Brain or Liver:

Fetal Priorities

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Haukeland University Hospital
Bergen

Tampere 2014

Peltonen

Hirvonen

Jouppila

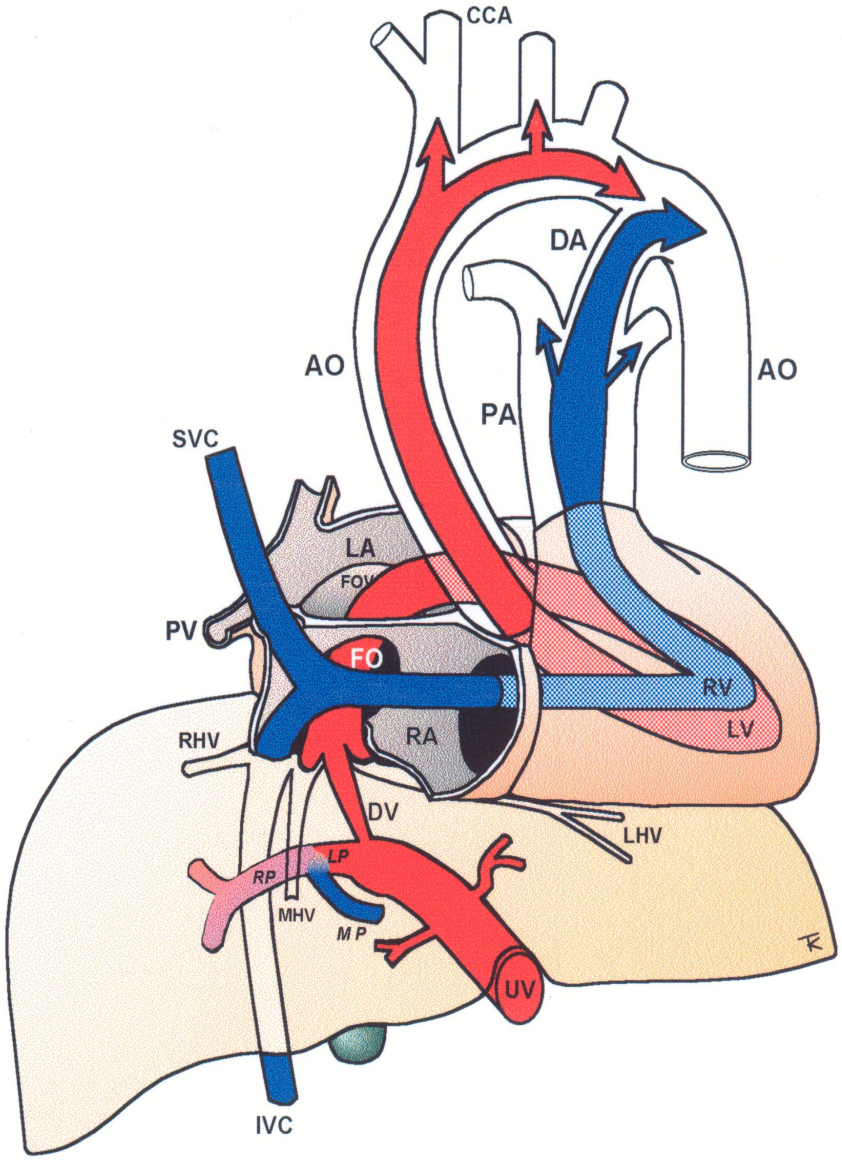
Kirkinen

Räsänen

Mäkikallio

Brain or Liver:

Fetal Priorities



Tampere 2014

Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

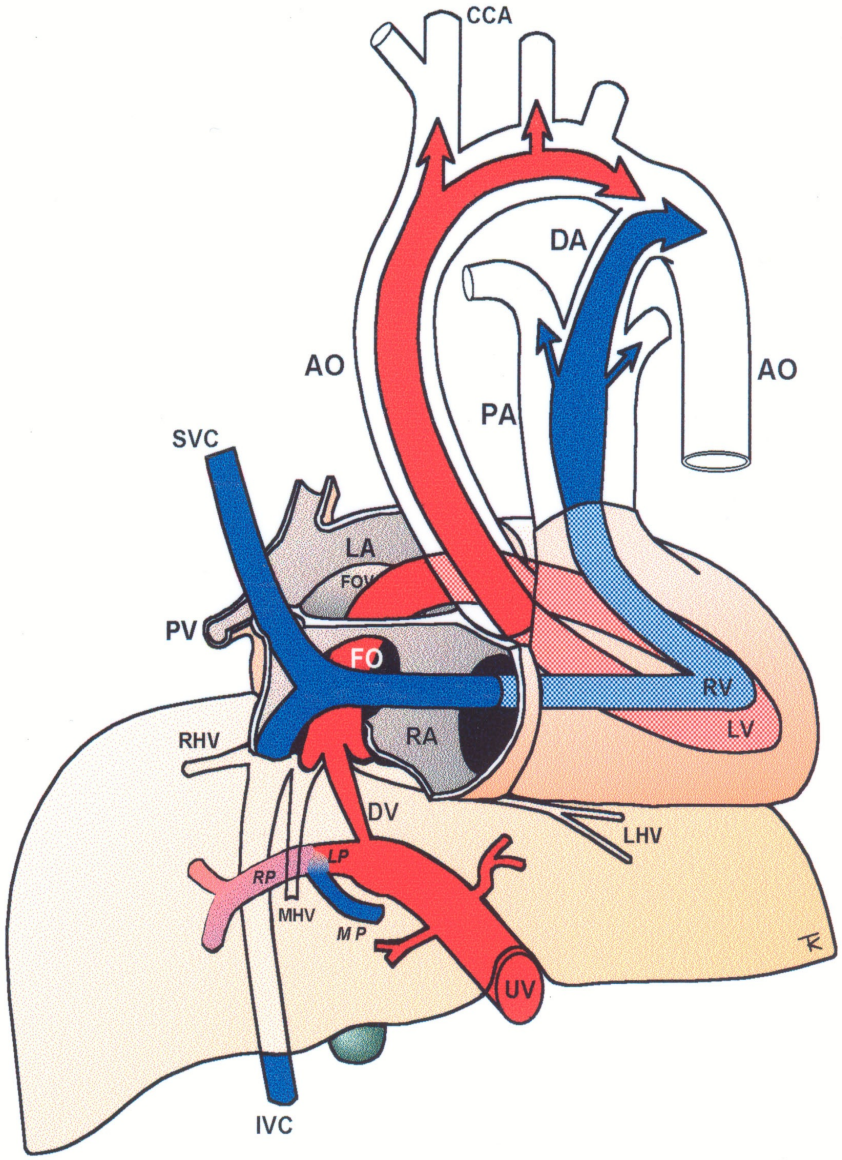
Brain or Liver:

Fetal Priorities

Via sinistra

&

Via dextra



Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Brain or Liver:

Fetal Priorities

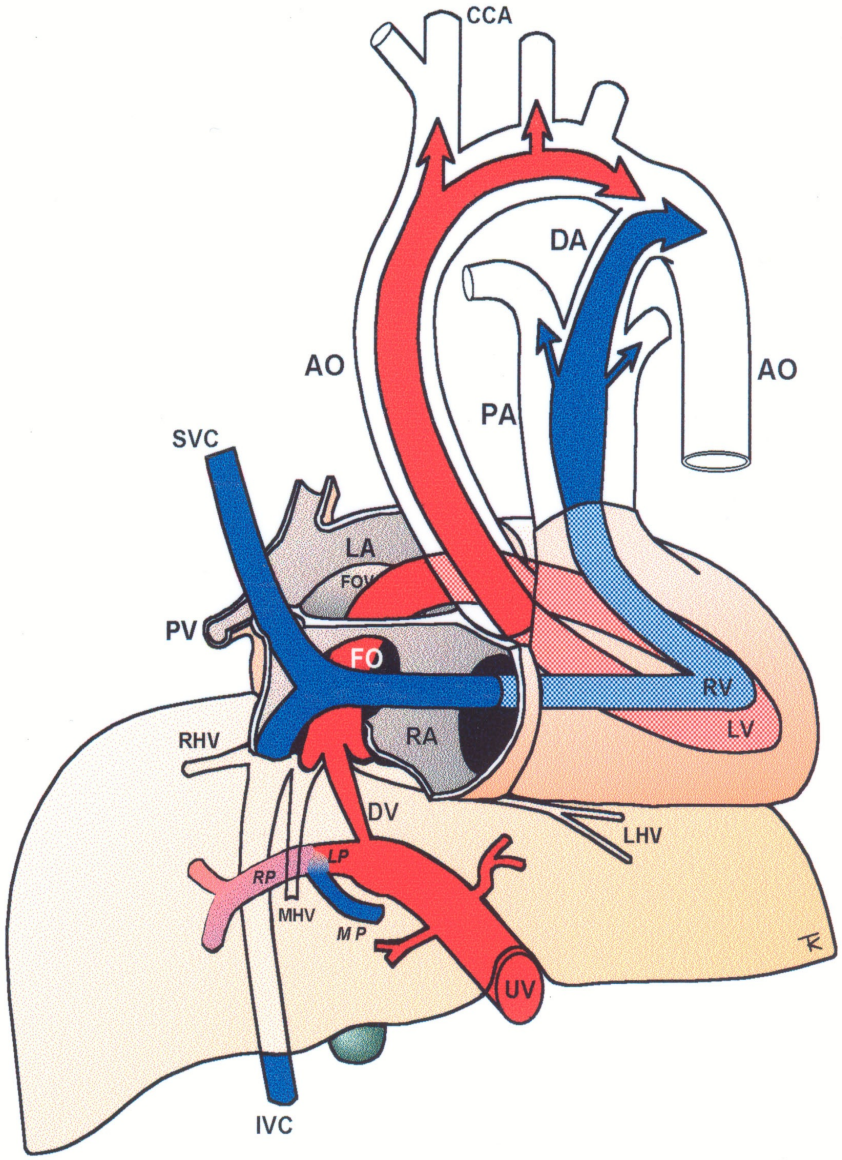
Ductus venosus shunting
(experimental results)

