

Cerebral blood flow and metabolism – Lecture 1

For 3rd year Students of Medicine

Prof. Ferenc Bari

September 5, 2018



The aim of the course

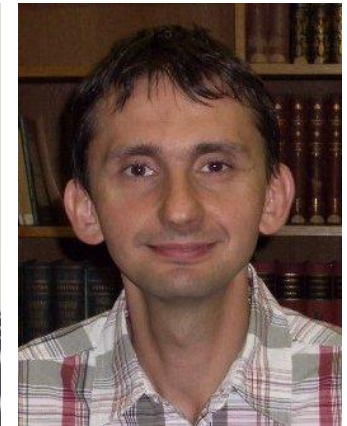
An overview of cerebral circulation

- Important for normal vital functions;
- Disease states: disturbed cerebral circulation affects motor, intellectual and autonomic functions
- Detection of (ab)normal cerebral circulation;
- Diagnostic tools



Speakers

- Prof. Ferenc Bari (Department of Medical Physics and Informatics)
- Dr. Ferenc Domoki (Department of Physiology)
- Dr. Tamás Kincses (Department of Neurology)
- Dr. Zoltán Ungvári (Reynolds Oklahoma Center on Aging
Department of Geriatric Medicine
University of Oklahoma Health Sciences Center)
- Dr. Eszter Farkas (Department of Medical Physics and Informatics)



Tentative structure of the course

English, Wednesday: 16:00-17:30		
Time	Topic	Lecturer
September 5, 2017	Introduction	Prof. Ferenc Bari
September 12, 2017	The blood brain barrier	Dr. Eszter Farkas
September 19, 2017	Physiology of the cerebral smooth muscle cell	Prof. Ferenc Bari
September 26, 2017	Regulation of cerebrovascular tone: the role of the endothelium	Prof. Ferenc Bari
October 3, 2017	Clinical neuroimaging	Dr. Tamás Kincses
October 10, 2017	Regulation of cerebrovascular tone: metabolic components	Dr. Ferenc Domoki
October 17, 2017	Neurovascular coupling	Dr. Eszter Farkas
October 24, 2017	Autumn break	
October 31, 2017	Regulation of cerebrovascular tone: neural components	Prof. Ferenc Bari
November 7, 2017	The regulation of the cerebral blood flow in the neonate	Dr. Ferenc Domoki
November 14, 2017	Students' Conference	
November 21, 2017	Aging and dementia	Dr. Zoltán Ungvári
November 28, 2017	Cerebral small vessel disease	Dr. Eszter Farkas
December 5, 2017	Written examination	Dr. Eszter Farkas

Content of the course

Is it too early (pathophysiology, pathology, internal medicine, radiology etc)?

Possibly, but

- you have basic knowledge (physiology, anatomy, biochemistry)
- you have motivation
- you can gain motivation



Content of the course

Is it too complex?

Possibly, but each part is exciting

Why take the course?

- Public health considerations (prevention, health education, rehabilitation etc)
- Basic science as well as applied science methods
- Just for some credit points? For some students, possibly – what can we do?



Visit the home page of our Department

<http://www2.szote.u-szeged.hu/dmi/eng/>

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Latest News

- Greetings 01 September 2016
 - LAMELIS 2016 28 June 2016
 - Conf. for undergraduate students 2016 02 March 2016
 - End-semester announcements 28 November 2015
 - Sectra 3D Human Body Visualization Table 17 November 2015
- More in Education Research Education



Dear first-year medical student, dear future colleague! On behalf of my colleagues I congratulate...



Greetings to our First-Year Students
Prof. Ferenc Bari, head of institute



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Latest News

Greetings 01 September 2016



Dear first-year medical student, dear future colleague! On behalf of my colleagues I congratulate...

LAMELIS 2016 28 June 2016

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End-semester announcements 28 November 2015

Sectra 3D Human Body Visualization Table 17 November 2015

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Greetings to our First-Year Students
Prof. Ferenc Bari, head of institute

- Undergraduate programmes
- Graduate programmes
- Pre-medical programme
- Exams
- International (JPEMS)
- Handouts

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Highlights

- LAMELIS 2014-2016
- JPEMS 2011-2016

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Faculty of Medicine - Cerebral blood flow and metabolism

[Cerebral lecture 1 \(Prof. Ferenc Bari\)](#)

[Cerebral lecture 2 \(Prof. Ferenc Bari\)](#)

[Cerebral lecture 3 \(Prof. Ferenc Bari\)](#)

[Cerebral lecture 4 \(Prof. Ferenc Bari\)](#)

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[Cerebral lecture 10 \(Dr. Ferenc Domoki\)](#)

[Cerebral lecture 11 \(Dr. Eszter Farkas\)](#)

[Cerebral lecture 12 \(Prof. Ferenc Bari\)](#)

[Cerebral lecture 12 supplement \(Prof. Ferenc Bari\)](#)

[Cerebral lecture 13 \(Dr. Eszter Farkas\)](#)

[Cerebral blood flow supplement1](#)

[Handouts 2014/2015 \(2nd semester\)](#)

[Handouts 2014/2015 \(1st semester\)](#)

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CooSpace kliens Android tableten!


Kedves Felhasználónk!


