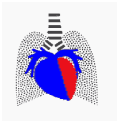
Fetal physiology

vaclav.hampl@lf2.cuni.cz

http://fyziologie.lf2.cuni.cz
http://vh.cuni.cz

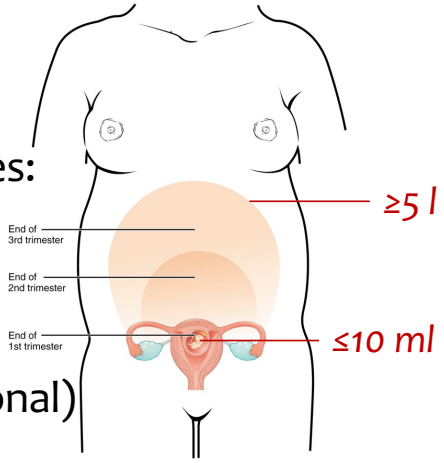
CHARLES UNIVERSITY
Second Faculty of Medicine



1

Pregnancy duration

- From ovulation:
  - 266 days = 38 weeks
- From the 1st day of last menses:
  - 280 days = 40 weeks
  - 10 lunar months
  - 9 calendar months
- Fetus from 9th week (gestational)
  - wk 25-28: lung developed to sustain extrauterine life



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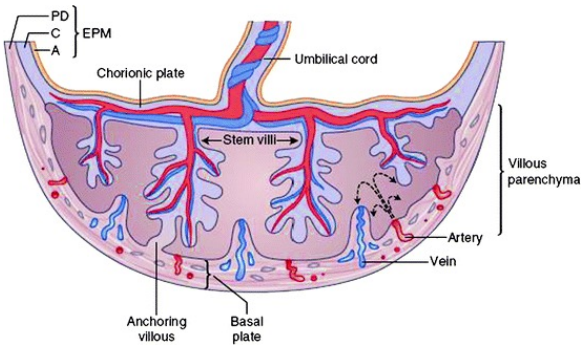
Placenta



- hemochorial
- function of:
  - lung
  - GIT
  - liver
  - kidneys
  - skin (thermoregulation)
- endocrine organ (hCG, hCS, progesterone, estrogens,...)
- high metabolism (~ brain)

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Histotrophic nutrition

- till 8-9 wk
- intervillous space filled by secretion from endometrial glands (& filtrate of maternal serum)
- trophoblast plugs in spiral arteries
- PO_2 ~ 20 mmHg (helps angiogenesis? – VEGF, HIF)
- by 10-12 wk completely replaced by maternal blood (after antioxidant defense have matured)

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Fetoplacental circulation

- similar role to pulmonary circulation
  - O_2 into blood, CO_2 out
- many similarities with lung circulation
  - low pressure, high flow – low vascular resistance
  - thin vascular wall
  - small (or no) role for nerves ...
- umbilical blood flow ~ 0.5 l/min
  - 17-25% for placenta & membranes nutrition

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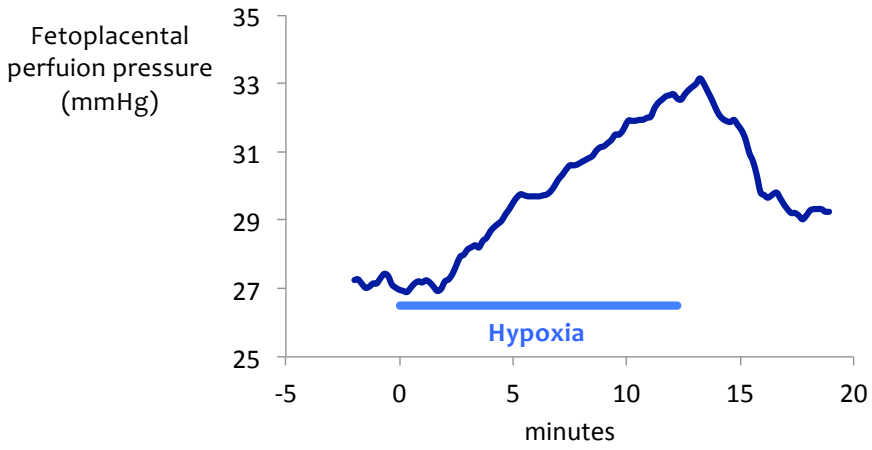
Hypoxic fetoplacental vasoconstriction



