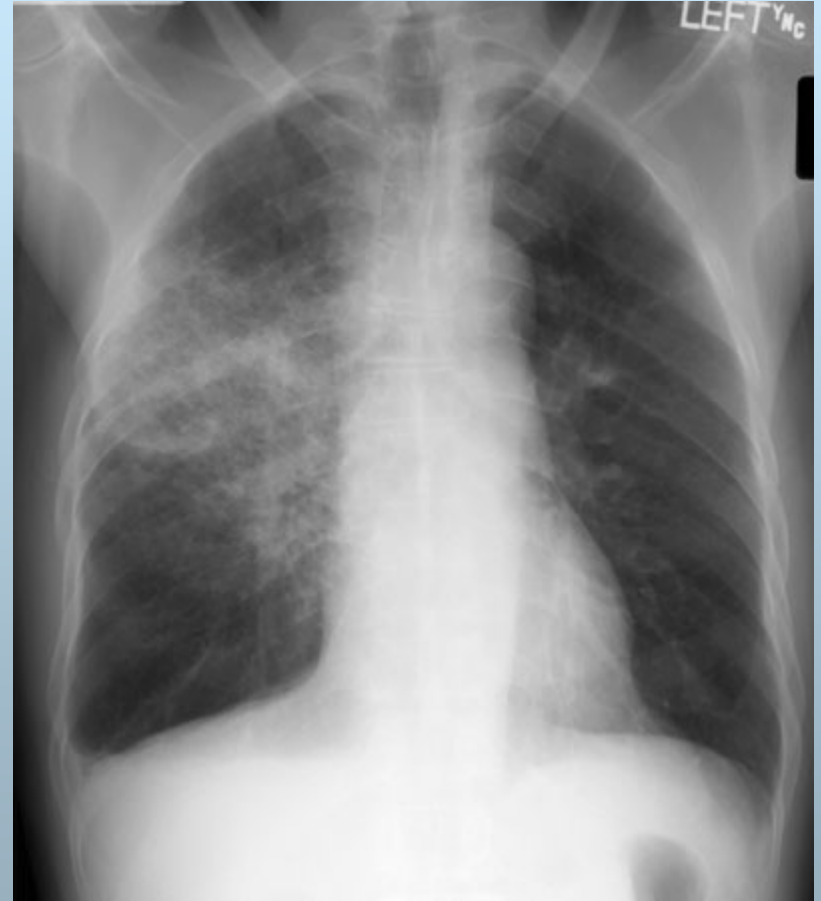
# Acute stroke and inflammation

- Inflammatory state exists after acute stroke
- IL6 associated with larger infarct size and poor recovery at 6 months
- Pro-inflammatory state in infection
- Ischaemic stroke results from damage to endothelial cells and thrombus formation over the damaged area
- Endothelial function linked with inflammation



# Systemic infections after stroke

- 25-65% of patients with acute stroke experience post-stroke infections (PSI)
- UTI and lower respiratory tract infections (LRTI) most common
- LRTI account for 22% of all deaths <1 month, and 26% of all deaths <1 year



# PSI and short term outcome

*Acta Neurol Scand* 2007; 115: 331–338 DOI: 10.1111/j.1600-0404.2006.00783.x

Copyright © 2007 The Authors  
Journal compilation © 2007 Blackwell Munksgaard

ACTA NEUROLOGICA  
SCANDINAVICA

## Infection after acute stroke is associated with poor short-term outcome

Kwan J, Hand P. Infection after acute stroke is associated with poor short-term outcome.

*Acta Neurol Scand* 2007; 115: 331–338.

© 2007 The Authors Journal compilation © 2007 Blackwell Munksgaard.