Örömmel értesítjük, hogy az iPad-re készített verzió után a CooSpace alkalmazás már **letölthető** Android platformra is. Ezzel az alkalmazással felhasználóink használhatják Androidos tabletekre is a

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7 Wednesday
September, 2016






September, 2016

	Su	Mo	Tu	We	Th	Fr	Sa
36	28	29	30	31	1	2	3
37	4	5	6	7	8	9	10
38	11	12	13	14	15	16	17
39	18	19	20	21	22	23	24
40	25	26	27	28	29	30	1
41	2	3	4	5	6	7	8














   

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Current	39
Change	35

Scenes     

PERMANENT

-  Medical Physics and Statistics ☆ MPS    
-  Oktatói Információs színtér ☆ OKTINF   
-  Zöld Egyetem - fenntarthatóság a Szegei Tudományegyetemen ☆ GREEN_UNIV   

2016-2017-1

-  Cerebral blood flow and metabolism ☆ *AOKKA1027celblood-1   
-  Demonstrátori tevékenység ☆ AOK-DEMO-FIZINF-1   
-  Fejezetek az agy vérellátásának szabályozásáról ☆ *AOKK10251-1   
-  Kutatásmódszertan ea. ☆ KITM0701E_L-1   
-  Szakdolgozat előkészítés, konzultáció ☆ AOK-SZD101Orv.Inf-1   
-  TEST-EN-Medical Physics and Statistics 1 practice* ☆ TEST-EN   
-  Medical Physics and Statistics 1st practice ☆ *AOK-KUA052-11   
-  Medical Physics and Statistics 1st practice ☆ *AOK-KUA052-5   

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Additional study material (e.g. journal articles)

The screenshot shows the CooSpace interface for a scene titled "Cerebral blood flow and metabolism". At the top, there is a navigation bar with the CooSpace logo, the text "Szegedi Tudományegyetem", and user information including a profile icon for "Farkas Eszter Dr.habil.", a notification badge with "246", and a language selector set to "EN". Below this is a toolbar with icons for "scenes", "folder", "today", "messages" (with a badge of "6"), "video", "my notes", "questions", "glossary", "trainer", and "news". A search bar is located on the right side of the toolbar.

The main content area features a left sidebar with navigation options: "Back", "New tool", "Rearrange tools", "Tag cloud", "Members", "Scene info", "Kimutatások", "Scene options", and "Scene settings". The main content area displays the scene title "Cerebral blood flow and metabolism" with a star icon and the identifier "*AOKKA1027celblood-1 2016-2017-1". Below the title, there are three main sections: "Newsboards" (with a sub-section "Hirdetmények" and "Last message"), "Forums" (with a sub-section "Kurzusforum" and "Last comment | Total comments 0"), and "Folders" (with a sub-section "Dokumentumok"). A red arrow points from the "news" icon in the toolbar to the "Newsboards" section.

At the bottom left, the date is displayed as "7 Wednesday September, 2016".

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CooSpace Szegedi Tudományegyetem

 2
 246
 Farkas Eszter Dr.habil.
 EN

scenes
 folder
 today
 6 messages
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 questions
 glossary
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 news

Journal of the American College of Cardiology
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ISSN 0735-1097/\$36.00
doi:10.1016/j.jacc.2009.12.072

STATE-OF-THE-ART PAPER

Stroke Prevention and Treatment

James D. Marsh, MD,* Salah G. Keyrouz, MD†
Little Rock, Arkansas

The decline in stroke incidence and mortality in the U.S. over the past 20 years is reaching a plateau, and the number of strokes may actually start to increase as the population ages. However, recent clinical trials have demonstrated that there are numerous opportunities to improve stroke prevention strategies and also opportunities to effectively intervene in and treat acute strokes. For patients with diabetes and for those with prior strokes or transient ischemic attacks, it has become evident that aggressive low-density lipoprotein lowering with statin medications will decrease the risk for total and fatal strokes. Optimal anticoagulation and antiplatelet therapy for primary and secondary stroke prevention in atrial fibrillation is being carefully defined. With numerous novel factor Xa and direct thrombin inhibitor drugs completing phase III clinical trials, it is likely that additional oral anticoagulant drugs will be clinically available for stroke prevention soon. Additionally, a major clinical trial is nearing completion that may resolve the role of carotid stenting and carotid endarterectomy in primary and secondary stroke prevention. There are recent notable advances in the acute treatment of stroke. It is likely that the time window for thrombolysis for appropriate patients with strokes will be increased from 3 to 4.5 h, permitting the inclusion of more patients in this treatment approach. There is ongoing investigation of intra-arterial thrombolysis and of acute intra-arterial thrombus extraction for treatment of selected patients with strokes. Unlike the progress in treatment of ischemic strokes, treatment of hemorrhagic stroke is progressing more slowly. (J Am

