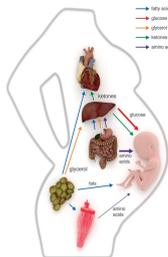


Physiology of fetal oxygenation during labor

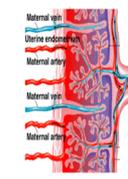
Branka M. Yli
Oslo University Hospital
Norway



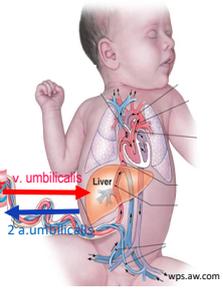
The O₂ supply is dependent on



Maternal respiration
Maternal circulation

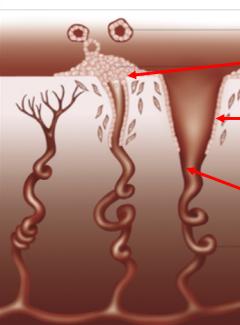


Placental perfusion
and gas exchange across
the placenta



Umbilical and
fetal circulations

It exists about 150 spiralarteries in the normal uterus



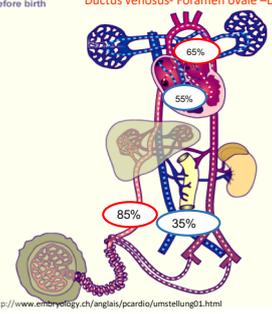
Conversion of the spiral arteries into the placenta bed

- Trophoblasts invasion of the placenta bed (decidua and internal myometrium) leads to the transformation of the spiral arteries into dilated in-elastic channels without smooth muscle media and where the endothelium is partially replaced by trophoblast results in the removal of mother's autonomous control
- Blood flow in the utero-placental vessels may normally increase up to 10%, unaffected by maternal vascular control

Fetal Circulation

shunt based: the most the O₂-rich blood to the heart and brain

Ductus venosus- Foramen ovale—Ductus arteriosus




The overarching mission of the cardiovascular system is to deliver sufficient oxygen to key organs

Acid-bases values in the healthy term fetus before birth, neonates after birth, along with the adult values for comparison

	Fetus Umbilical vein ¹	Umbilical cord artery	Umbilical cord vein	Adults ⁴
pH	> 7.38	7.27 (7.09- 7.38) ²	7.35 (7.21-7.46) ²	7.36-7.44
pCO ₂ (kPa)	< 5.6	7.1 (5.1-10.0) ²	5.2 (3.7-7.1) ²	4.7-5.9
BDecf (mmol/l)	< 3	2.2 (-1.8- 8.1) ²	3.5 (-0.4-8.7) ²	- 3.0-3.0
pO ₂ (kPa)	> 2.93	2.1 (0.7- 4.1) ³	3.5 (1.7- 4.9) ³	10-14 kPa

¹ Results obtained by cordocentesis, from Huch A, Huch R, Booth G. Guidelines for blood sampling and measurement of pH and blood gas values in obstetrics. Based upon a workshop held in Zurich, Switzerland, March 19, 1993 by an Ad Hoc Committee. Eur J Obstet Gynecol Reprod Biol 1994; 54: 169-76.

² Median (IQR, 95% percentile), 11881 term infants, spontaneous vaginal deliveries, no epidural analgesia, no induction, 5 minute Apgar score >7. Kro-GSB et al. BJOG 2010

³ Data from 1145 term neonates with 5 minute Apgar score >7 after spontaneous vaginal deliveries from Arlikan GM, Scholz HS, Petru E, Haeussler MC, Haas J, Welts PA. Cord blood oxygen saturation in vigorous infants at birth: what is normal? BJOG 2000; 107: 987-94.

⁴ 95% reference interval from *Dep. for medical biochemistry at OsloUniversity Hospital, www.kjellerer.no

Yli BM, Kjellmer I. Pathophysiology of foetal oxygenation and cell damage during labour. Best Practice & Research Clinical Obstetrics and Gynaecology 2015.

Fetus is living on the top of Mount Everest!

The fetus lives in low O₂ environment

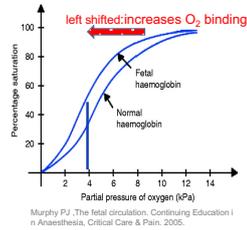
Does the fetus spends months with inadequate oxygenation?