≈50%

Behrman & al 1970
Edelstone & al 1979-1980

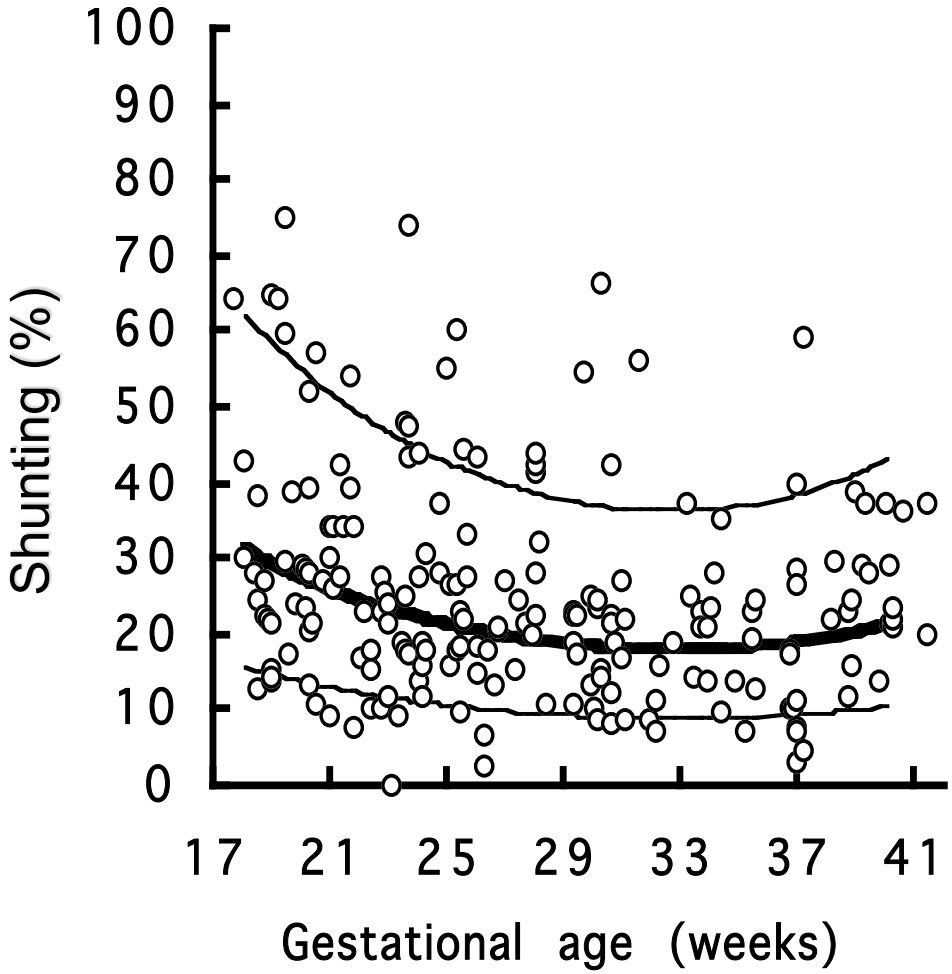
≈55% (human)