7 Wednesday
September, 2016

DEPARTMENT OF MEDICAL PHYSICS AND INFORMATICS

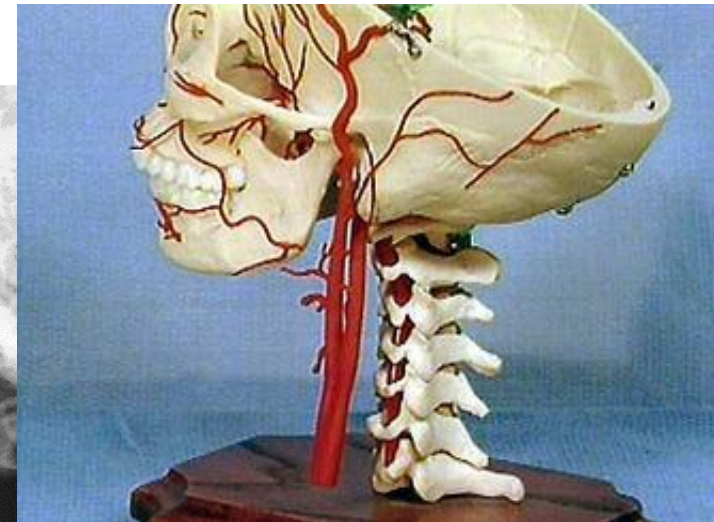
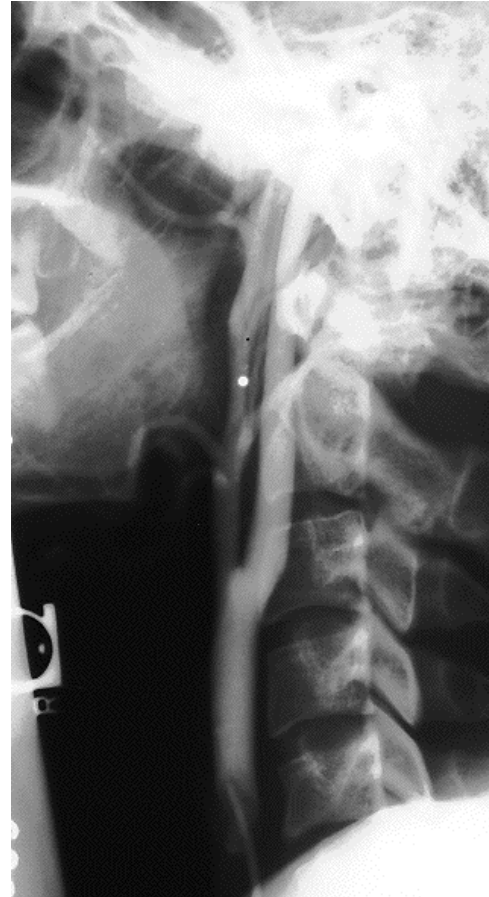
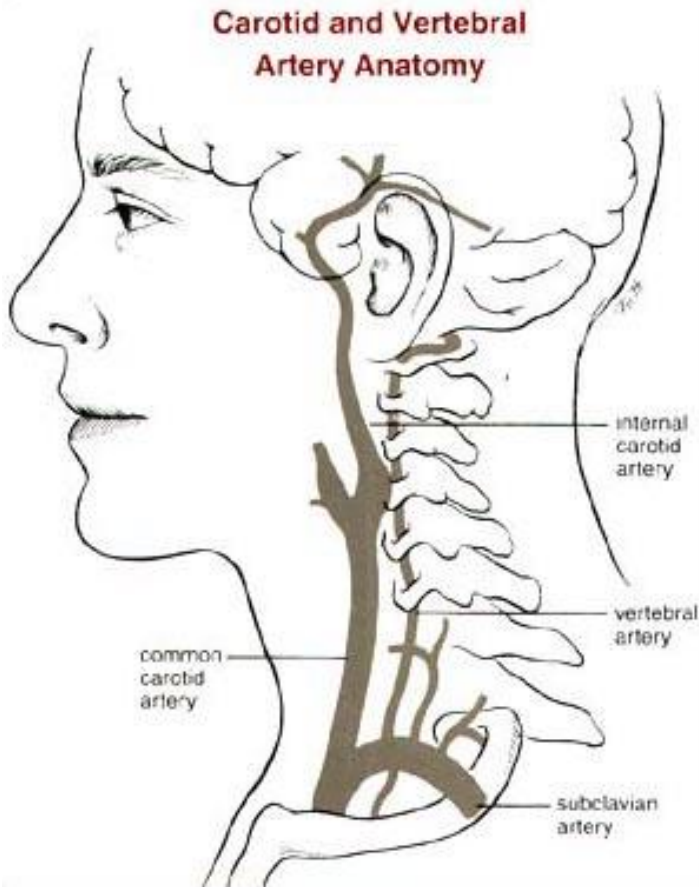
University of Szeged, Faculty of Medicine, Faculty of Science and Informatics

Requirements and exam

- Attendance will be checked
- Teaching material: on the website and papers recommended
- Exam: MCQ, the last week of the semester



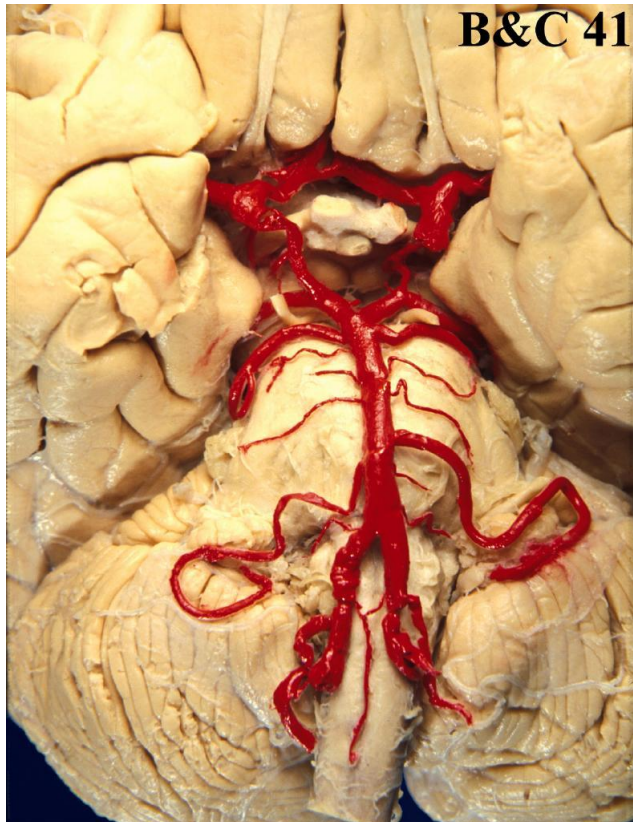
Blood supply to the brain: extracranial vessels