**J. Kwan<sup>1</sup>, P. Hand<sup>2</sup>**

<sup>1</sup>Department of Medicine for the Elderly, Royal Bournemouth Hospital, Bournemouth, UK; <sup>2</sup>Department of Neurology, Royal Melbourne Hospital, Parkville, Vic., Australia

- 439 consecutive stroke admissions – 73 (17%) had PSI <5 days of admission
- Patients with PSI were on average 5 years older, frailer pre-stroke, had more severe strokes, and had urinary catheter in situ

# PSI and short term outcome

- PSI associated with poor short term outcome
- Patients with PSI were more likely to develop hypoxia, pressure sores and seizures
- PSI was associated with higher risk of in-hospital death (OR 2.5, 1.27-4.9) and institutionalisation (OR 1.9, 1-3.4)

**Table 5** Occurrence of chest and urinary tract infections in the present study compared with previous recent studies

	Patient ( <i>n</i> )	Period of assessment	Chest infection (%)	UTI (%)
Present study	439	5 days	10	7
Chamorro et al. (1)	136	7 days	13	4
Aslanyan et al. (22)	1455	7 days	14	17
Roth et al. (25)	1029	During rehabilitation	4	31
Langhorne et al. (3)	311	During hospital stay	22	23
Grau et al. (23)	119	7 days	10	3
Johnston et al. (7)	279	10 days	10	11
Davenport et al. (5)	607	During hospital stay	12	16
Kalra et al. (24)	245	During rehabilitation	12	25
Dromerick and Reding (2)	100	During rehabilitation	7	44

UTI, urinary tract infection.

# PSI – unanswered questions

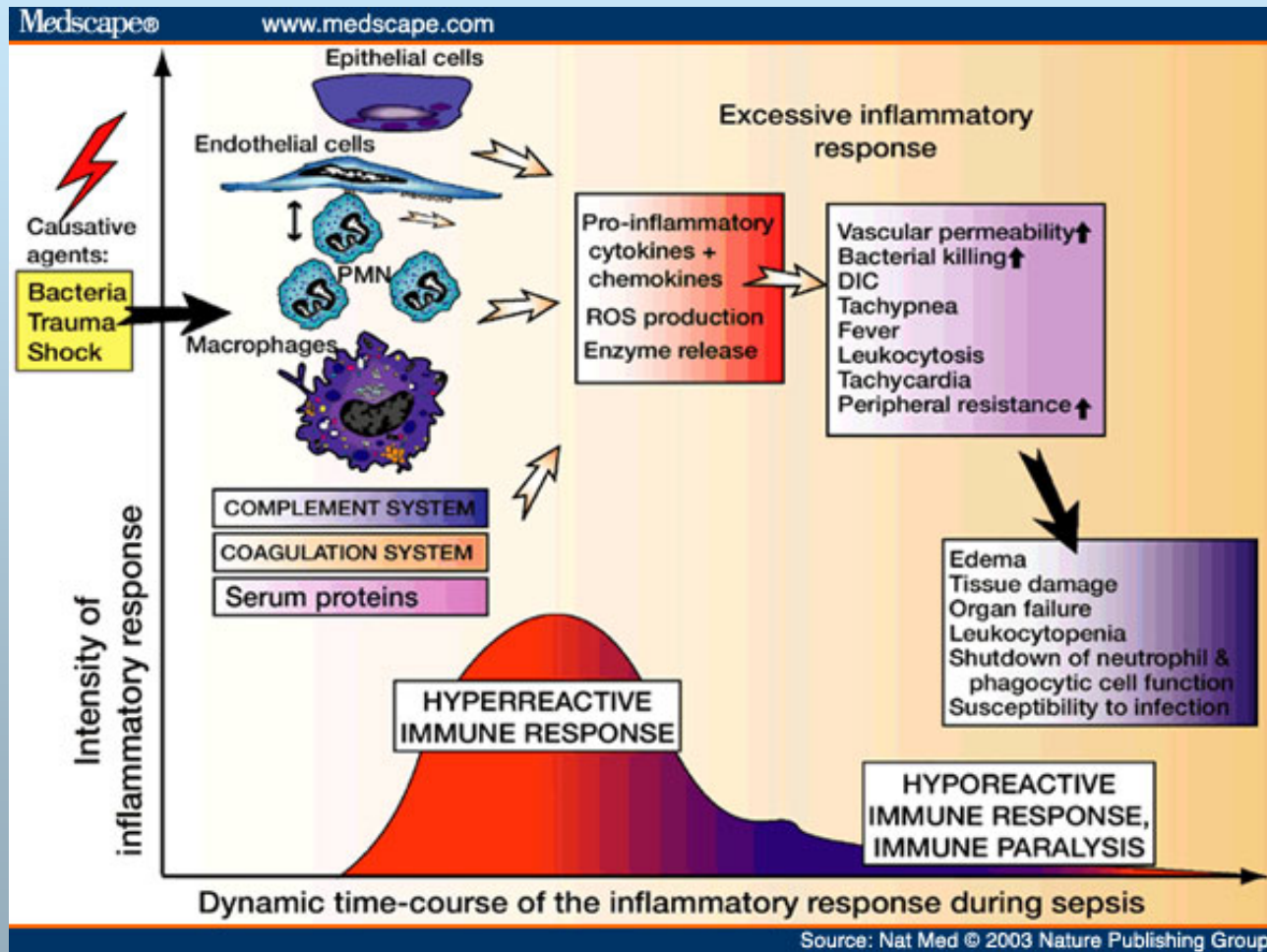
- What are the effects of PSI on long term outcome?
  - Functional recovery, cognitive, mood, QoL
- Why do infections adversely affect early recovery?
  - Role of inflammation and endothelial cell activation
- Why are stroke patients at high risk of infections?
  - Neurological deficits (↓LOC, dysphagia, poor cough urinary catheterisation)
  - Stroke-induced immuno-suppression
  - Microglial activation

