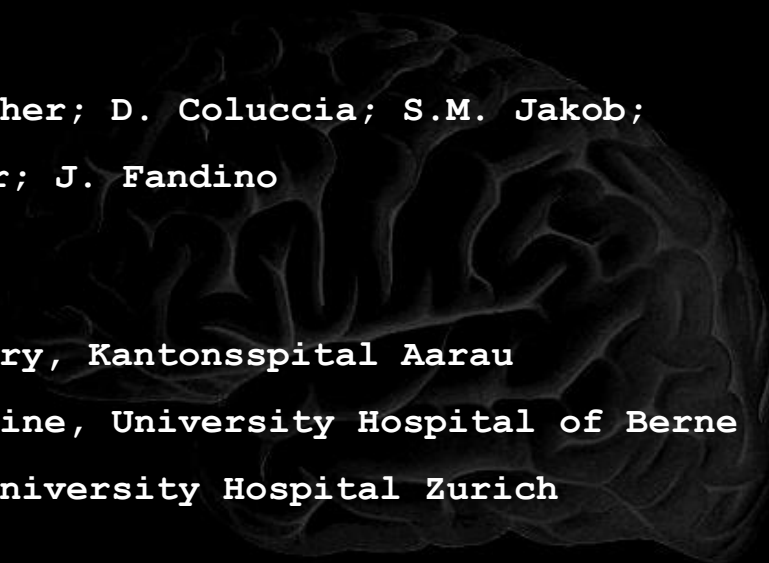


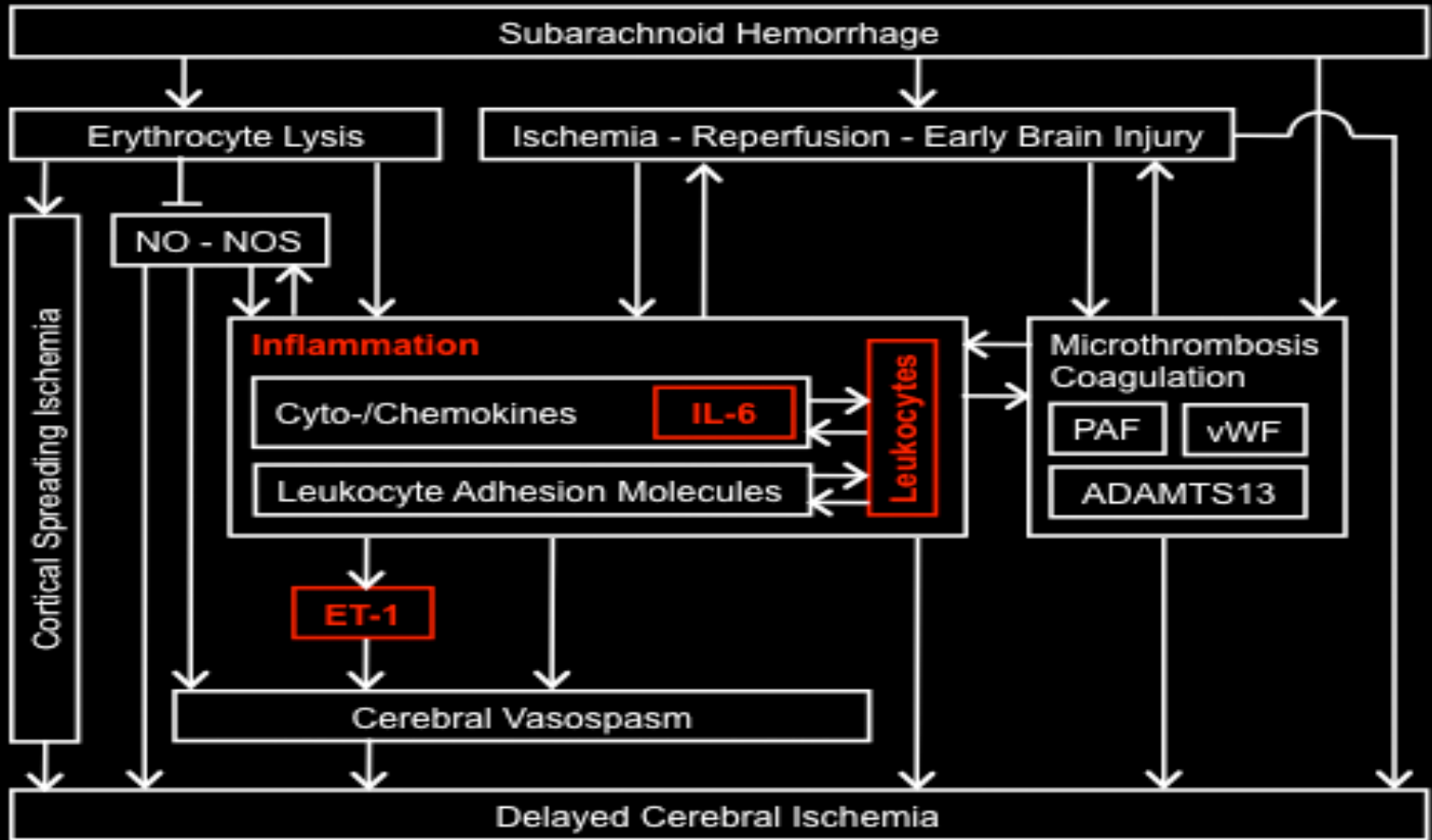
Relationship between Cerebrospinal Fluid
Endothelin-1 and Interleukin-6 Levels in Cerebral
Vasospasm after Experimental Subarachnoid
Hemorrhage in the Rabbit