Sir Joseph Barcroft 1946

The mechanisms that facilitate oxygenation of the fetus

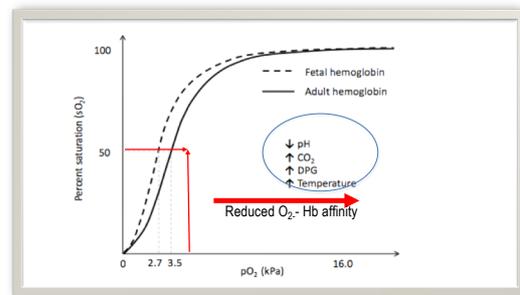
- The fetal hemoglobin (HbF) versus adult hemoglobin (HbA) has a greater affinity for O₂ at the same pO₂, which drives the oxygen-dissociation curve left
- Increased concentration of HbF compared with adults increases the oxygen-carrying capacity.
- High fetal heart rate, high basal blood flow
- Unique vascular shunts
- Cardiac output is approximately four times higher in the fetus than in the adult and secures higher perfusion rates of both central and peripheral organs



Yli BM, Kjellmer I. Pathophysiology of foetal oxygenation and cell damage during labour. Best Practice & Research Clinical Obstetrics and Gynaecology 2016.

Pyrexia

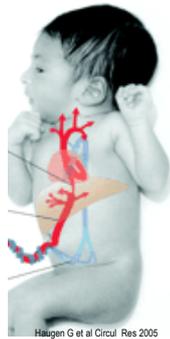
Might aggravate fetal hypoxia because of:
 ↑ tissue O₂ consumption
 shift of the O₂-Hb dissociation curve to the right



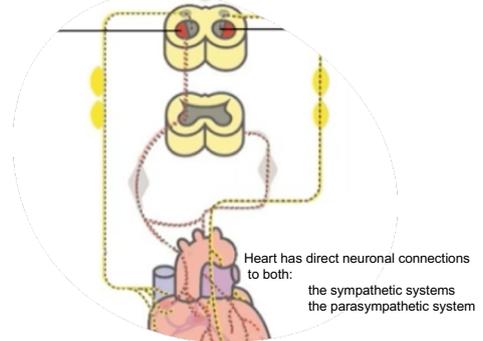
less available O₂ to the fetus due to right shift of ODC!

Development of O₂ deficiency

- Hypoxemia:** reduced O₂ in blood
- Hypoxia:** reduced O₂ supply to a tissue
- Asphyxia** where the hypoxia extends to the **central organs** the heart, brain and adrenal glands and potentially leads to progressive hypoxemia and metabolic acidosis

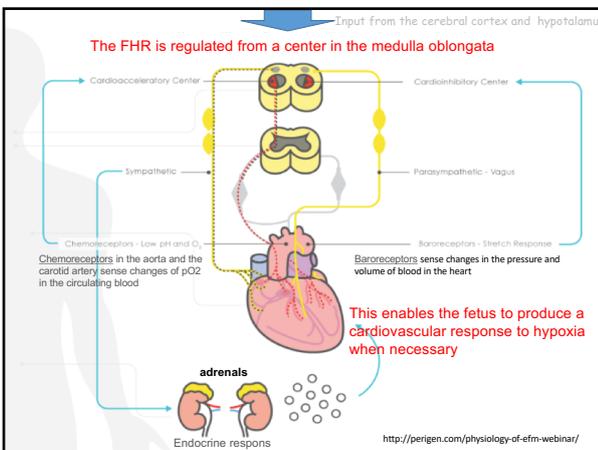


The FHR is regulated from a center in the medulla oblongata



<http://perigen.com/physiology-of-efm-webinar/>

The FHR is regulated from a center in the medulla oblongata

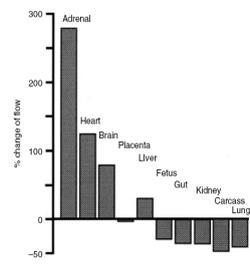


The hemodynamic response of the fetus to hypoxia in labor (intermittent)

Chemoreflex (aorta and carotid bodies)