# PSI and long term outcome

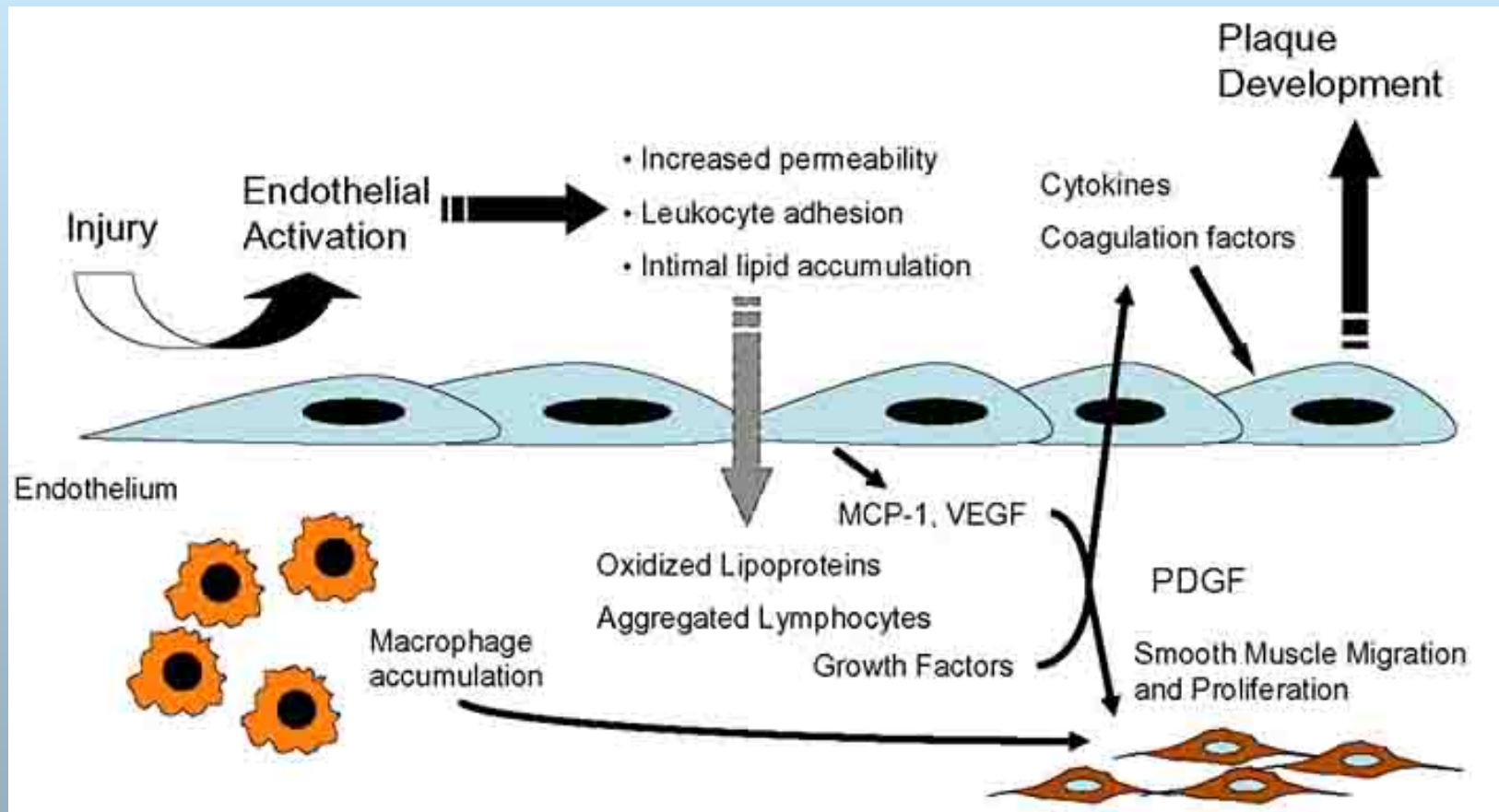
- STARR programme funded by Stroke Association with collaboration between RBH and Soton (Ashburn)
- 416 consecutive stroke admissions in RBH
- Follow up to 4 years
- Outcomes: mortality, functional recovery, mood, cognitive function, quality of life
- Data on occurrence of seizures, PSI (30%), physiological disturbances, blood tests
- Influence of PSI on long term outcome?