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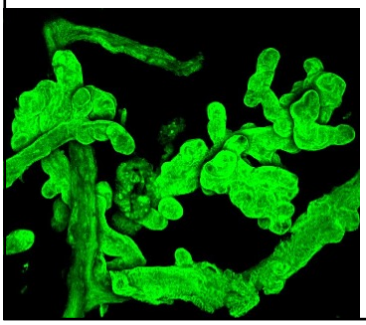
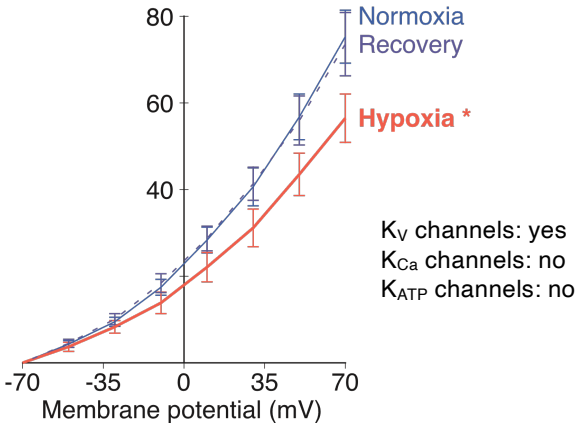
Hypoxia inhibits K channels in fetoplacental VSM cells





K_V channels: yes
K_{Ca} channels: no
K_{ATP} channels: no

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Hampl et al, *AJP* 2002

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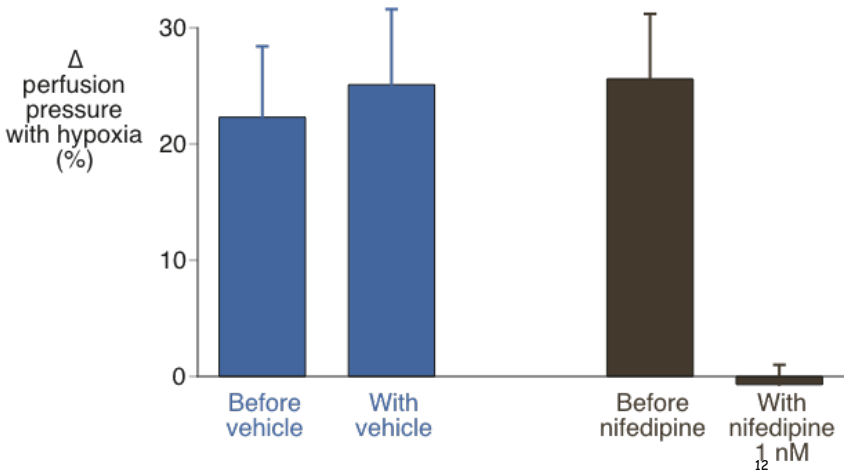
Voltage-gated Ca channels are essential in HFPV



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Jakoubek et al, *Placenta* 2006

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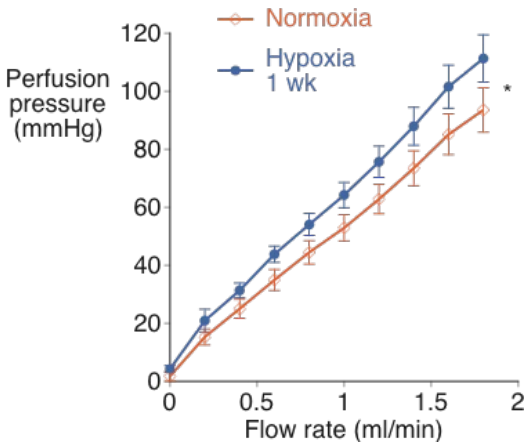
Chronic hypoxia increases vascular resistance in placenta



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Jakoubek et al, *AJP* 2008

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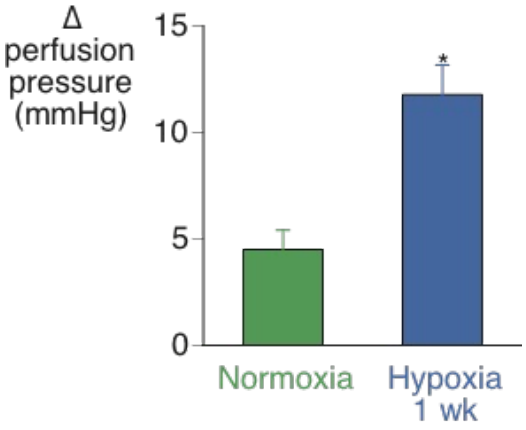
Chronic hypoxia potentiates reactivity to acute hypoxia