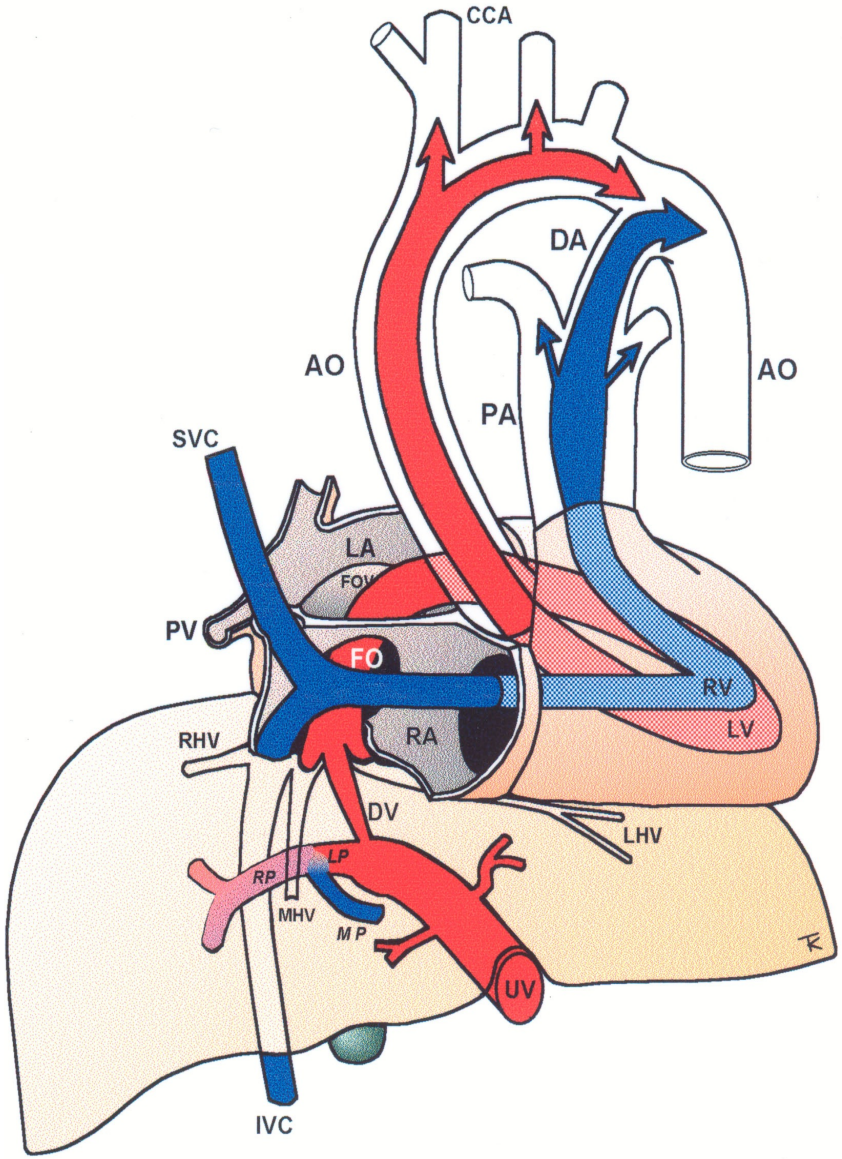
Rudolph & al 1971



Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

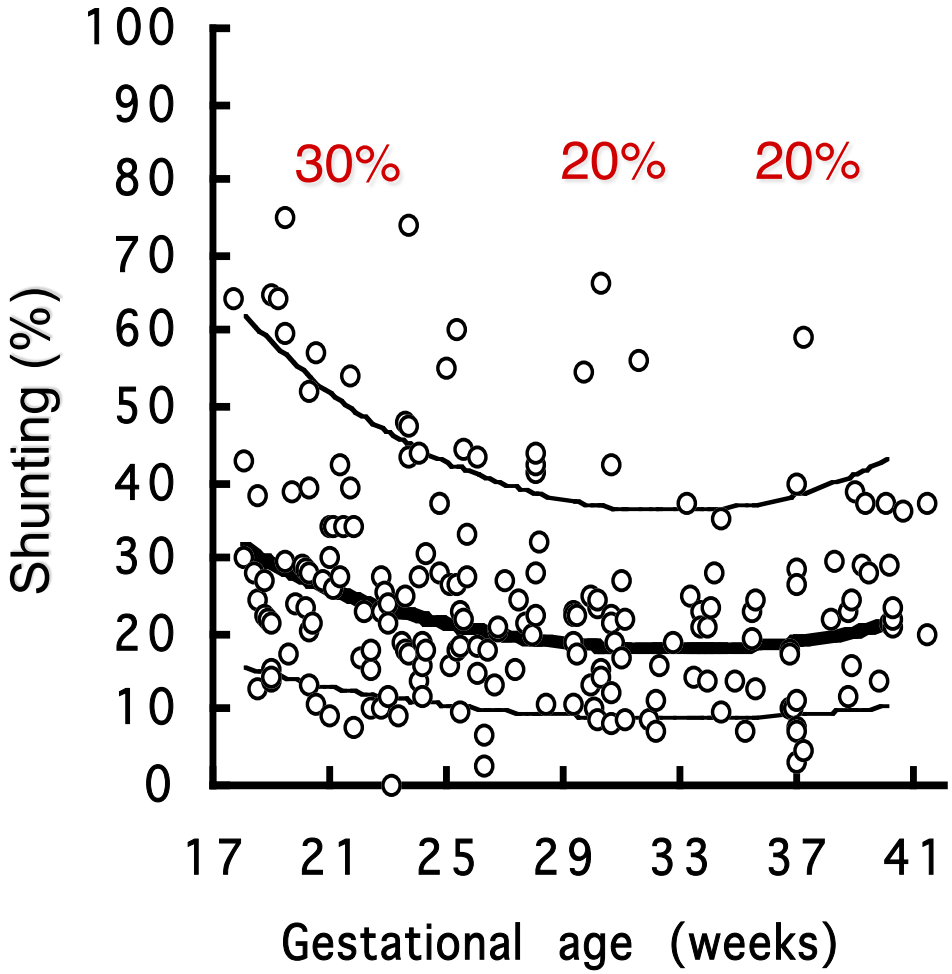
Ductus venosus shunting

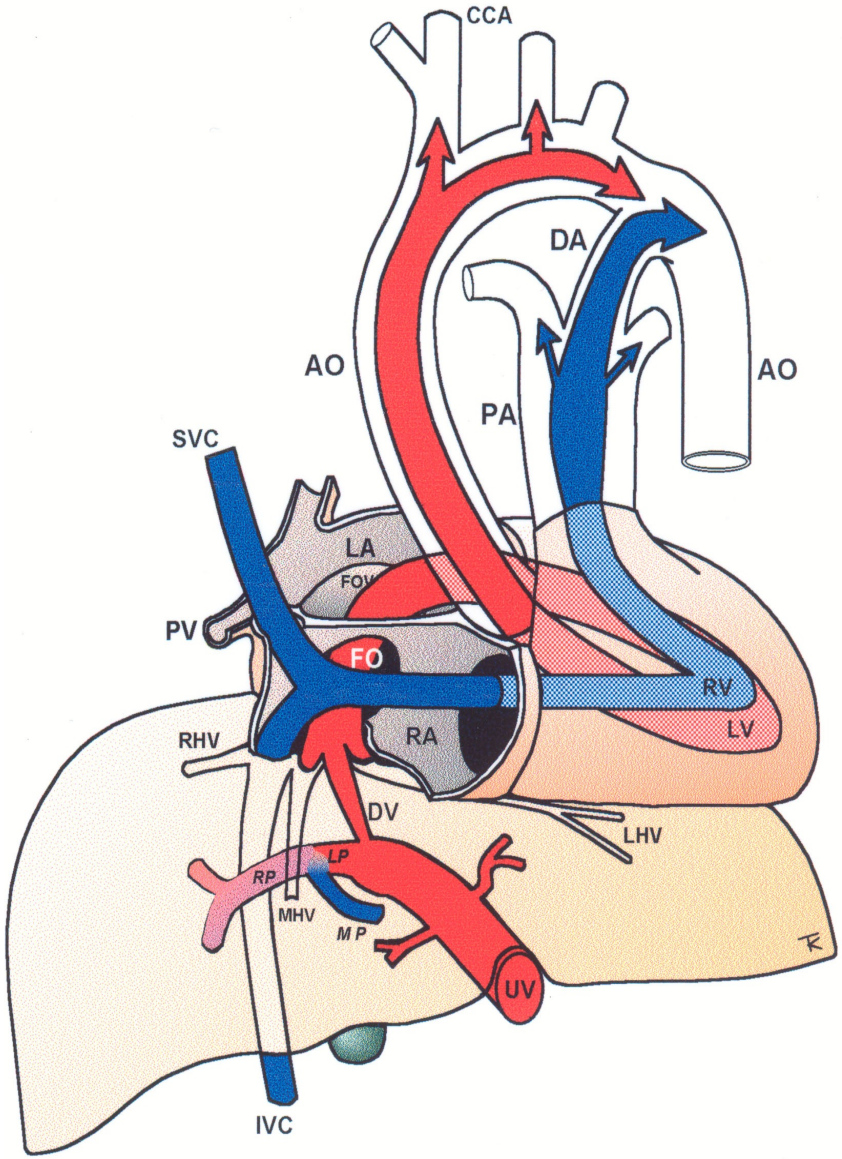




Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Ductus venosus shunting



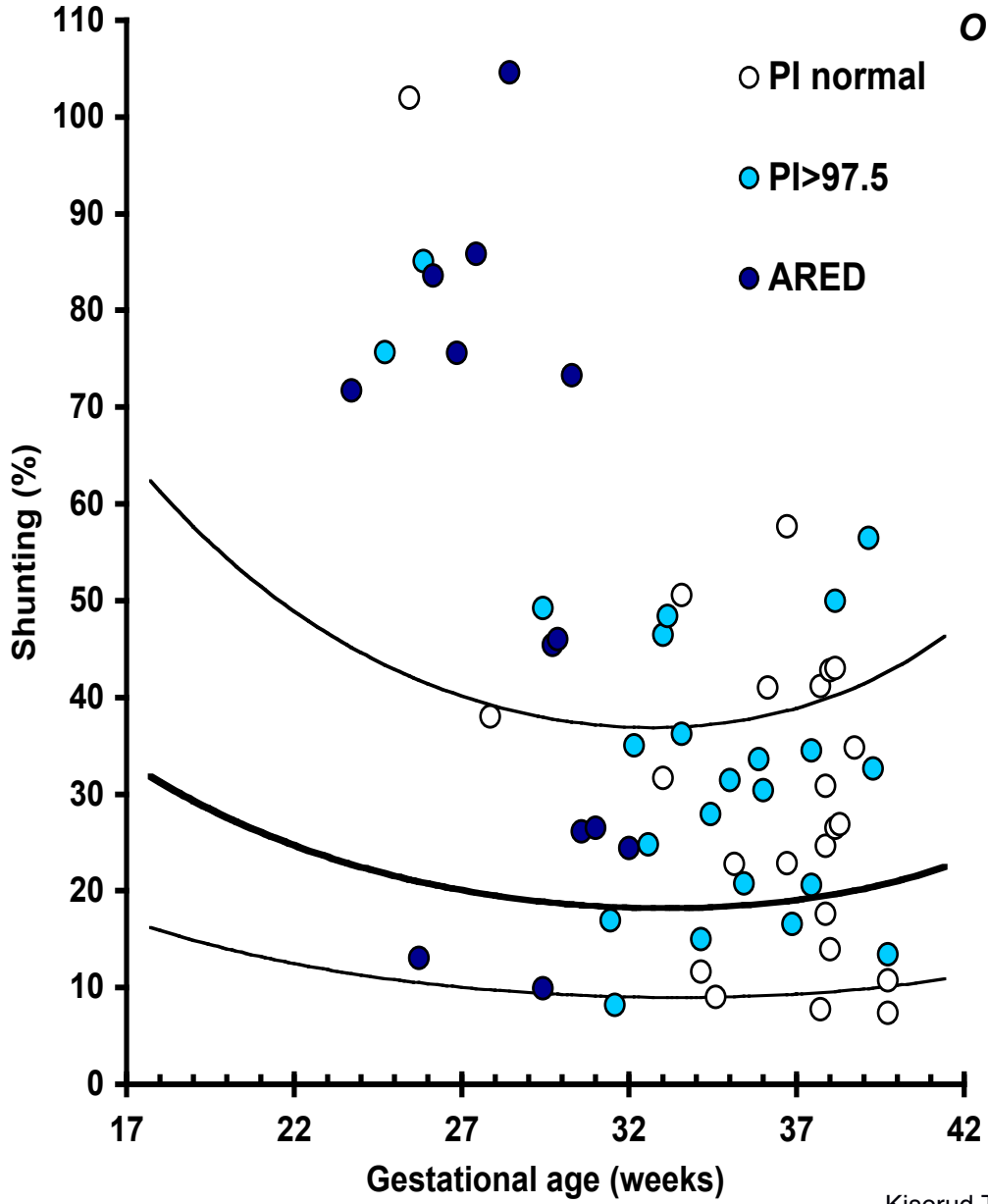


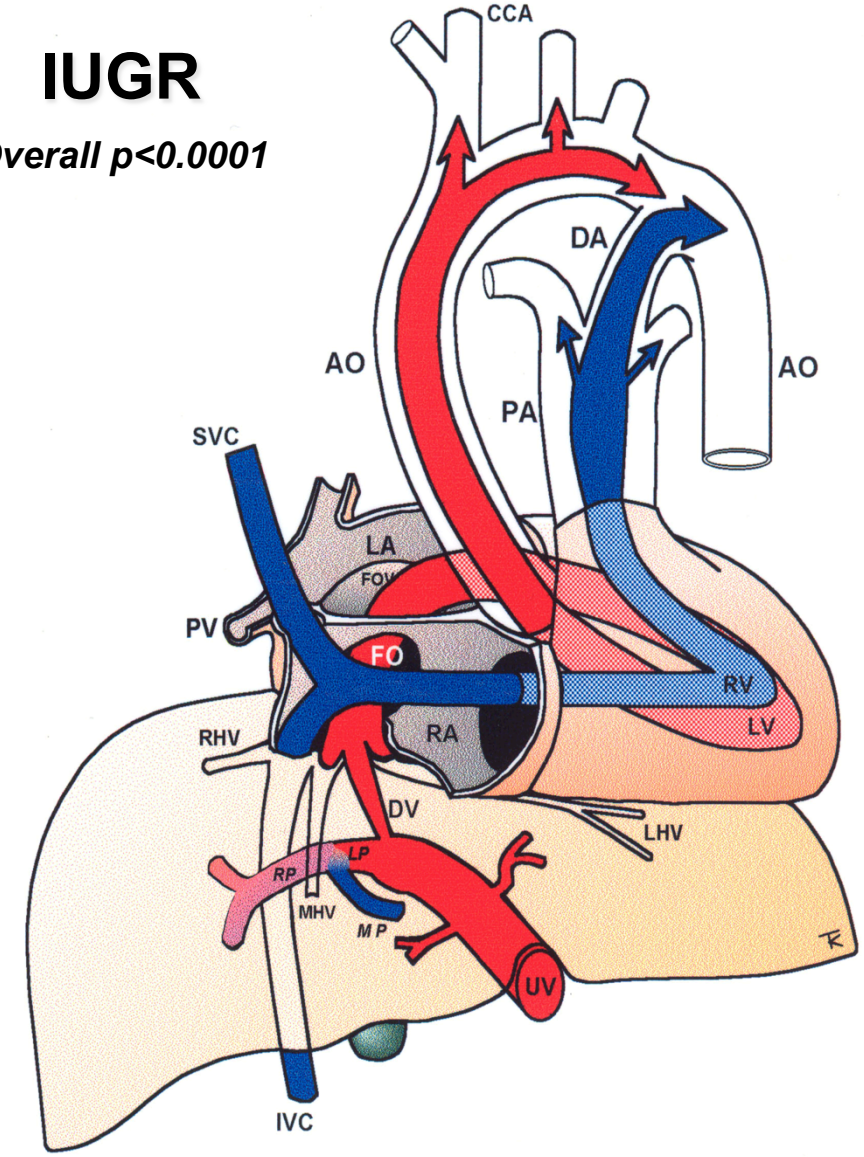
Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Ductus venosus shunting (%)