# PSI, inflammation & endothelial cell activation

Stroke →



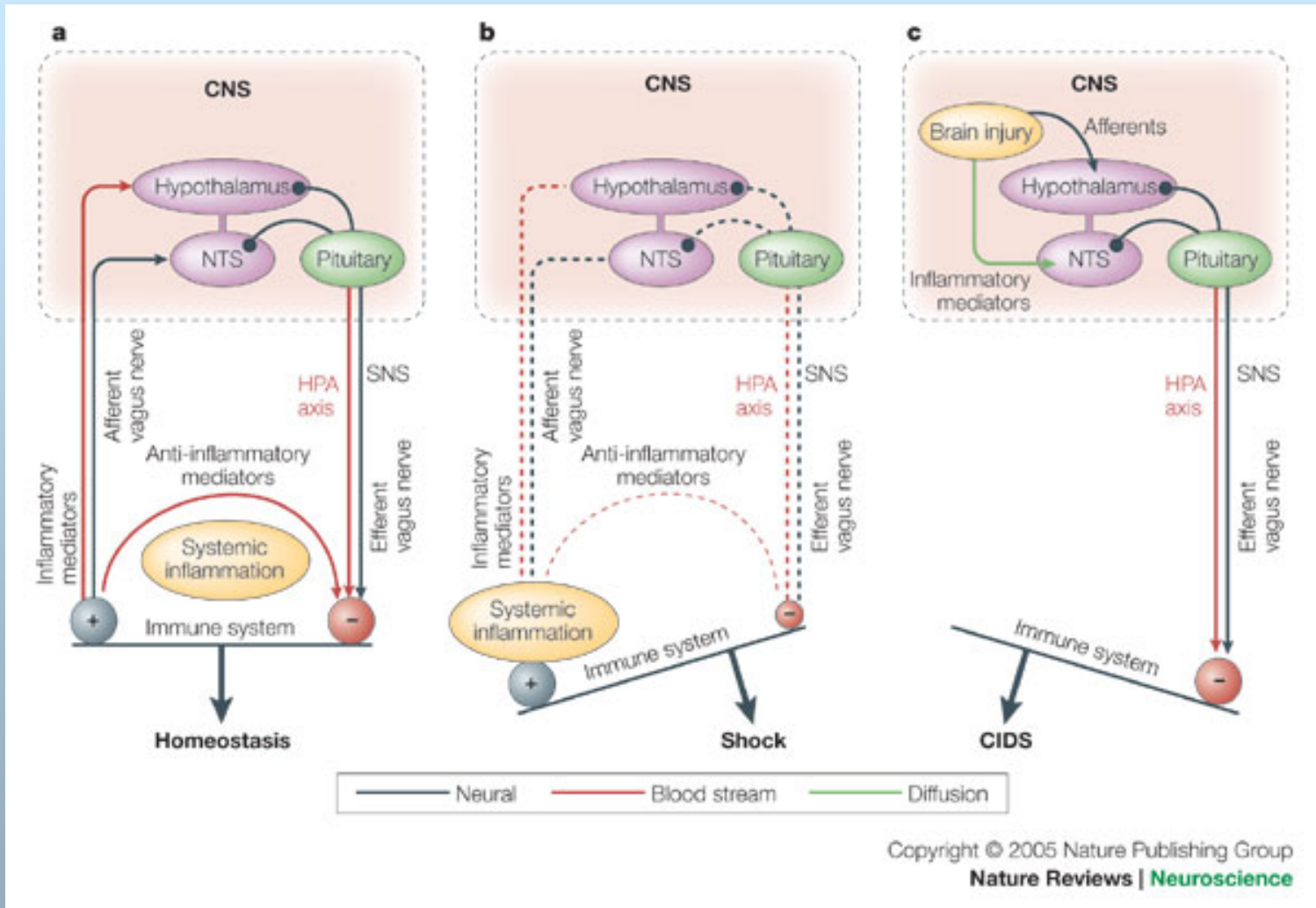
# PSI, inflammation & endothelial cell activation