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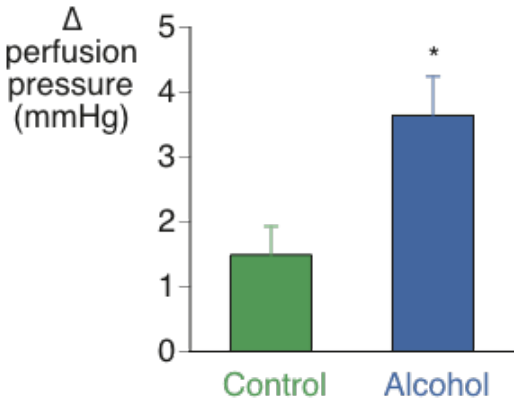
Chronic maternal alcohol intake: ↑ reactivity to angiotensin II



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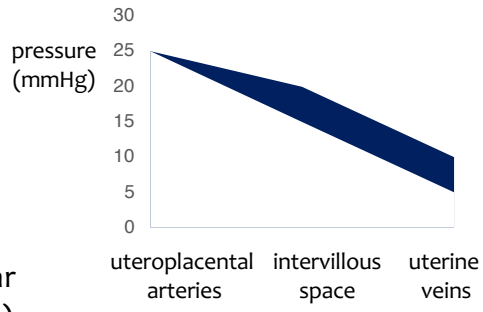
Maternal blood flow in placenta

- placenta contains ~150 ml of maternal blood
- uterine arteries flow = 10-20 % CO
  - 20-27% to myometrium & cervix
- low pressure system
  - invading trophoblast: spiral ⟶ uteroplacental arteries
  - maternal SBP not transmitted to intervillous space (no extravascular compression of fetoplacental vessels)
  - small A-V pressure gradient
  - ↓ NE receptors ⟶ ↓ SNS responsiveness (instead placental PGI_2)



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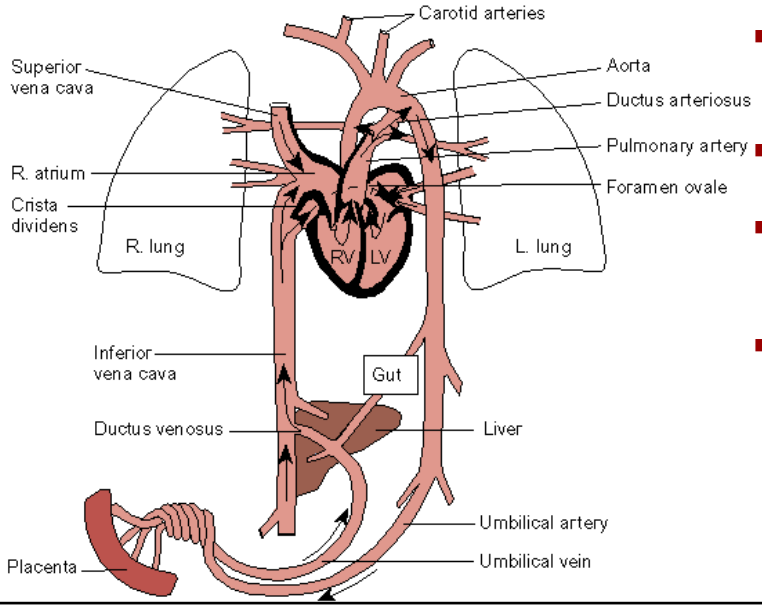
Fetal circulation



- ~50% placental flow returns via ductus venosus
- remainder through liver
- separate streams in IVC (crista dividens)
- stream from d.v. → foramen ovale → LV → carotids

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High fetal pulmonary vascular resistance

- low O_2 → hypoxic vasoconstriction
- no ventilation → un-distended, convoluted vessels
- shunts ~90% of CO through ductus arteriosus (enters aorta distal to origin of carotid arteries)