- Project Outline -

C. Muroi; E. Keller; S. Marbacher; D. Coluccia; S.M. Jakob;
M. Hugelshofer; J. Fandino

Department of Neurosurgery, Kantonsspital Aarau
Department of Intensive Care Medicine, University Hospital of Berne
Neurocritical Care Unit, University Hospital Zurich





Inflammatory response and occurrence of cerebral vasospasm (CVS) represent a common pathogenic pathway

Interleukin (IL)-6

- Linked with occurrence of CVS and outcome in clinical studies
- Topic application induced CVS in animal models

Osuka et al. Acta Neurochir 1998

- Neutralizing AB showed attenuation of CVS

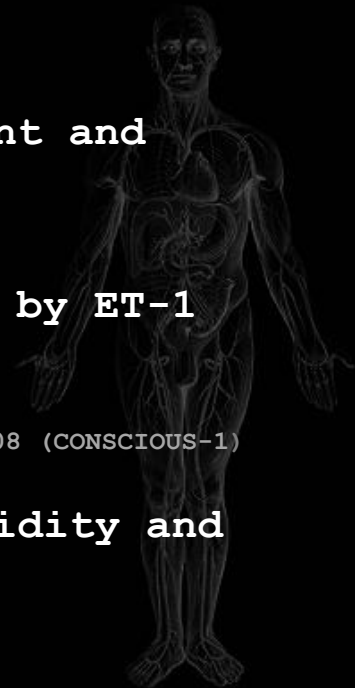
Bowmann et al. Neurosurgery 2004

Endothelin (ET)-1

- One of the primary suspect in direct development and propagation of CVS
- Randomized phase 2b trial showed decreased CVS by ET-1 Receptor Antagonist

Mc Donald et al. Stroke 2008 (CONSCIOUS-1)