IUGR

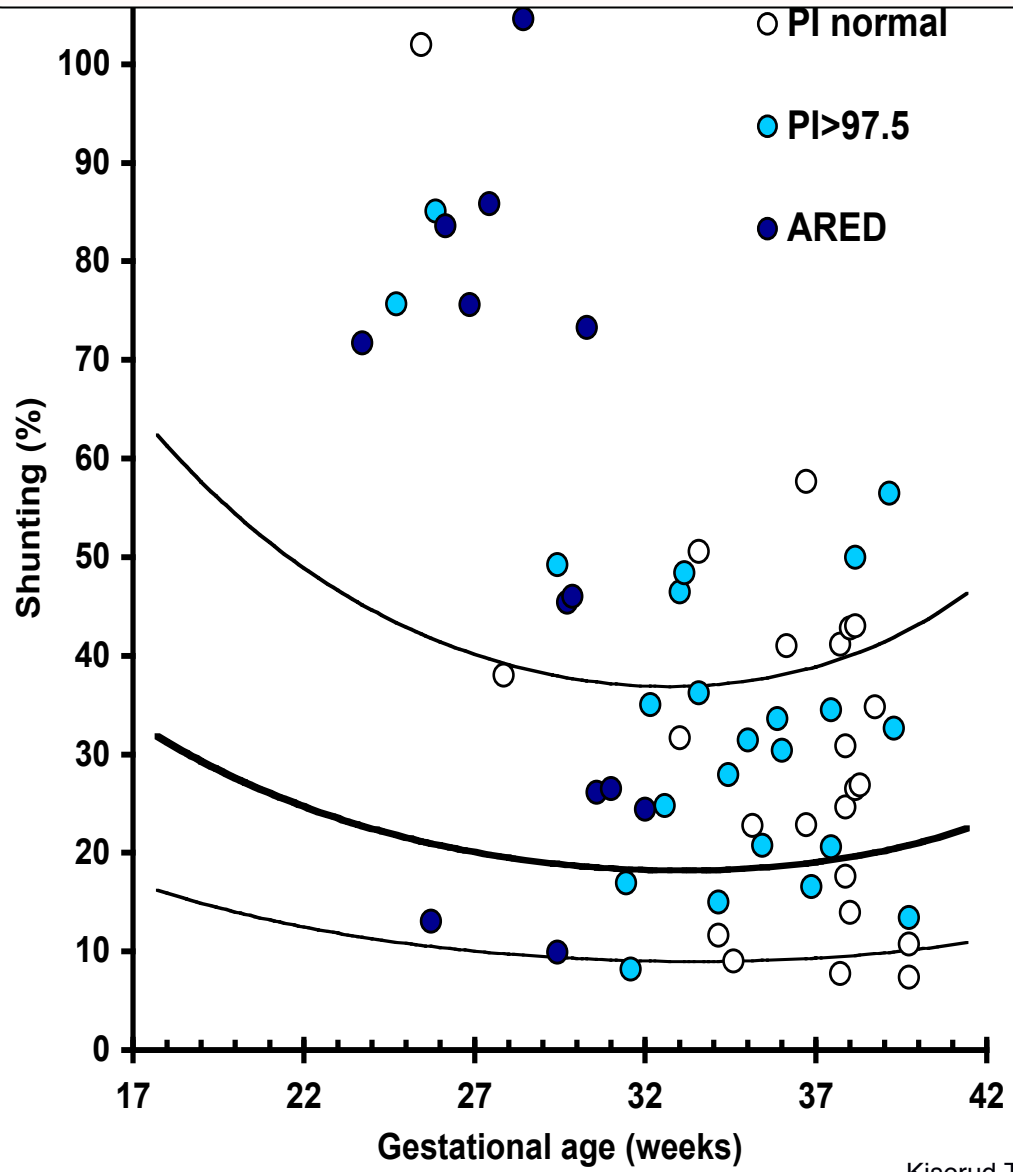
Overall p<0.0001

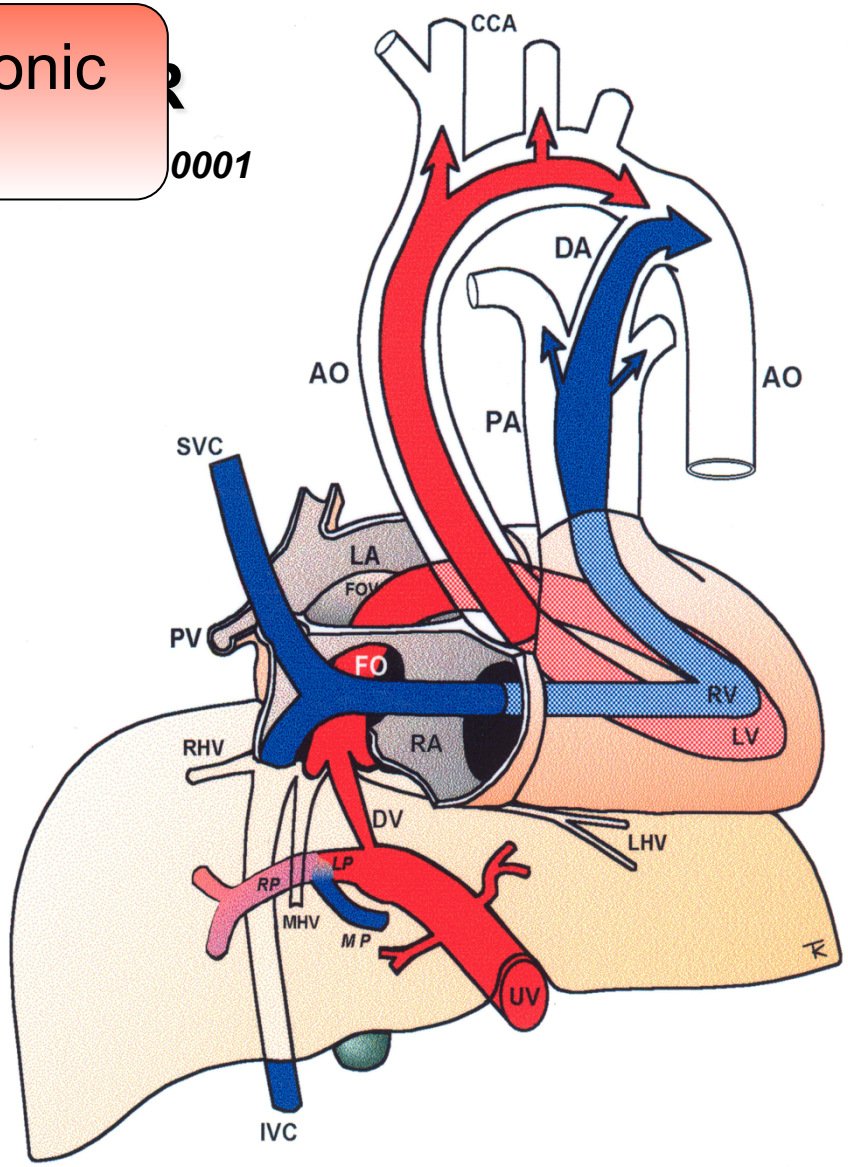




Kiserud T et al.
Ultrasound Obstet Gynecol 2006

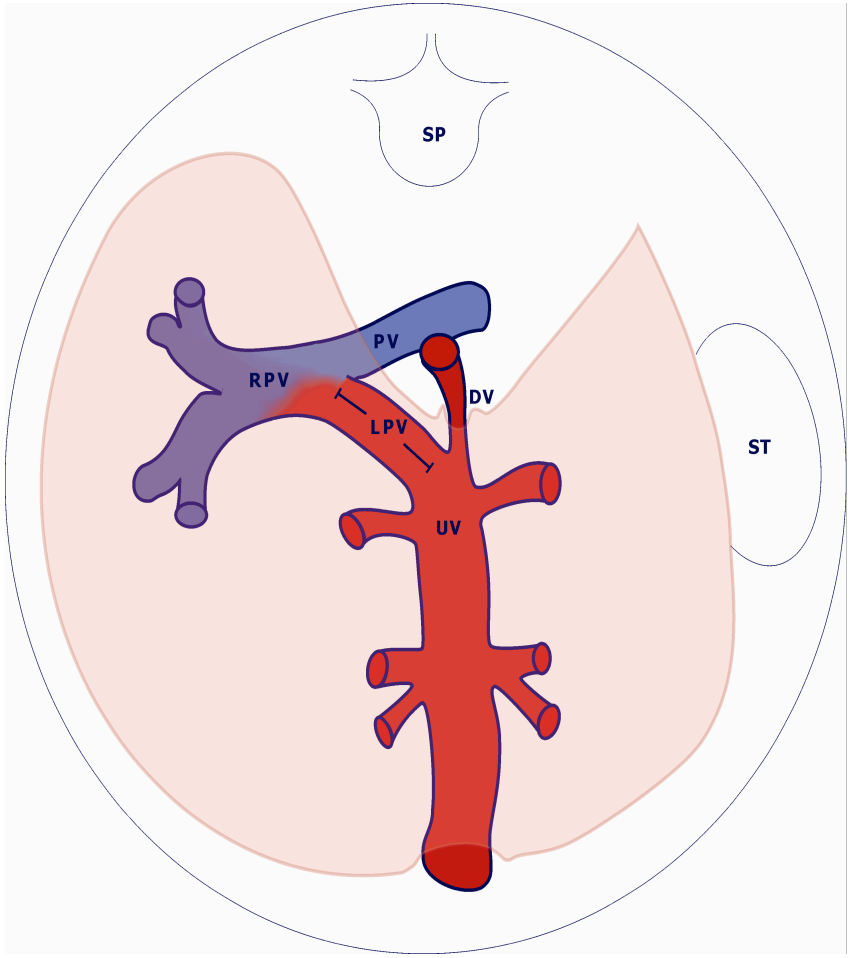
1. Brain is prioritised in acute & chronic placental compromise