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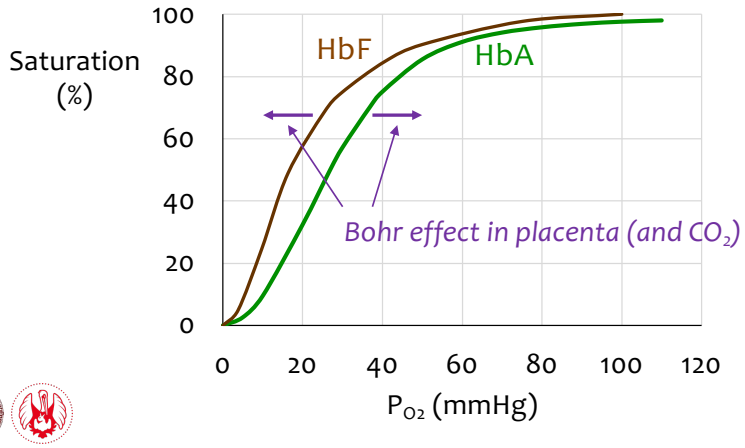
Fetal Hb (Hb F: $\alpha_2\gamma_2$)

- BPG binding: γ<α< β
- γ has less + charges that attract the - charges on BPG
- ↑ BPG formation in placenta



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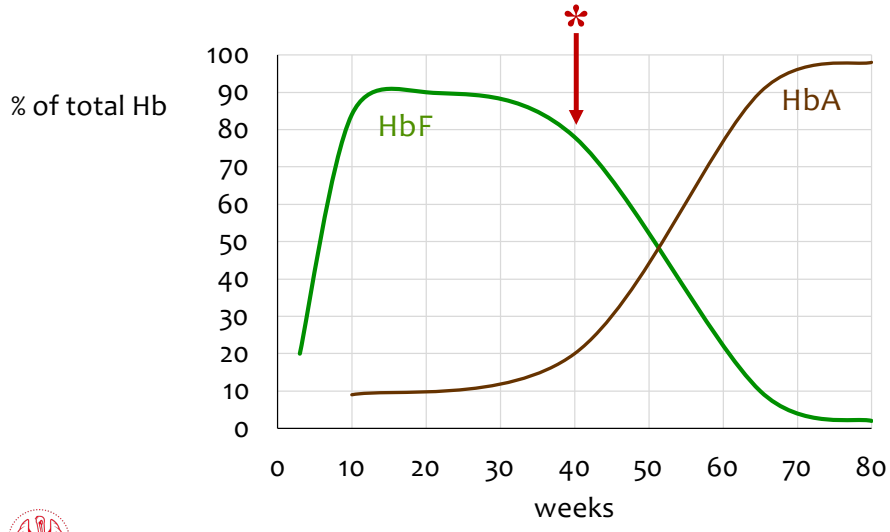
Fetal Hb



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Rh incompability

- mother Rh^-, father Rh^+
- 2nd and subsequent Rh^+ child after the 1st Rh^+

- what to do?

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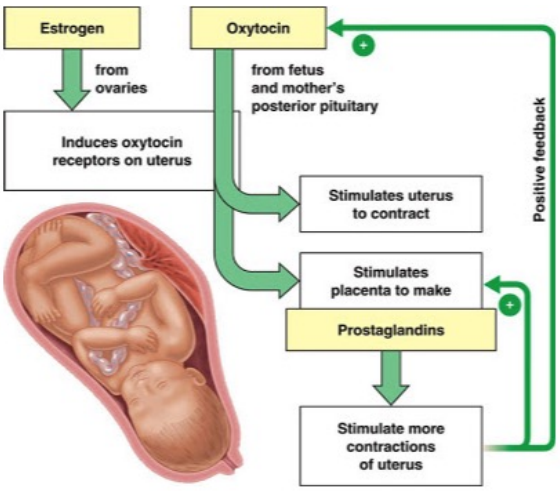
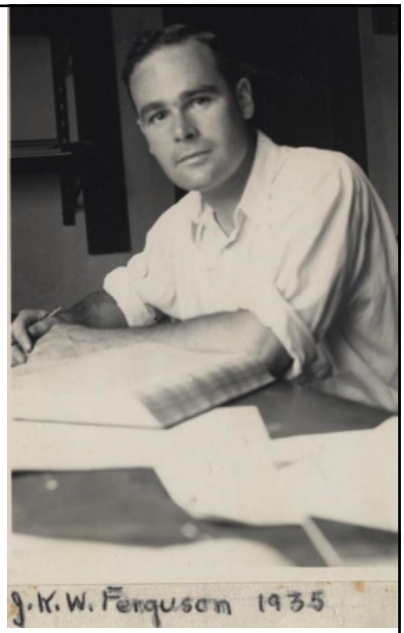
Ferguson reflex