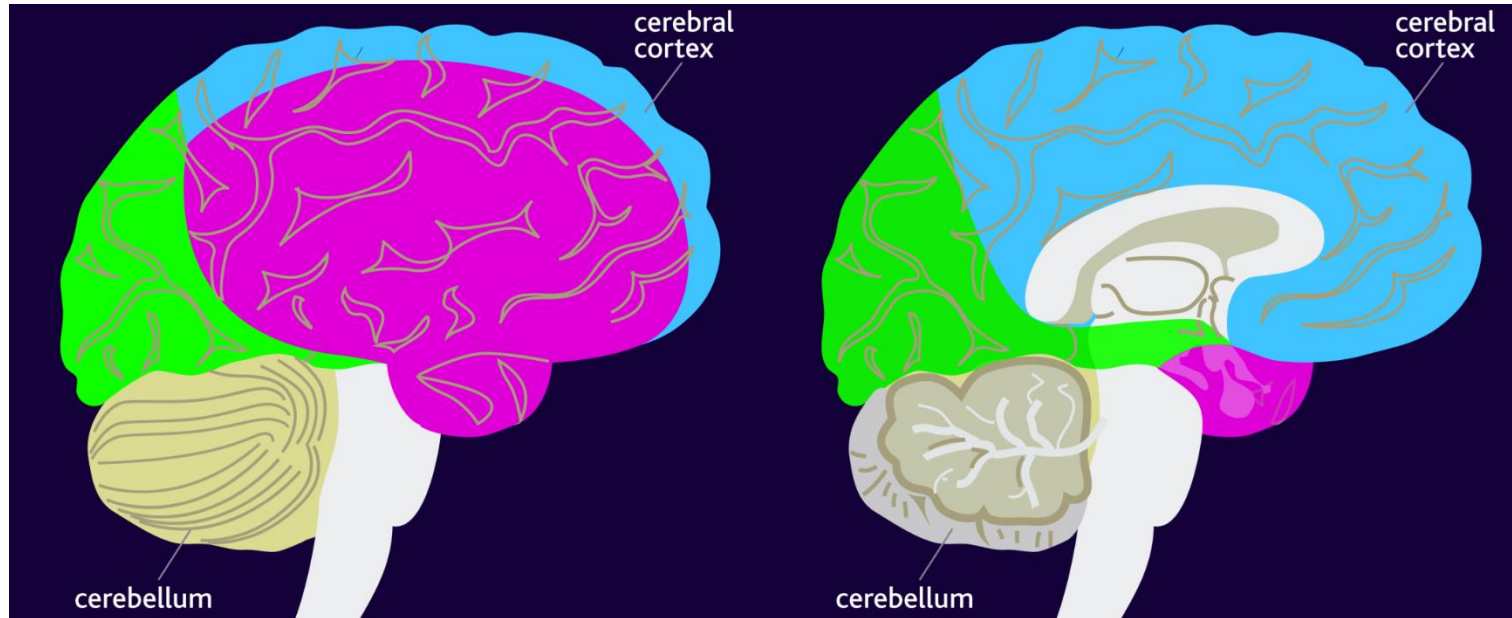
- common carotid → internal carotid
 - vertebral → basilar
- ⇒ circle of Willis

Blood supply to the brain: Circle of Willis

Circle of communicating arteries at the base of the brain



Blood supply to the brain: intracranial vessels



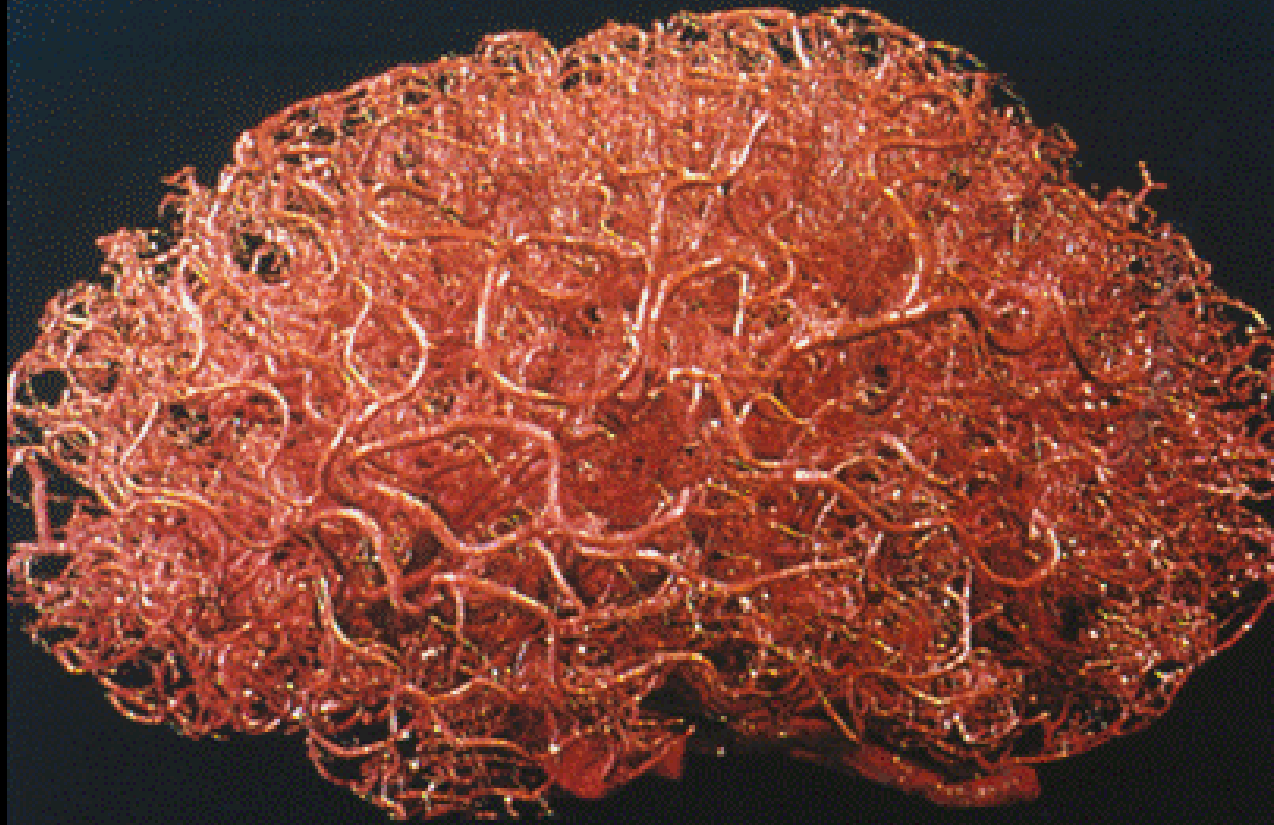
Basilar A.