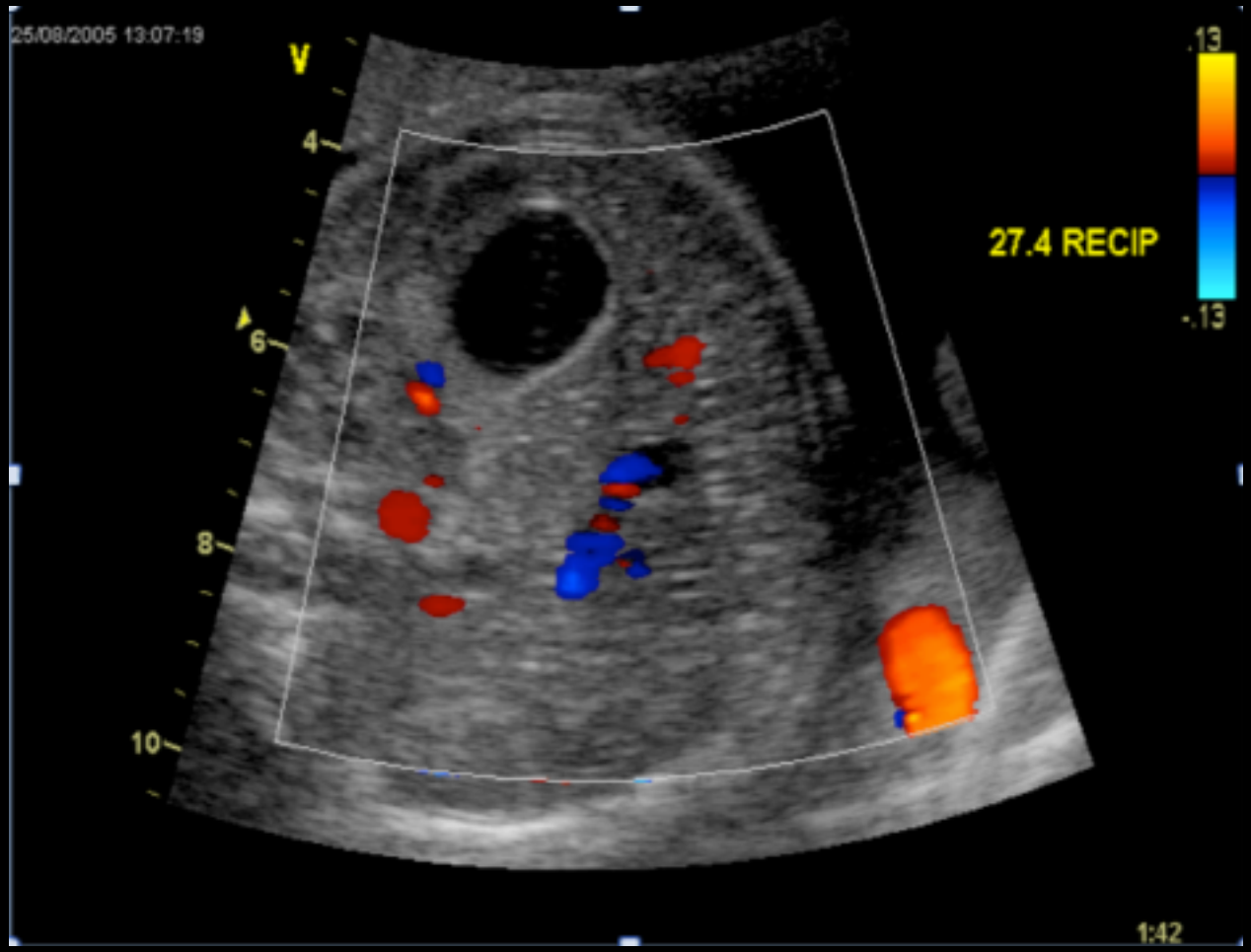


Kiserud T et al.
Ultrasound Obstet Gynecol 2006

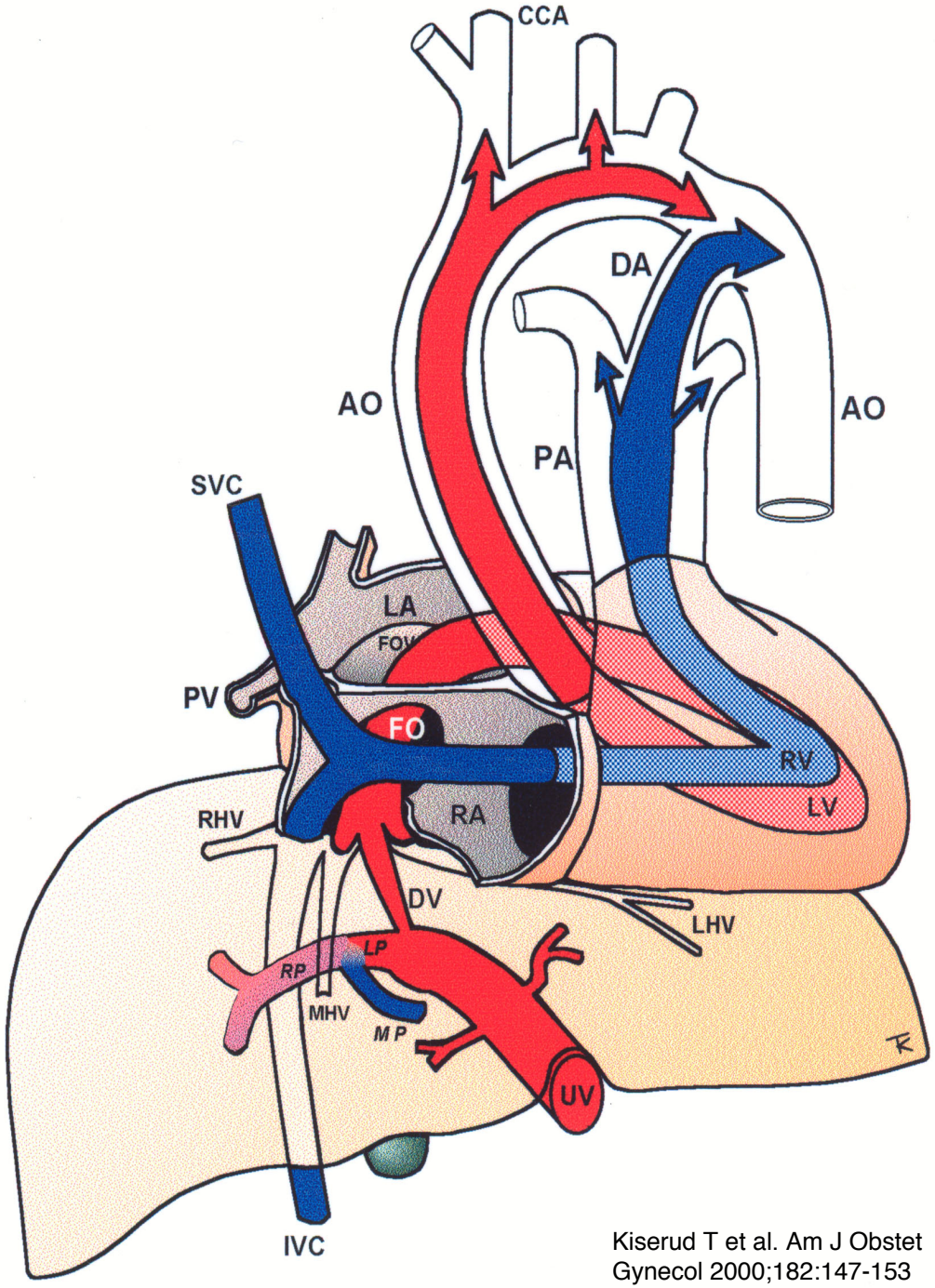
Watershed area: left portal vein



J Kessler et al. 2007

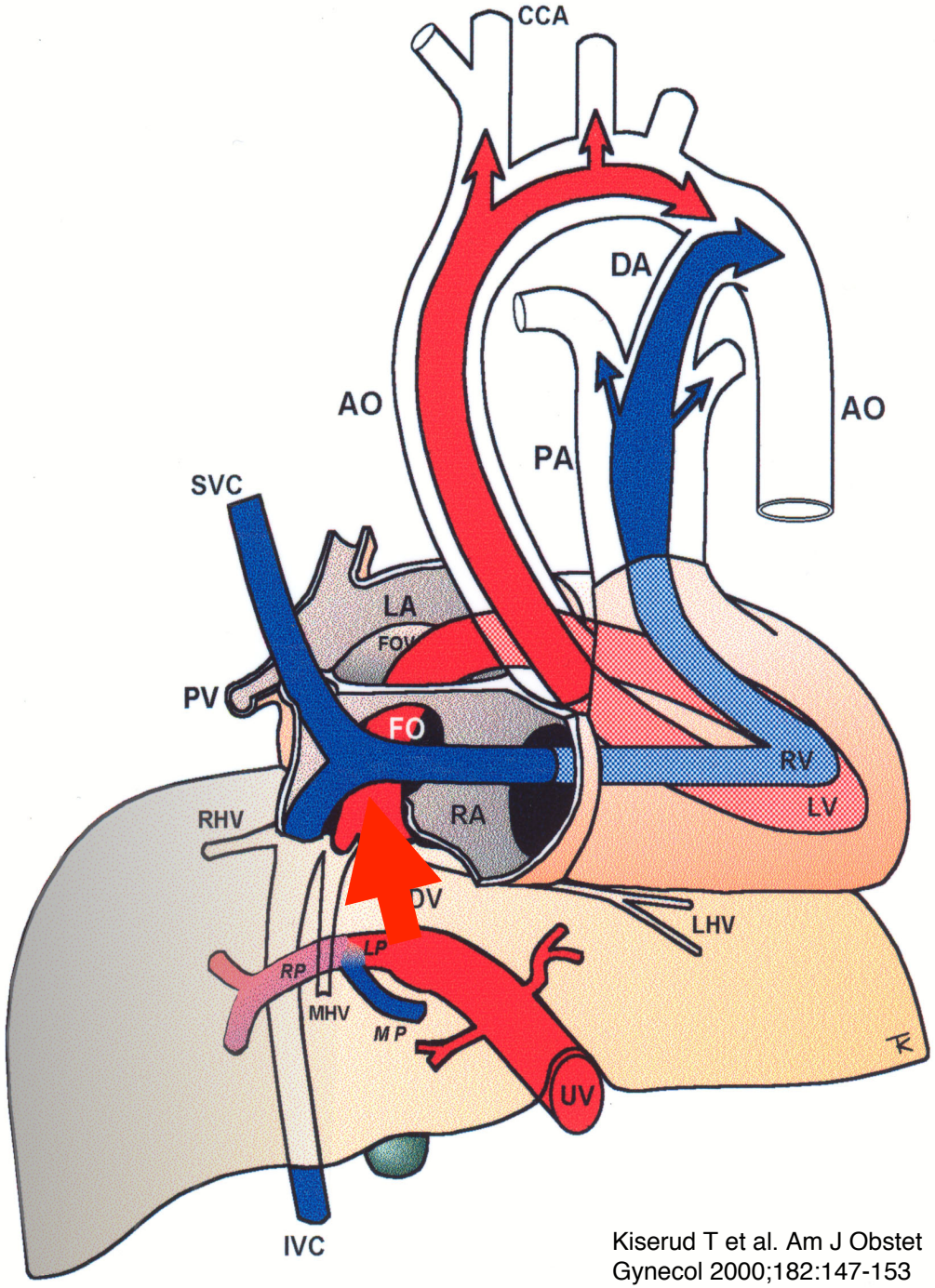

25/08/2005 13:07:19
V
4
6
8
10
27.4 RECIP
.13
-.13
1:42

Portal watershead



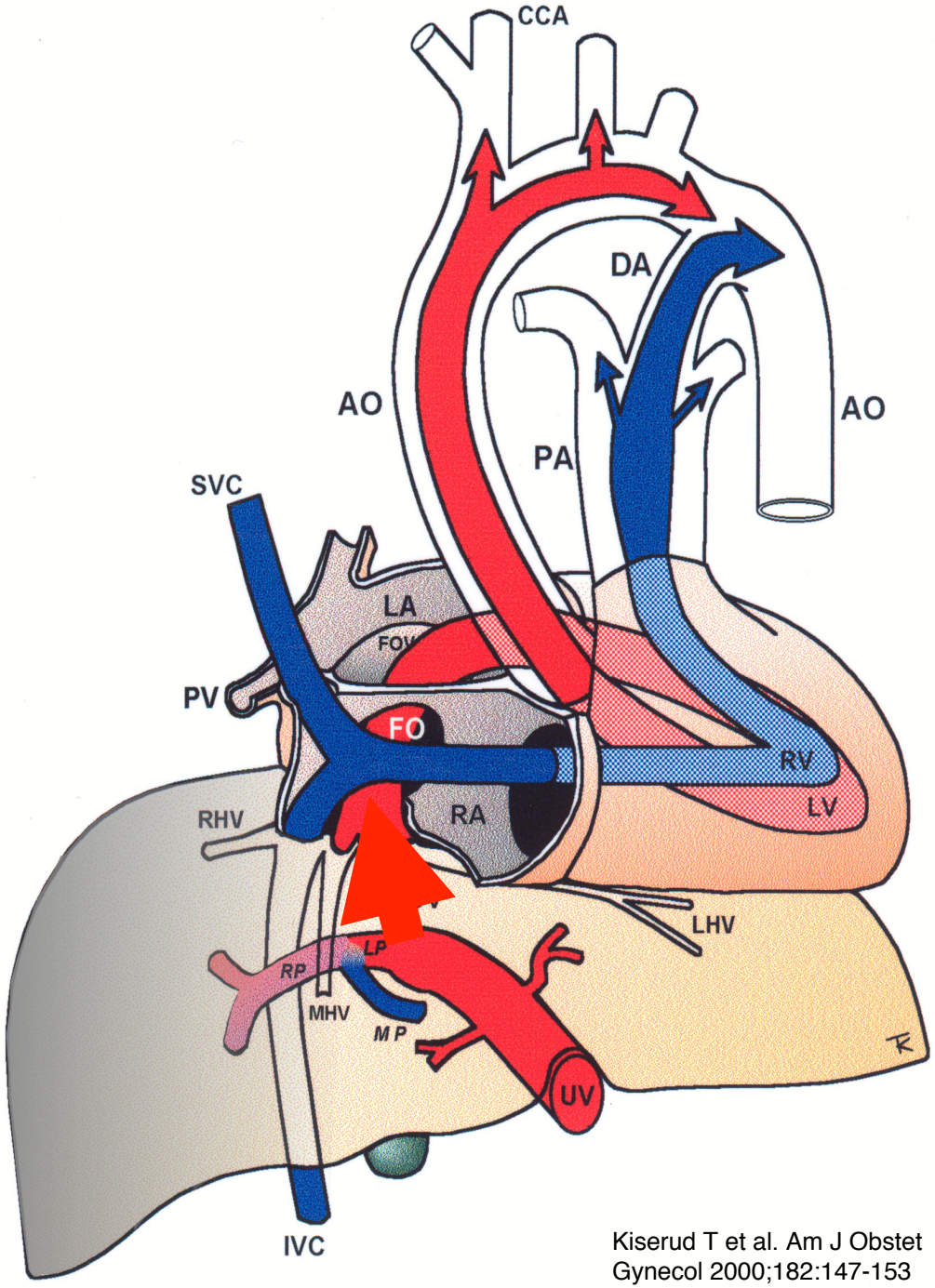
Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Portal watershead