Ferguson, J.K.W.:
A study of the motility of the intact uterus at term. *Surg Gynecol Obstet*. 73: 359-66, 1941

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"Placental transfusion"

- umbilical arteries constriction:
  - starts 5 sec after birth
  - complete by 45 sec
- umbilical vein constriction
  - starts 15 sec after birth
  - complete by 3-4 min

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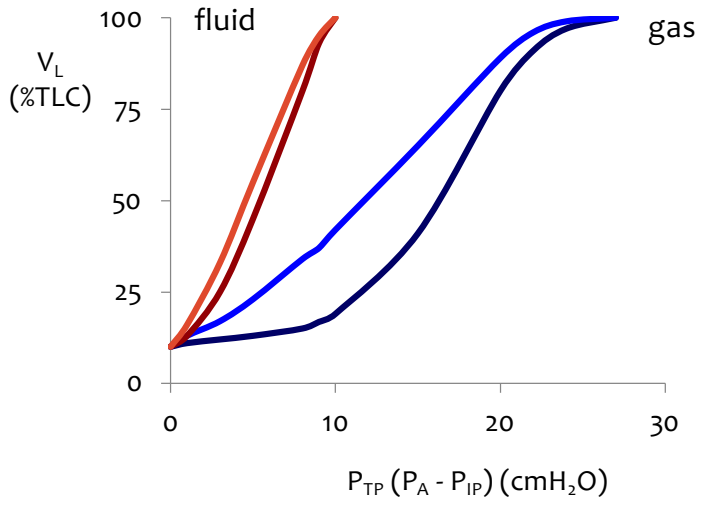
Static compliance & surface tension



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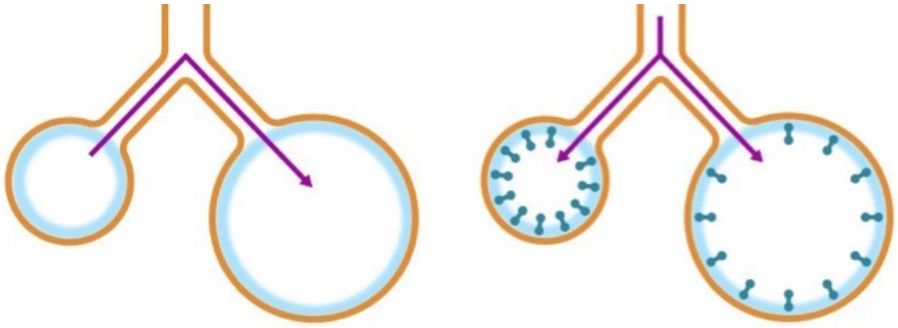
Surfactant prevents alveolar collapse

$$P = 2T/r \rightarrow T_1/r_1 = T_2/r_2$$

no surfactant

with surfactant



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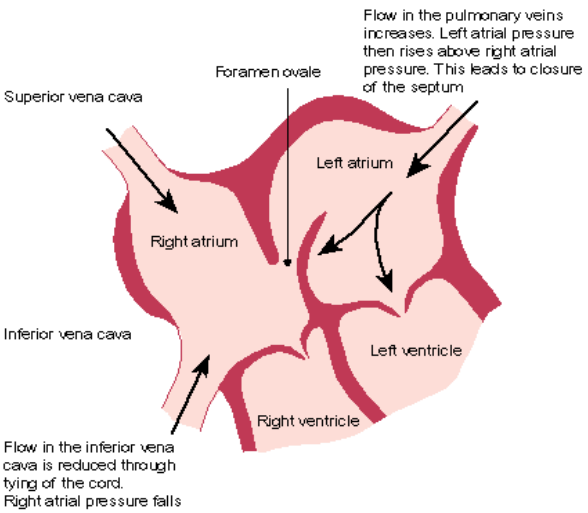
Birth

- Umbilical vessels constrict (if not tied)
- Ductus venosus closes (mech. ??)
- ↑ CO_2 → breathing
- ↑ arterial pO_2 constricts ductus arteriosus (via ↓ vasodil. PGs, Bk; also K channels)