- + Phase 3 trial: no significant CVS-related morbidity and all-cause mortality

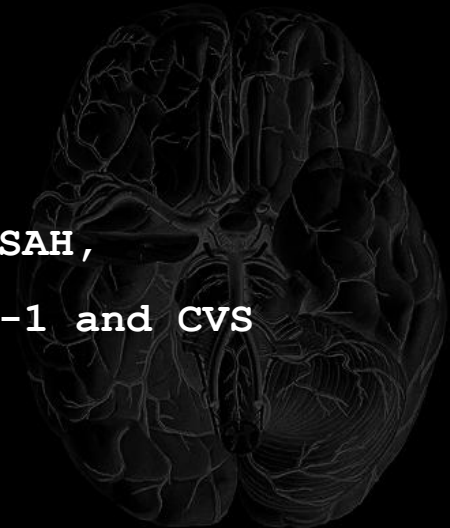


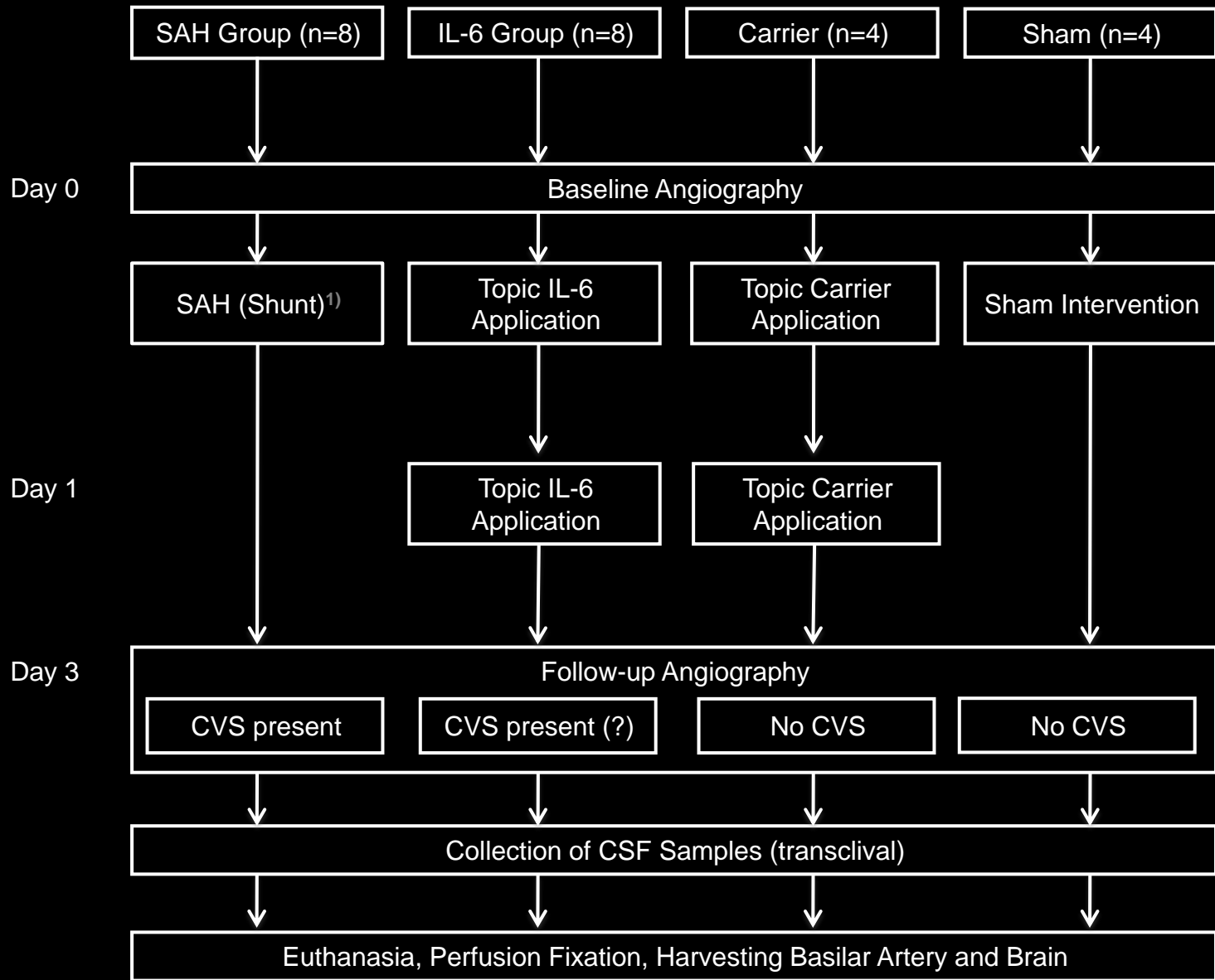
- Mechanism of ET-1 release and its origin unclear
- Inflammatory response and occurrence of CVS represent a common pathogenic pathway
- ET-1 production occurs by activated leukocytes with accompanying inflammatory response

Fassbender K et al. Stroke 2000

- IL-6 may promote CVS by the involvement of activation of inflammatory cells to produce ET-1 (??)