# PSI, inflammation & endothelial cell activation

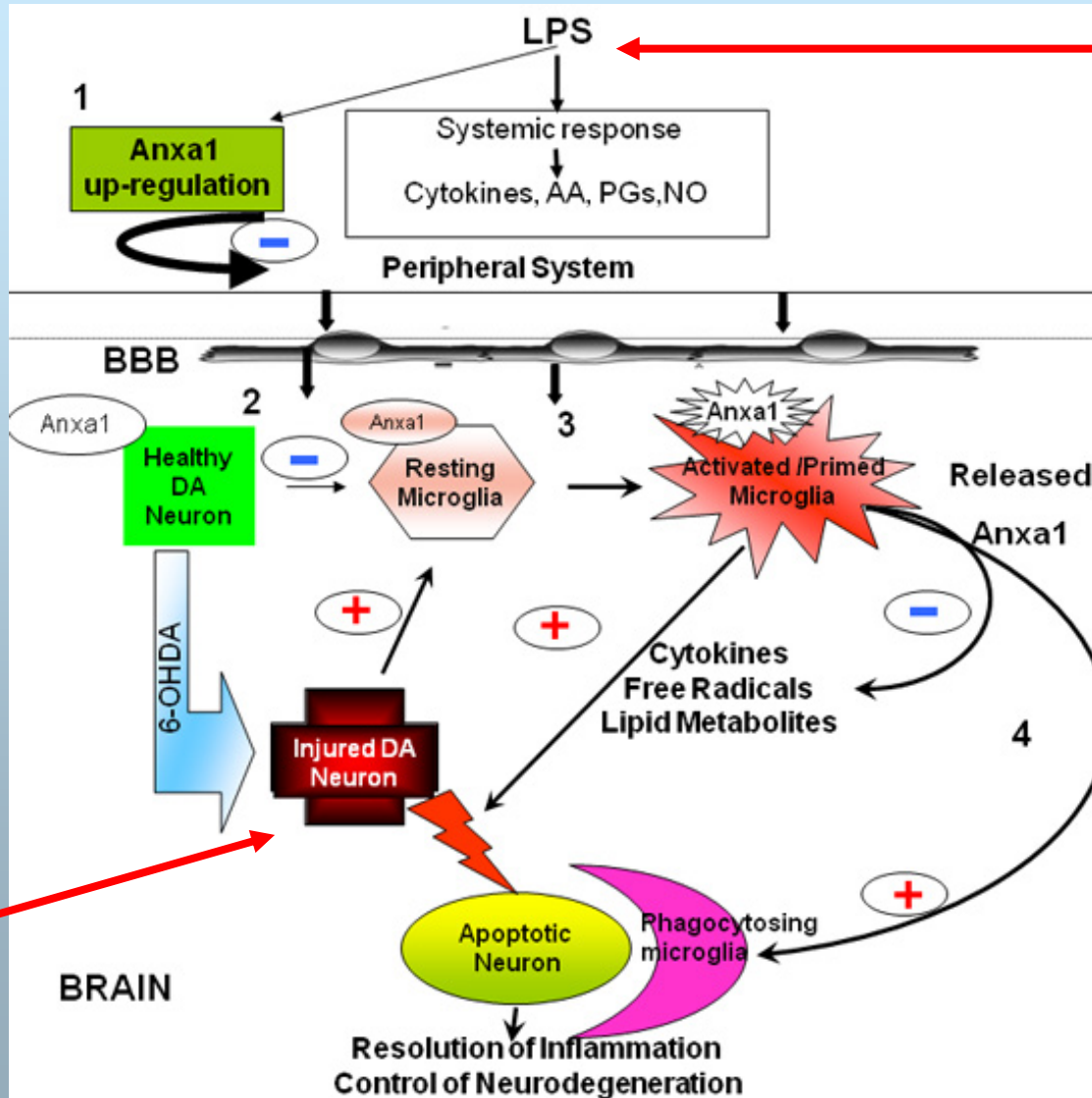
- Collaboration between RBH and Soton (Englyst)
- 85 patients with acute ischaemic stroke
- Follow up for 6 months and 2 years
  
- Outcomes: functional recovery, infarct volume on CT
- Data on occurrence of PSI (53%), cytokines (IL6, TNF $\alpha$ , IL1 $\beta$ ), endothelial cell activation (vWF, soluble thrombomodulin)
  
- PSI, inflammation and endothelial cell activation independently predicted recovery at 6 months and 2 yrs

# Stroke induced immunosuppression



# Microglial activation

Infection



Stroke

# Infection & autonomic dysfunction

- Part time PhD studentship in BU, based at RBH
- 40 in-patients with infection vs. 40 in-patients without infection vs. 40 healthy controls
- Follow up to 6 weeks
  
- Outcomes: autonomic function, cognitive function
- Data on cytokines (IL6, TNF $\alpha$ , IL1 $\beta$ , IL10)
  
- Association between autonomic function, cognitive function and inflammation

# Infection, inflammation & immunity after stroke

- Joint research programmes with RBH Haematology unit – measure level of immunity after stroke + correlate with PSI occurrence
- Joint research programme with Soton Uni – translational work looking at role of microglial activation / inflammation in PSI
- Joint research programme with Leipzig Uni – measure autonomic function and cardiac rhythm disturbance with/without PSI