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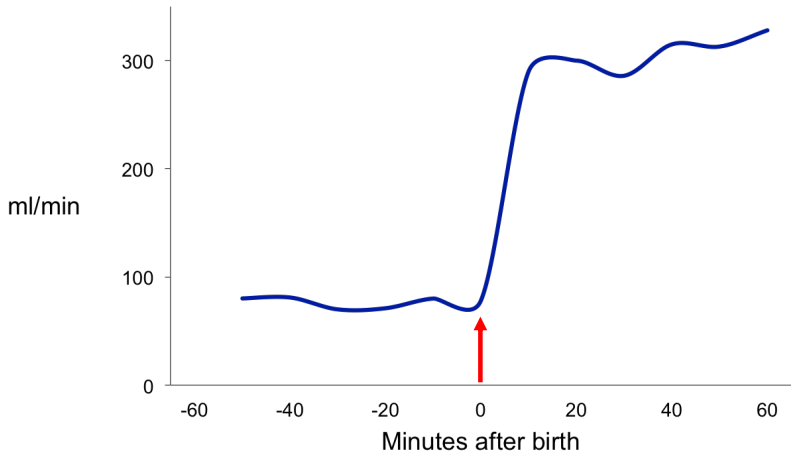
Lung blood flow at birth



NOTHING LIKE THIS EVER AGAIN

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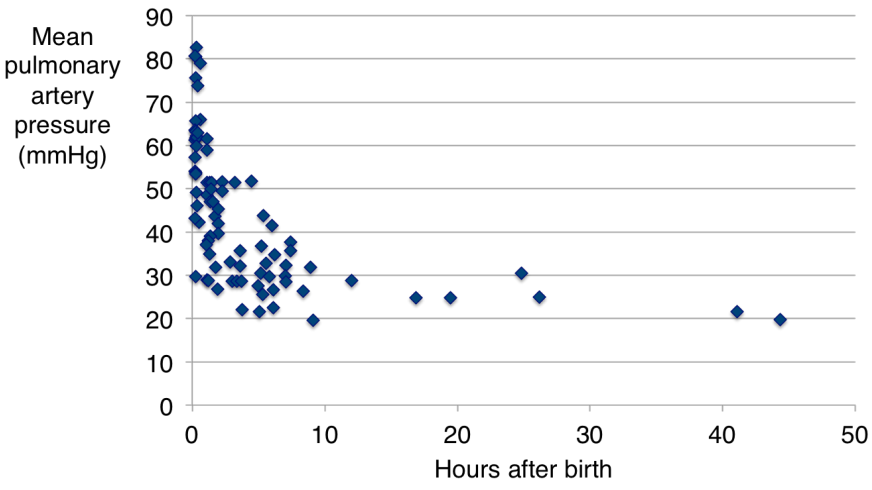
Pulmonary vasodilation at birth



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Placenta delivery

rapid ↓ uterus volume
⟶ ↓ placenta contact surface (to Ø ~10 cm)
⟶ placenta compression & shearing

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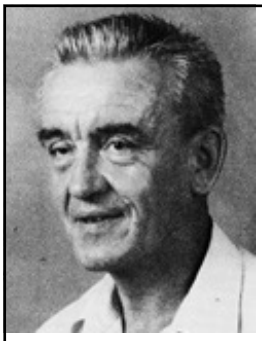
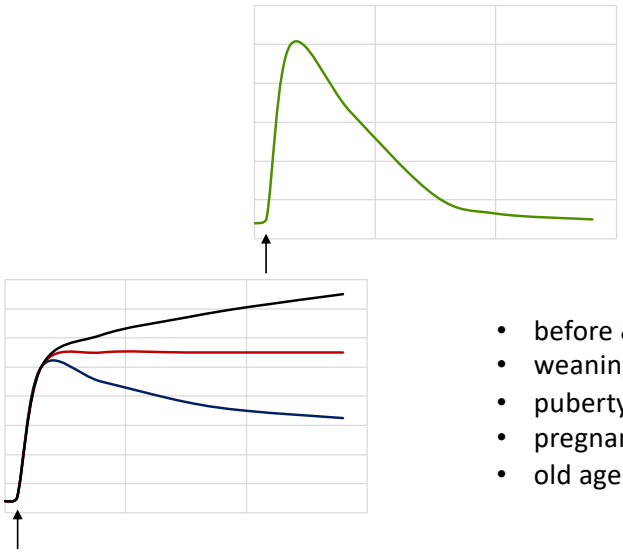


prof. Jiří Křeček
(1923 - 2014)