- ant-inf. Cerebellar A.
- int. Auditory A.
- Pontine Aa.
- sup. Cerebellar A.
- **POSTERIOR CEREBRAL A.**

Carotidian system ~ ICA

- Hypophyseal A.
- Ophthalmic A.
- post. Communicating
- **MIDDLE CEREBRAL A.**
- **ANTERIOR CEREBRAL A.**

Microvessels



<http://brainwaves.corante.com/Vasculature.gif>

Blood vessels are responsible for 25-30% of total brain volume

400 miles of microvessels (with 20 m² surface area) provide adequate cerebral perfusion at all times

Microvessels

A lot more to come:
Blood-brain barrier lecture



Physiology: some interesting facts

Brain weight: ~2% of body weight (1400-1500g)

The brain:

- Receives 15% of the cardiac output (700-750 ml)
- Consumes 20% of the oxygen used by the entire body

Has no metabolic reserve:

- 10 seconds of interruption of blood flow to the brain leads to unconsciousness
- 2-10 minutes interruption of blood flow may cause brain death



Physiology: some interesting facts

Continuous oxygen requirement: Neurons are predominantly aerobic



Few minutes of ischemia causes irreversible injury

- Oxygen extraction = 35%
- Oxygen supply is 3 times bigger than demand

Sensitive areas

Adults:

- Hippocampus,
- 3,5th & 6th layer of cortex,
- Purkinje cells
- Border zone (watershed areas)

Infants:

- Brain stem nuclei in infants.

Typical features of cerebral circulation

- The Monroe-Kelly hypothesis
- Autoregulation
- No sympathetic tone of blood vessels
- Blood-brain barrier
- The origin of interstitial fluid



The Monroe-Kelly hypothesis

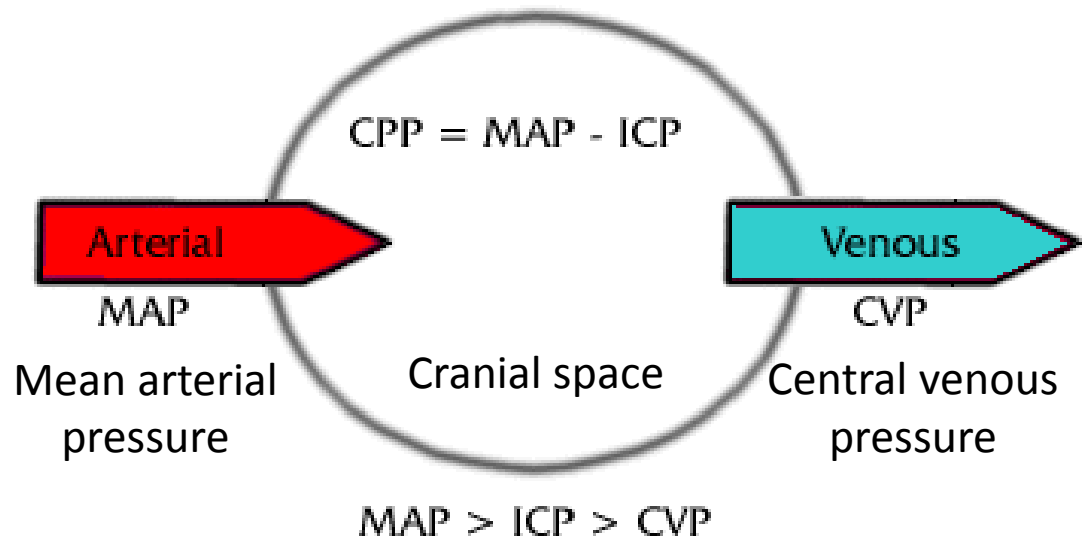
Describes the pressure relationship between cranial compartments

- Closed cranium: fixed volume - incompressible
- Compartments:
 - Brain parenchyma: 88%
 - Cerebrospinal fluid (CSF): 7-8%
 - Blood: 4-5%
- State of volume equilibrium: any increase in volume of one of the cranial constituents must be compensated by a decrease in volume of another
- Maintenance of normal intracranial pressure (ICP) at any change in volume less than approximately 100–120 ml (buffers: CSF, venous blood)
- Pathophysiologic increase in any one of the components: at the expense of the other two, increased ICP



Cerebral perfusion pressure (CPP)

- Responsible for blood supply to the brain
- Cerebral perfusion pressure (CPP) = mean arterial pressure (MAP) – intracranial pressure (ICP)
- Normal value: 70-80 mmHg
- < 50 mmHg: insufficient blood supply (ischemia)



Cerebral blood flow

- Definition: the blood supply to the brain in a given time (ml/min, v. ml/min/100g)
- Adult:
 - 750 ml/min (15% of resting cardiac output)
 - 50 ml/min/100g
- Defining variables: $CBF = \frac{CPP}{CVR}$ $CPP = MAP - ICP$

(CVR: cerebrovascular resistance)

Cerebral blood flow regulation

Categories:

Affected area:

- Global
- Local

Type:

- Myogenic
- Neurogenic
- Metabolic
Chemical

Origin of stimulus:

- Parenchyma
- Endothelium
- Blood



Cerebral blood flow regulation

A lot more to come!