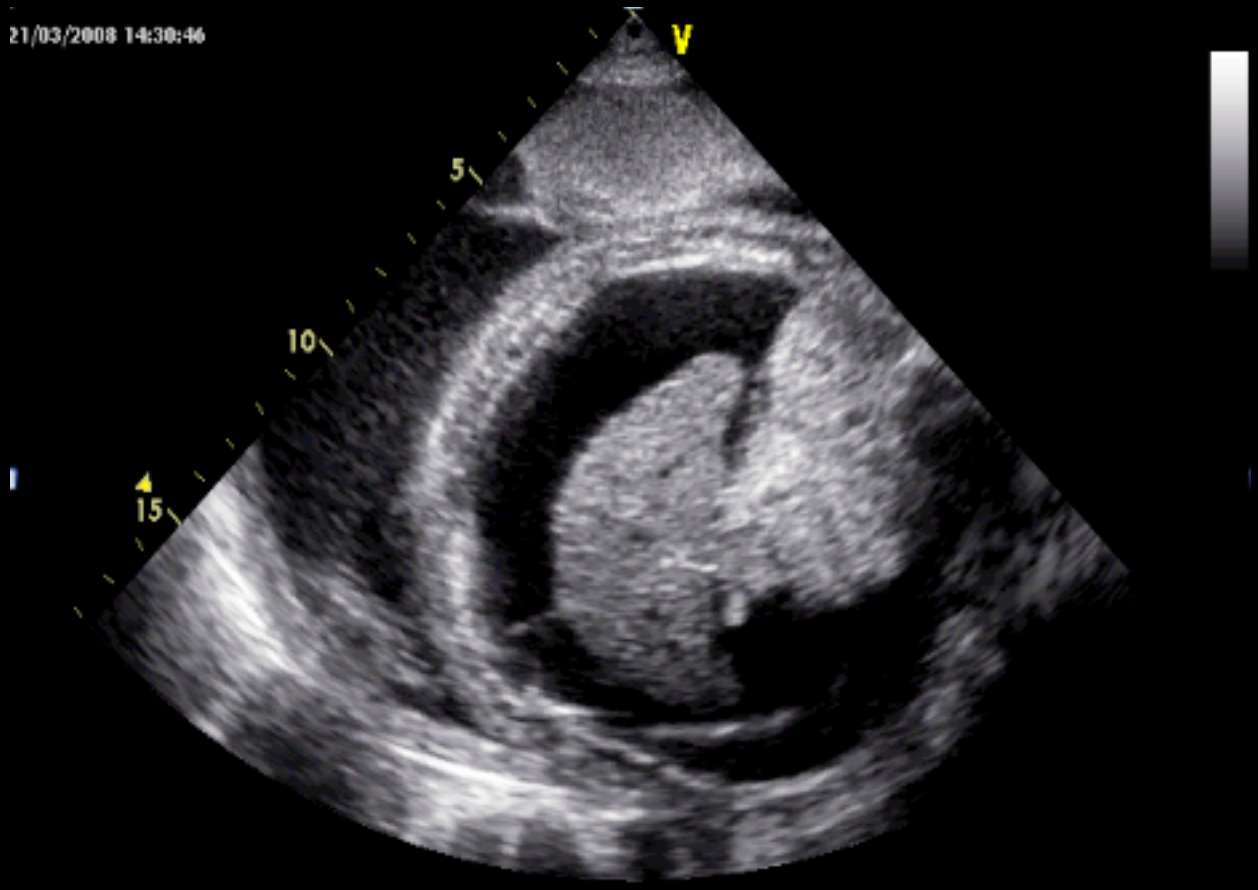


Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Portal watershead



Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153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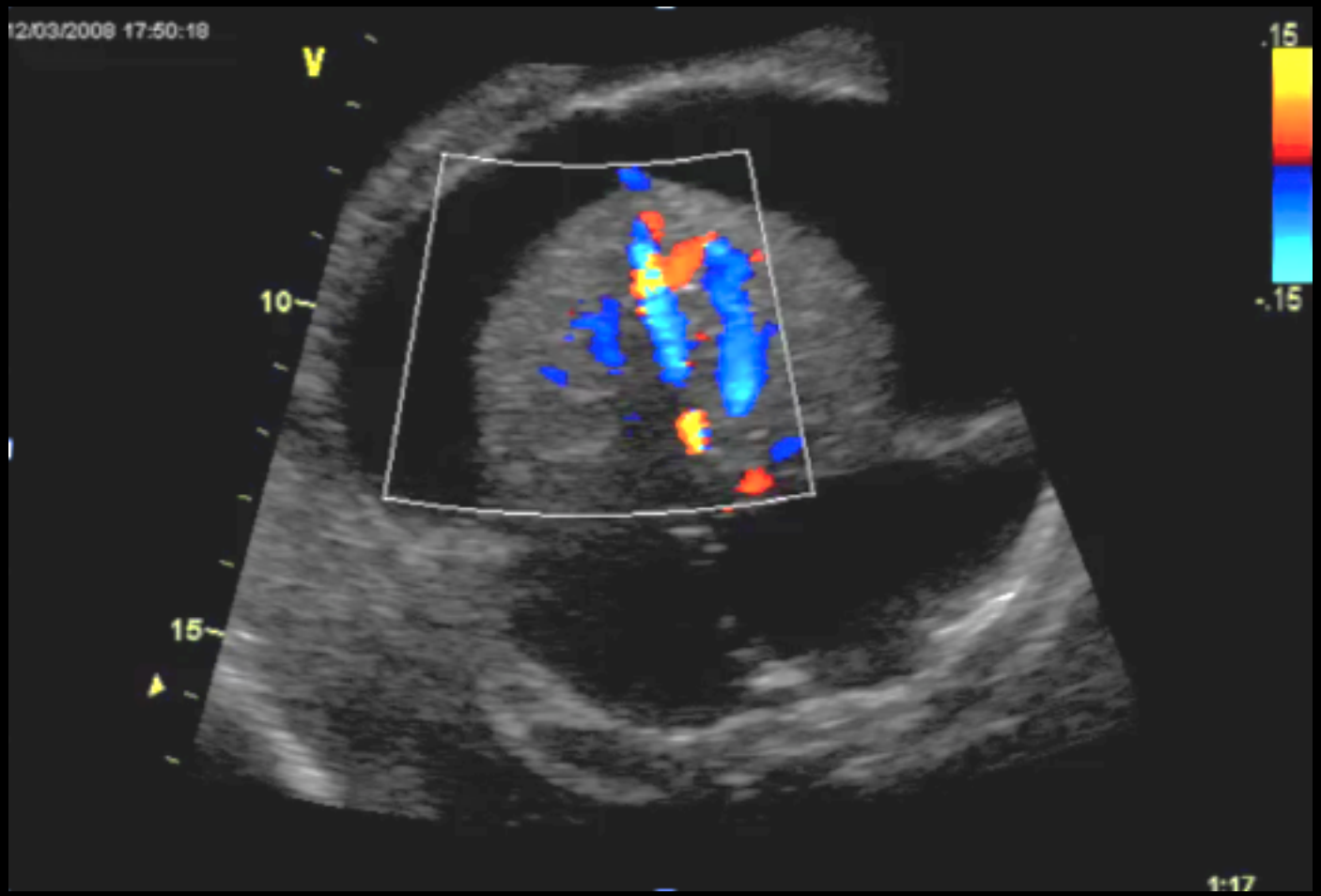
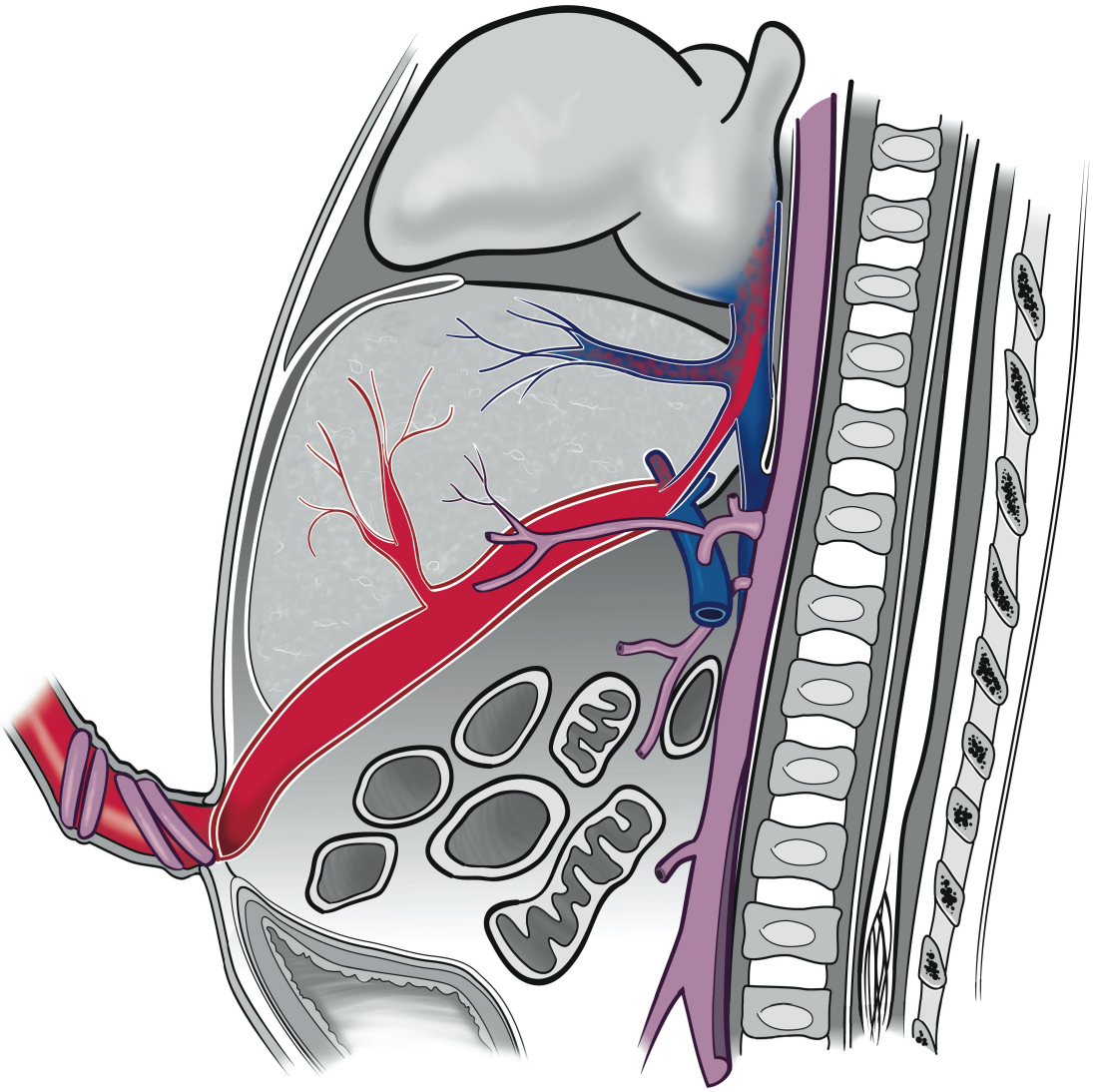
V
5
10
15