Critical periods of development



- before & after birth
- weaning
- puberty
- pregnancy
- old age

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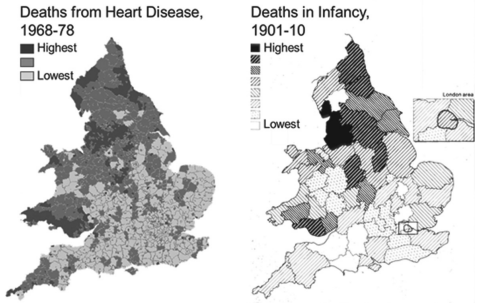
"Barker hypothesis"

- Fetal origin of adult diseases (fetal programming)
- David James Purslove Barker (1938-2013)
  Lancet 1986
  - correlation of neonatal mortality 1910s-1920s and cardiovascular mortality 60-70 years later
  - maternal nutrition in pregnancy affects child's cardiovascular risk in adulthood



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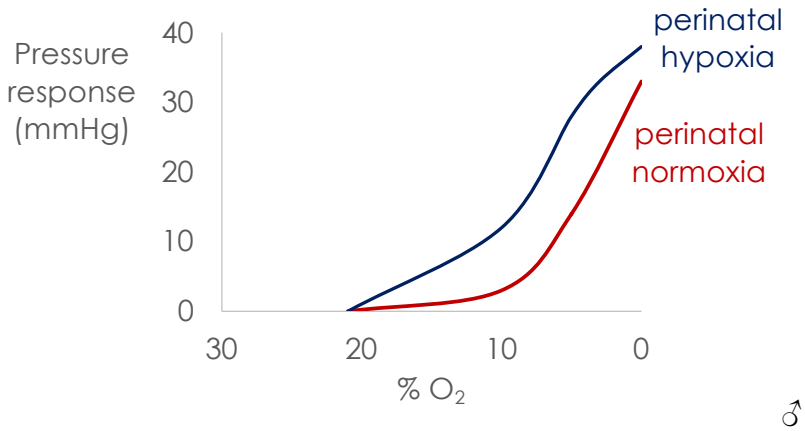
Perinatal hypoxia: ↑ response to acute hypoxia during recovery from hypoxia in adulthood



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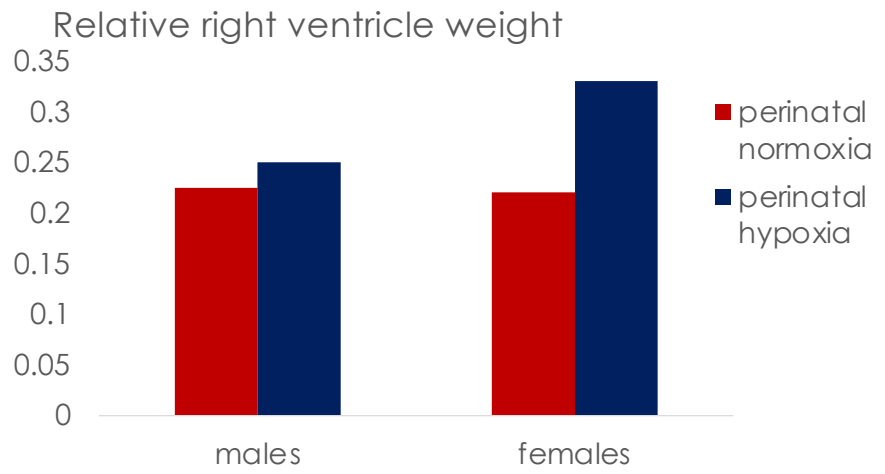
Sex differences in long-term effects of perinatal hypoxia



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Long-term effect of indomethacin before delivery on lung vessels