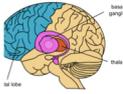
- Parasympathetic**
 FHR ↓ decelerations
- Sympathetic**

- Peripheral vasoconstriction: redistribute cardiac output to central organs
- Endocrine response: adrenals catecholamines



Effects relatively slow reflecting their half-life of 2 to 3 minutes
 alpha-receptors regulate the degree of constriction of the peripheral vessels; FHR ↑ heart contractility stroke volume
 beta-receptors: metabolic reactions such as glycolysis

Jensen A et al J Dev Physiol 1991;15:309-323
 Lear CA. 2016. J Physiol 2016; 594:1265-1277



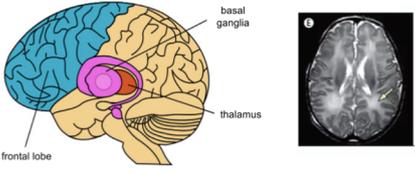
The brainstem-sparing model

Simultaneously, a redistribution of the blood flow within the brain takes place. The blood flow flows from the cerebral cortex to the deeper central nuclei basal ganglia and thalamus.

Blood supply reflex: Blood is redistributed in superficial hemispheres deeper central nuclei (the ganglia and thalamus).

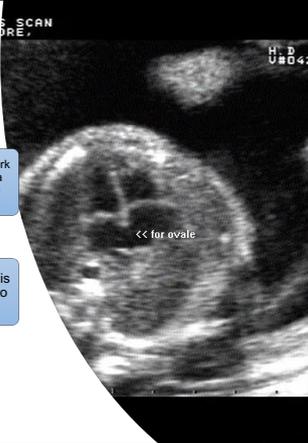
Behrman RE, et al. Distribution of the circulation in the normal and asphyxiated fetal primate. Am J Obstet Gynecol 1970;108(6):956-69.
Richardson BS. Fetal adaptive responses to asphyxia. Clin Perinatol 1988;16(3):595-611.

This brainstem-sparing model protects the respiratory and vasomotor centers in medulla oblongata.

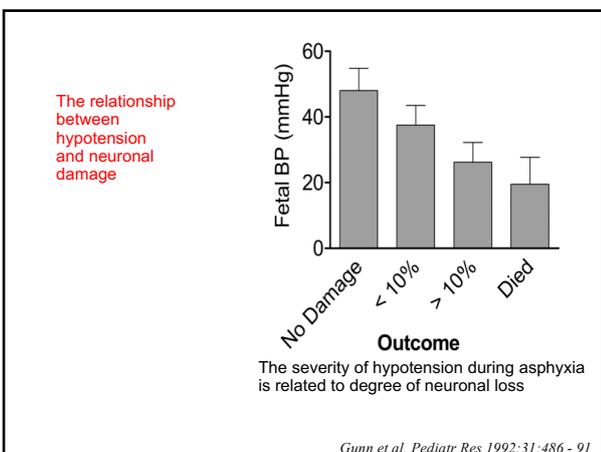
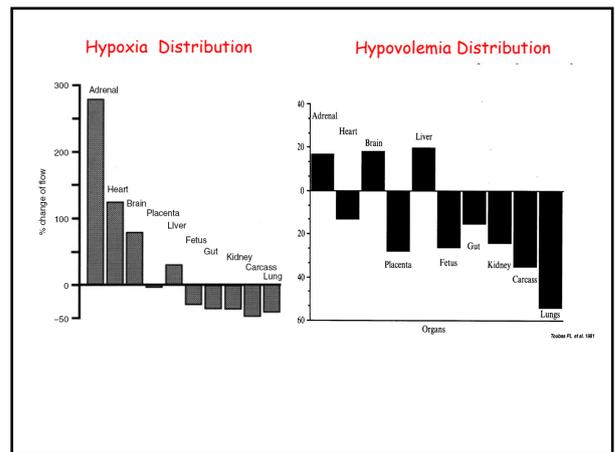


Watershed injury: Extensive white matter involvement predicts cognitive deficits, microcephaly.

Can the heart spare?