Cerebrovascular diseases

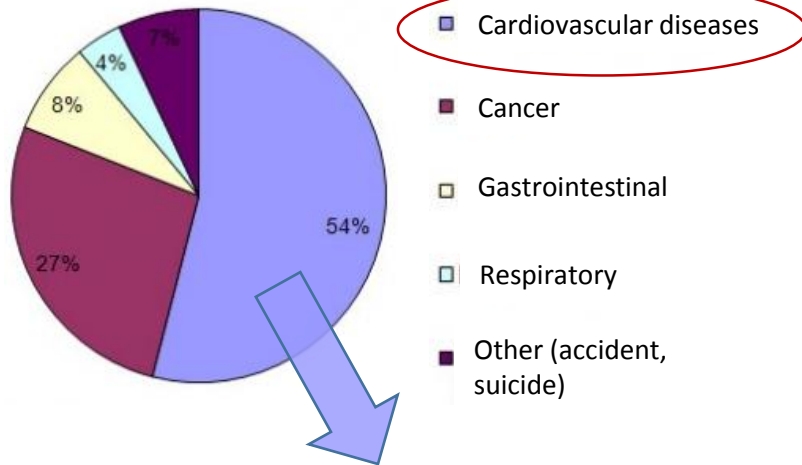
- Common denominator: ischemia
- What is ischemia?

An inadequate blood supply to an organ or part of the body \Rightarrow shortage of oxygen and glucose needed for cellular metabolism



Cerebrovascular diseases

Major causes of death



Cardiovascular diseases:

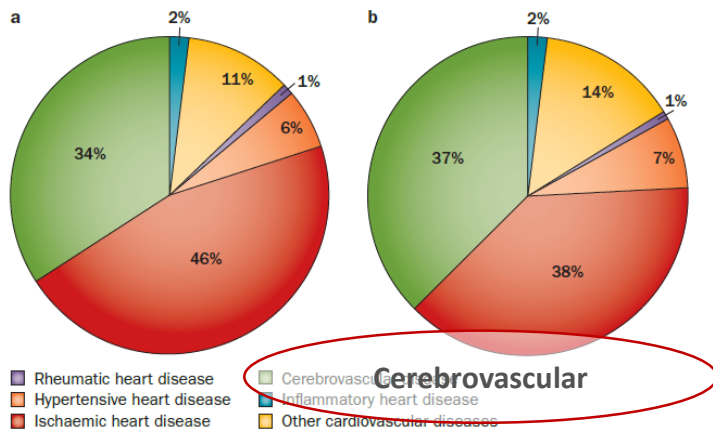
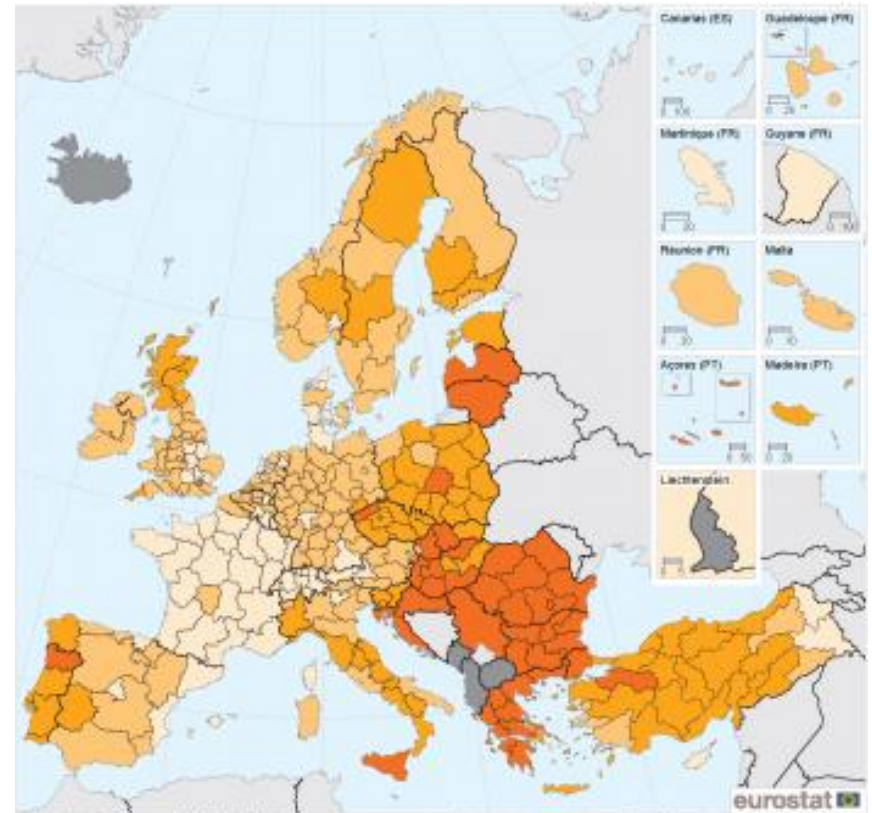


Figure 1 | The proportions of cardiovascular deaths caused by ischaemic heart disease, cerebrovascular disease, inflammatory heart disease, rheumatic heart disease, hypertensive heart disease, and other cardiovascular diseases in



Deaths due to cerebrovascular diseases in people aged 65 and over, by NUTS 2 regions, 2013 (1) (crude death rates per 100 000 inhabitants)

Source: Eurostat

(1) 2012 data for ARB (Greece), French (United Kingdom) and Turkey, Serbia (1)



Alzheimer's disease

White matter lesions

Vascular Cognitive Impairment

Stroke

Clinical Categories of Inadequacy

1. Global Ischemia

Hypotension, hypoxemia, anemia



Hypoxic encephalopathy

2. Focal Ischemia

Obstruction to blood supply to focal area

Thrombosis, embolism or hemorrhage



Global ischemia

Etiology:

- Impaired blood supply - Lung & Heart disorders
- Impaired O₂ carrying – Anemia/Blood disorders

Morphology:

- Laminar necrosis, damage in: Hippocampus, Purkinje cells
- Border zone infarcts – “Watershed”
- Sickle shaped band of necrosis on cortex.