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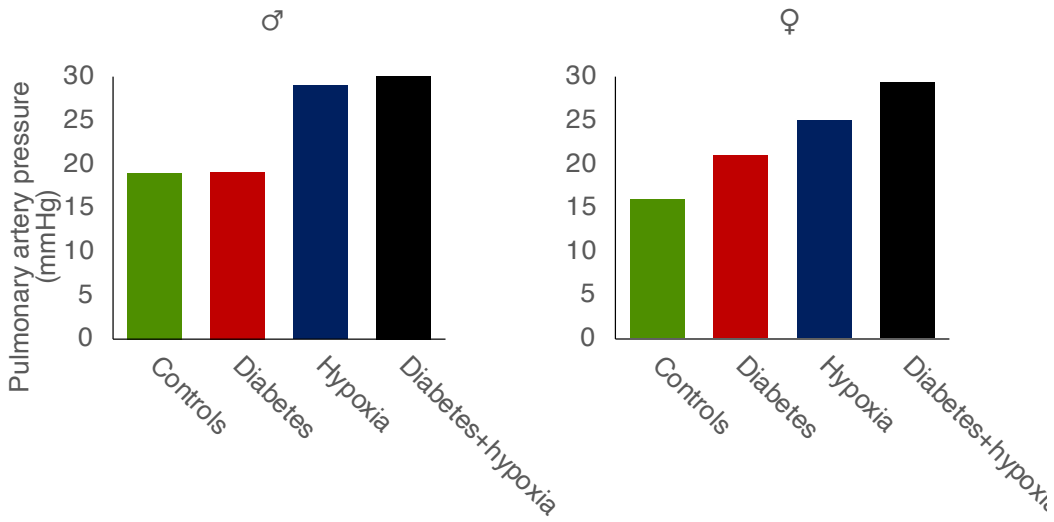
Maternal diabetes exacerbates hypoxic pulmonary hypertension in daughters



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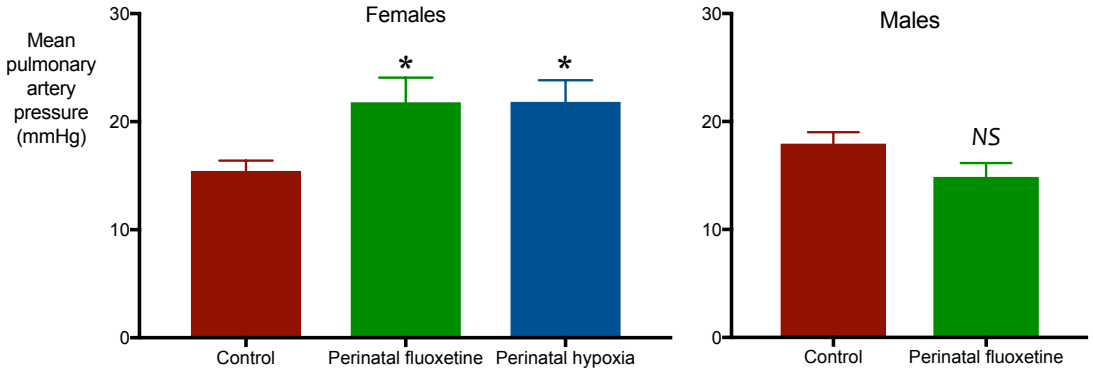
Perinatal fluoxetine induces pulmonary hypertension in adult daughters



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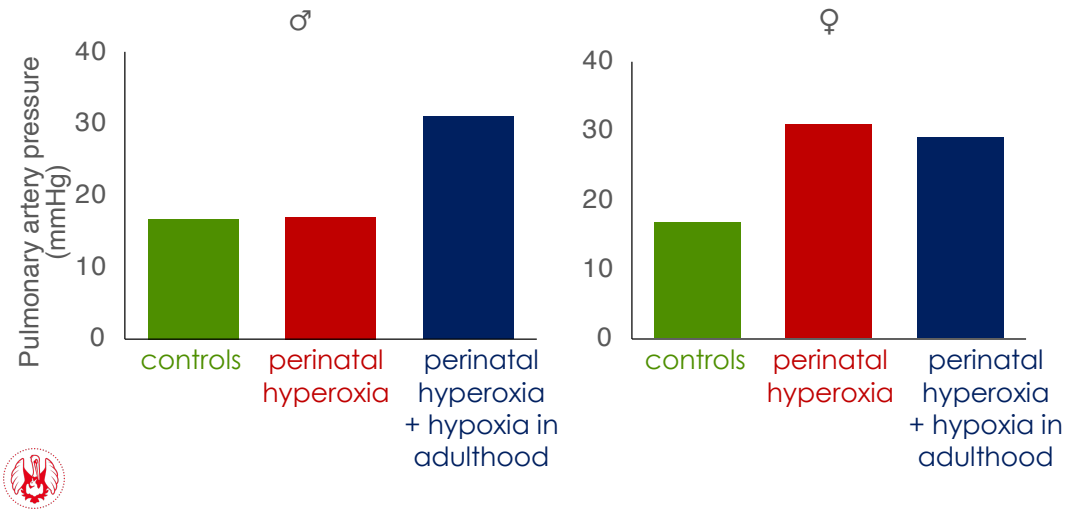
Perinatal hyperoxia: pulmonary hypertension in daughters



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