Objective: enlighten the relationship between SAH, Inflammatory response with IL-6 expression, ET-1 and CVS

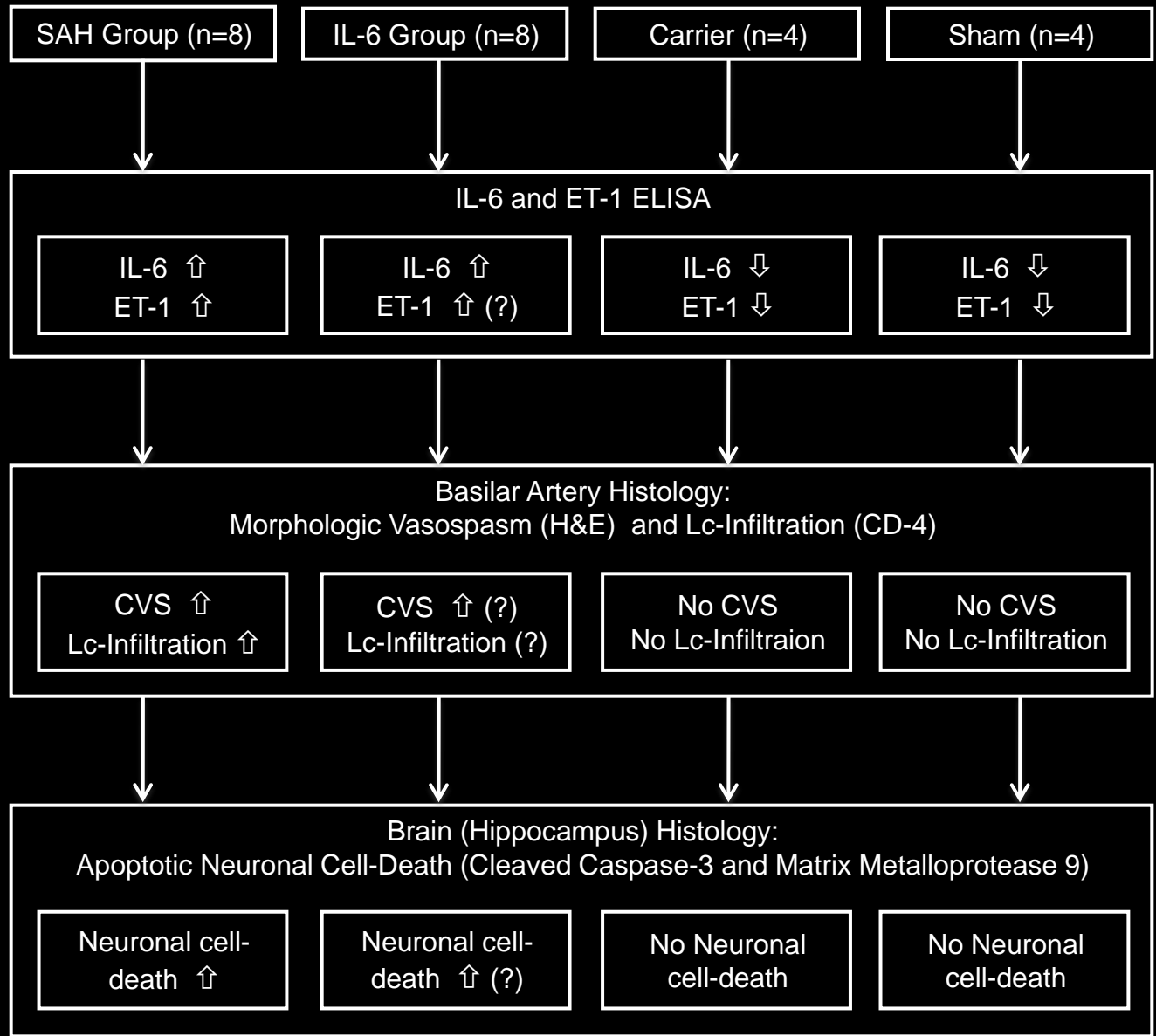




Neurological Assessment q12h 1)

1) Marbacher et al. J Neurosci Methods 1998

P o s t
M o r t e m
A n a l y s i s



- Does IL-6 trigger ET-1 release? Correlation?
- Does IL-6 cause CVS irrespective of ET-1?
Since ET-1 RA might be insufficient...
- Does IL-6 cause neuronal cell damage without CVS?
CVS is not the only cause of DCI...
- Might IL-6 blocking strategies be an option?
IL-6 RA have been validated in Rheumatoid diseases...
- Monitoring of IL-6 Levels in clinical practice?
A point-of-care test for IL-6 is available...

*** Thank You ***