Clinical Features:

- ↓ Mild transient confusion state
- ↓ Severe irreversible brain death; flat EEG, vegetative state, coma

Global ischemia

Mild cognitive impairment

Dementia

- Alzheimer's Disease, cerebral amyloid angiopathy
- CADASIL (Cerebral Autosomal-Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy): mutations of the Notch 3 gene on chromosome 19
- Cerebral microhemorrhage - results from rupture of small blood vessels
- Multi-infarct dementia - multiple strokes (disruption of blood flow to the brain)



Alzheimer's disease

An upcoming lecture dedicated to the topic!



Focal ischemia

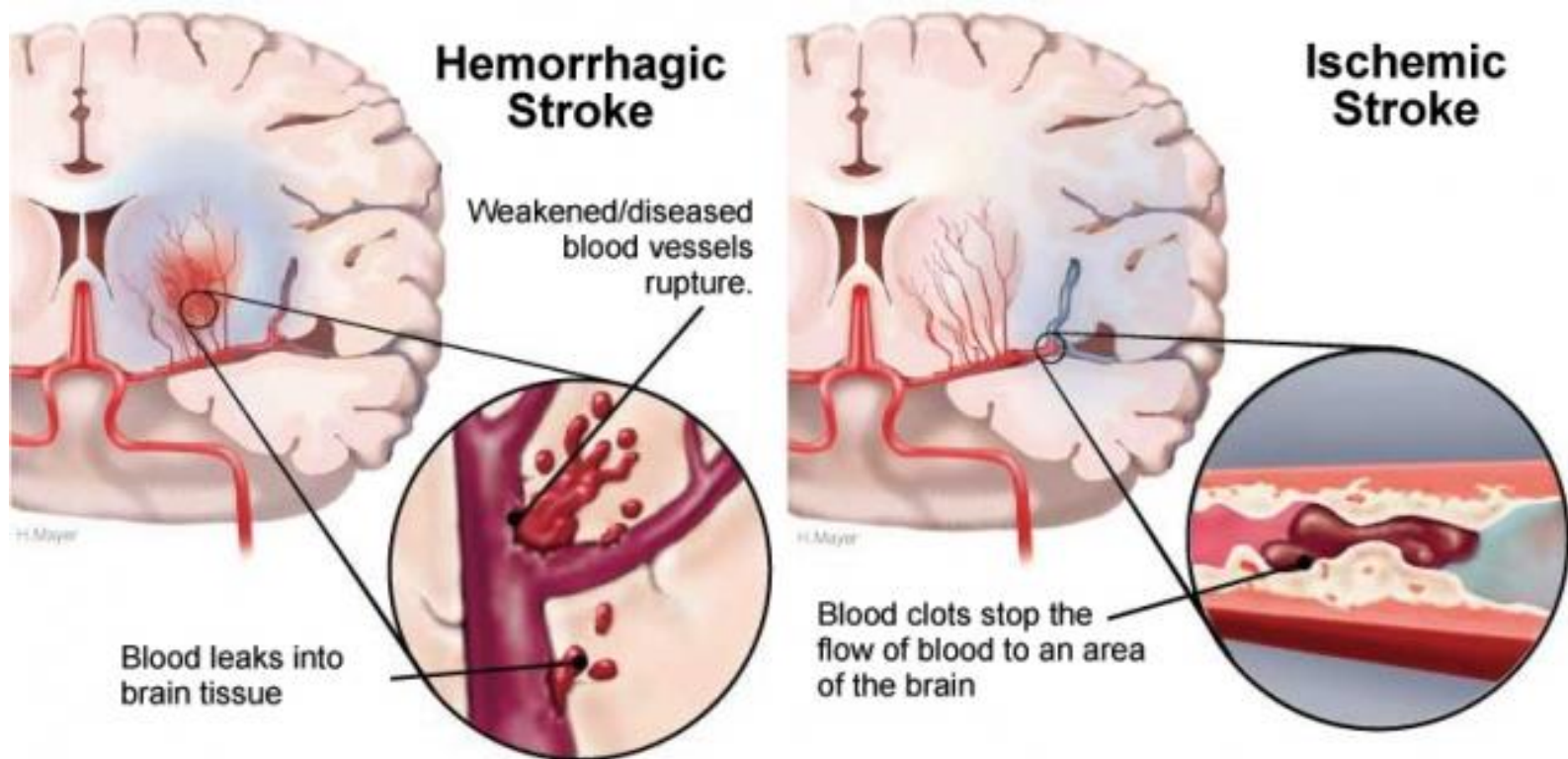
Cessation of blood circulation, oxygen and nutrients in a particular region of brain

~ **Stroke**



Definition of stroke

Cerebro-vascular disorder caused by **insufficient cerebral circulation**, and resulting in sudden neurological deficits.



© Heart and Stroke Foundation of Canada

Incidence

- **Hemorrhage:** bleeding, within the skull

Incidence 20% - mortality 80%

- Intracerebral or subarachnoid
- Aneurysm (hypertension/congenital), arteriovenous malformation