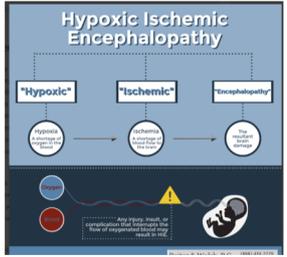


The heart can not reduce its O₂ requirements during hypoxia. It is forced to work harder due to a catecholamine surge. Results of severe myocardial hypoxia are bradycardia, hypotension. Thus, the fetal heart is often the last organ to fail during hypoxia. **cardiovascular collapse**.



Fetus has a good strategy for hypoxia

It is much more vulnerable to hypotension/hypovolemia and cerebral hyperperfusion **Ischemia**.



The severity of damage is determined by the occurrence of fetal hypoxia-induced hypotension.

Obstetrics catastrophes
acute profound hypoxia-ischemia

uterine rupture, cord prolapse, abruption of the placenta

Lack of O₂ develops rapidly
 With complete cessation of the blood flow

Little or no time for compensatory mechanisms to take effect

Risk for basal ganglia and thalamus injury



Basal ganglia and thalamus injury associated with Cerebral Palsy

What may contribute to brain damage

Fetal Asphyxia
 degree duration recurrent

no brain damage → brain damage

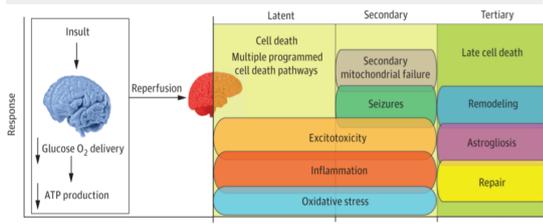
Fetal Cardiovascular Compensation
 infection

James A. Low *Obstet. Gynaecol. Res. Vol. 30, No. 4: 276-286, August 2004*

The JAMA Network

Hypoxic-Ischemic Encephalopathy: A Review for the Clinician

JAMA Pediatr. 2015;169(4):397-403. doi:10.1001/jamapediatrics.2014.3289



Latent (0-30 min): Cell death, Multiple programmed cell death pathways, Excitotoxicity, Inflammation, Oxidative stress

Secondary (6-12 h): Secondary mitochondrial failure, Seizures

Tertiary (≥3 d to Months): Late cell death, Remodeling, Astrogliosis, Repair

Reperfusion

Response: Glucose O₂ delivery, ATP production

Schematic Overview of the Pathophysiological Features of Hypoxic-Ischemic Encephalopathy: ATP indicates adenosine triphosphate; O₂, oxygen.

- At the cellular level, the neuronal injury develops in two phases:
 - an initial ischemic phase characterized by cell death within areas of poor blood perfusion,
 - and a reperfusion phase after 2-6 h with apoptotic cell death and extension of the affected areas

Am J Physiol Regul Integr Comp Physiol, 2019 Apr 24; doi: 10.1152/ajpregu.00008.2019. [Epub ahead of print]

Current Paradigms and New Perspectives on Fetal Hypoxia: Implications for Fetal Brain Development in Late Gestation.

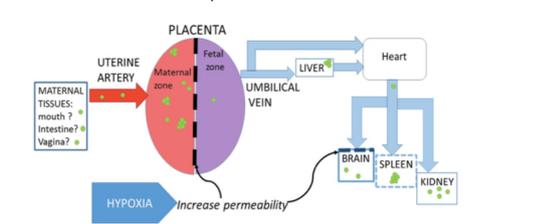
Wood CE¹, Keller-Wood M².

Recent studies demonstrate that availability of oxygen may not tell the whole story.

Transient hypoxia in the fetal sheep stimulates transcriptomics responses that mirror inflammation.

Transcriptomics is the study of the transcriptome – the complex set of RNA transcripts that are produced by the genome under specific conditions.

This response is accompanied by the appearance of bacteria in the fetal brain and other tissues, likely resulting from a hypoxia-stimulated release of bacteria from the placenta!



PLACENTA: Maternal zone, Fetal zone

UTERINE ARTERY

MATERNAL TISSUES: mouth?, Intestine?, Vagina?

HYPOXIA → Increase permeability

UMBILICAL VEIN → LIVER, Heart, BRAIN, SPLEEN, KIDNEY

Wood CE, Keller-Wood M; 2019

EDUCATION IS THE MOST POWERFUL WEAPON WE CAN USE TO CHANGE THE WORLD

- NELSON MANDELA