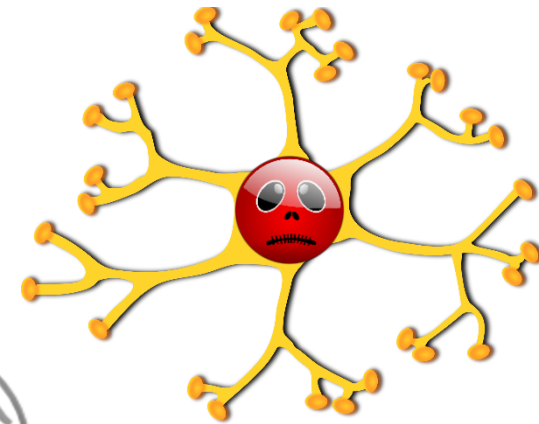
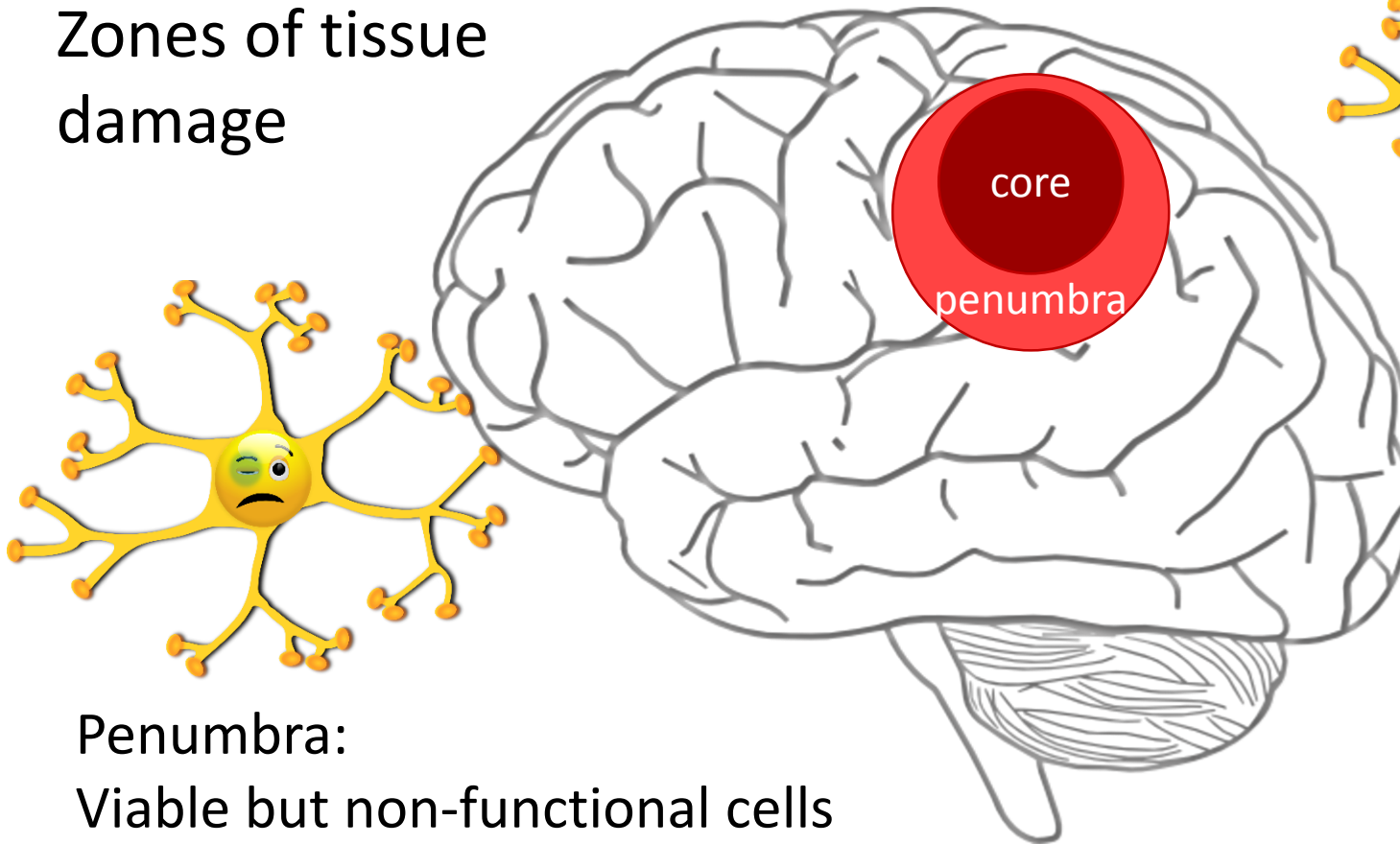
- **Infarction:** tissue death (necrosis) due to a local lack of oxygen caused by obstruction of the tissue's blood supply.

Incidence 80% - mortality 40%

- 50% - Thrombotic – atherosclerosis
 - Large-vessel 30% (carotid, middle cerebral)
 - Small vessel 20% (lacunar stroke)
- 30% Embolic (heart disease/atherosclerosis)
 - Young, rapid, extensive

Infarction (ischemic stroke)

Zones of tissue damage



Core (umbra):
Infarcted area
– non-viable
cells

Penumbra:
Viable but non-functional cells

Residual blood flow

Collateral circulation helps to maintain some CBF to post obstruction area

- Core \sim CBF < 10 ml/100gm/min

Early irreversible membrane rupture & cell death

- Penumbra \sim CBF < 20 ml/100gm/min

Rapid energy depletion & loss of neuronal activity
(electrically silent)

Infarct maturation

Reduced blood supply \Rightarrow hypoxia/anoxia

Altered metabolism \Rightarrow Na/K pump block

Glutamate receptor activation \Rightarrow Ca influx



1-6 min – ischemic injury

>6 min – cell death

Duration of ischemia \Rightarrow infarct maturation

- Animal models & human studies (MRI, PET) of acute ischemia shows:

< 2 hrs

reversible neuronal deficit


> 6 hrs

irreversible neuronal deficit



Clinical studies & current therapies aim for **reperfusion**
within 2 to 6 hrs (*therapeutic window*)

Stages of infarct maturation

- 
- Immediate – 6 hours; no change (both macro & micro)
 - Acute stage – 2 days; edema, loss of grey/white matter border, inflammation, red neurons, neutrophils
 - Intermediate stage – 2 weeks; demarcation, soft friable tissue, cysts; macrophages, liquifactive necrosis
 - Late) stage – after 4 weeks; fluid filled cysts with dark grey margin (gliosis), removal of tissue by macrophages
 - Gliosis – proliferation of glia, loss of architecture

Stroke

An upcoming lecture dedicated to the topic!