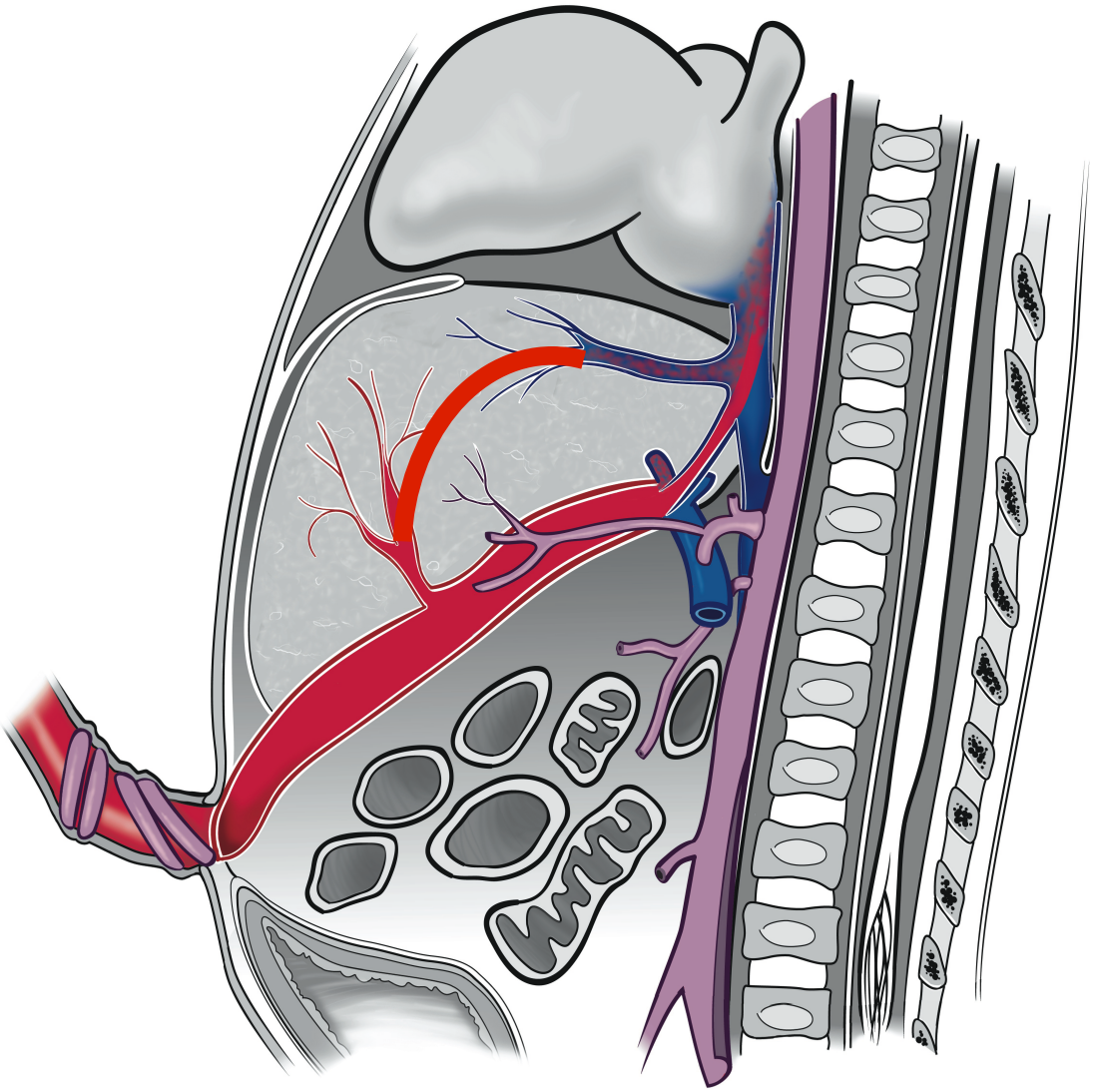
12/03/2008 17:31:43
V
6
8
10
12


12/03/2009 17:50:19
V
10
15
.15
-.15
1:17



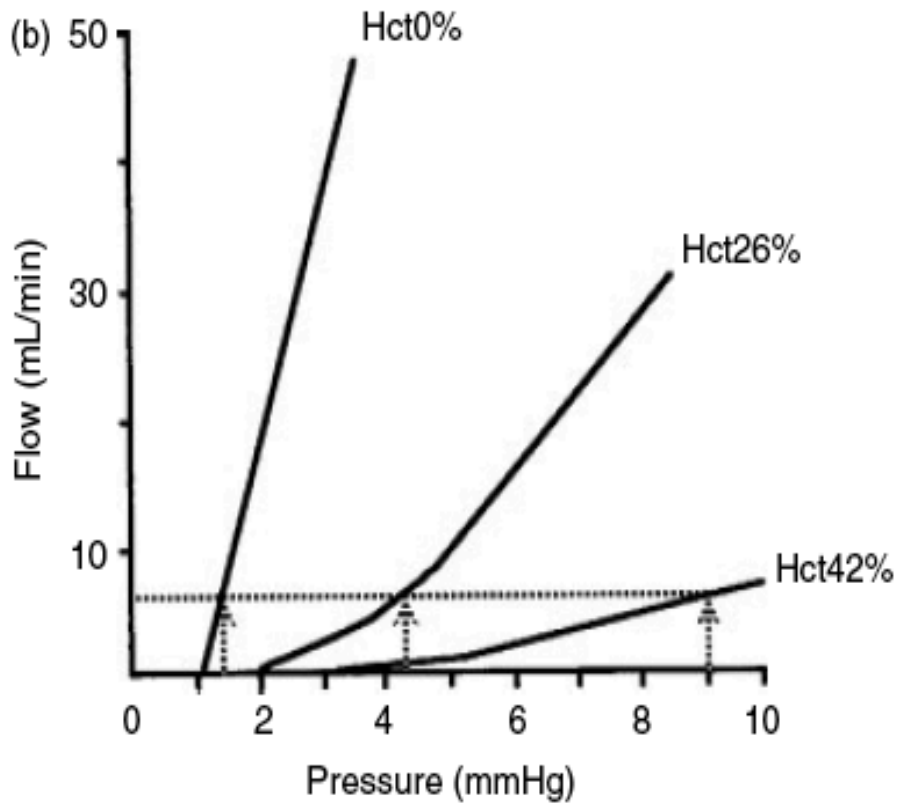
Ebbing C et al. Reproduct Sci 2008

Portosystemic shunt



Viscosity – Resistance

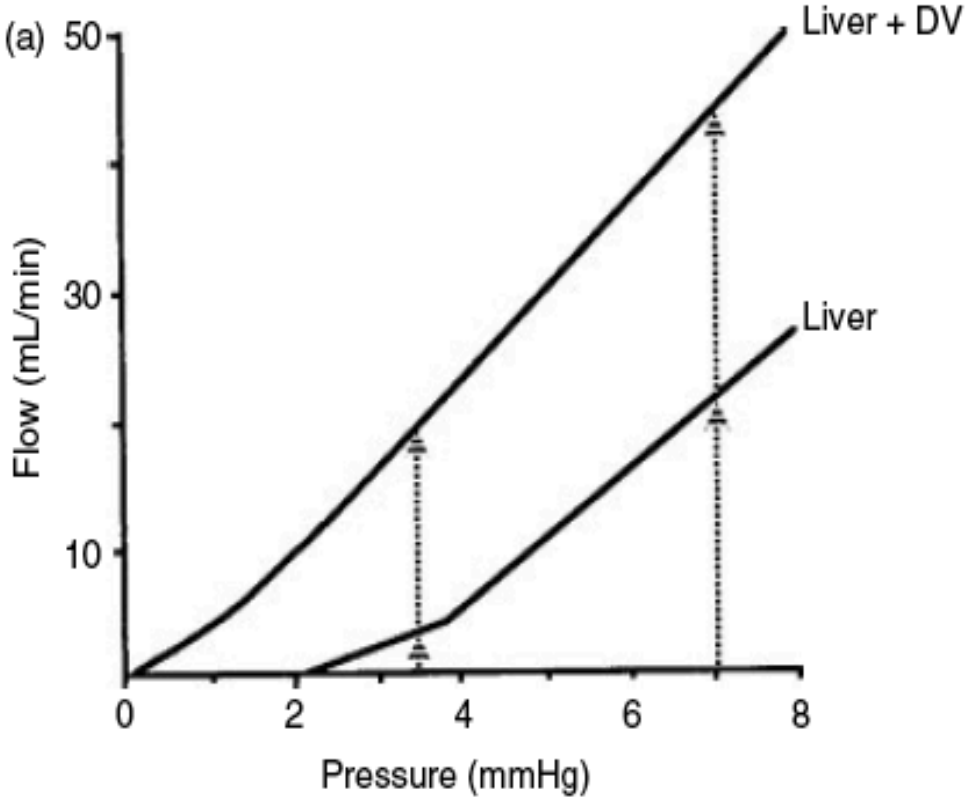
Liver only



Kiserud T et al. Am J Obstet Gynecol 1998

Viscosity – Resistance

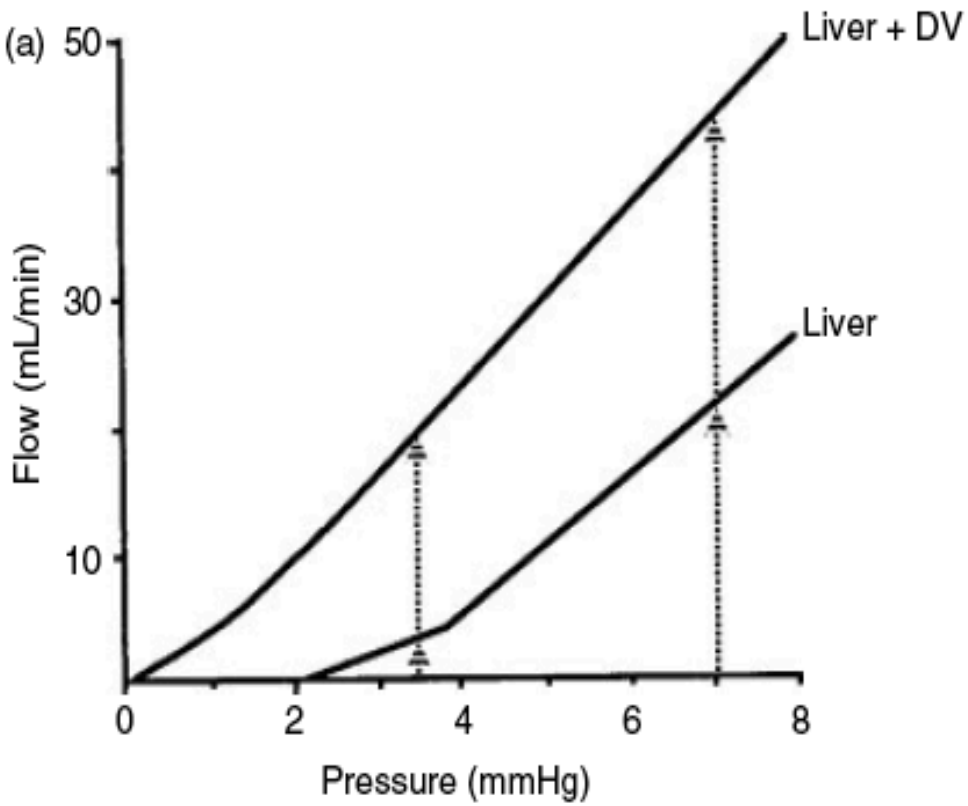
Liver +/- DV



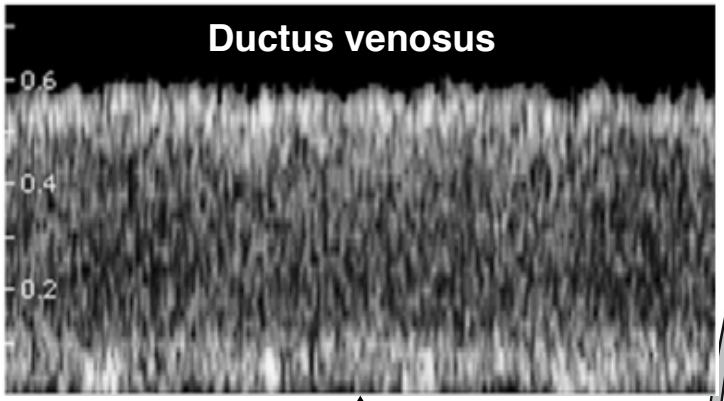
Liver only

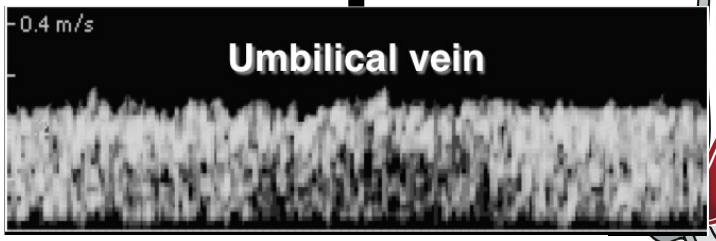
Kiserud T et al. Am J Obstet Gynecol 1998

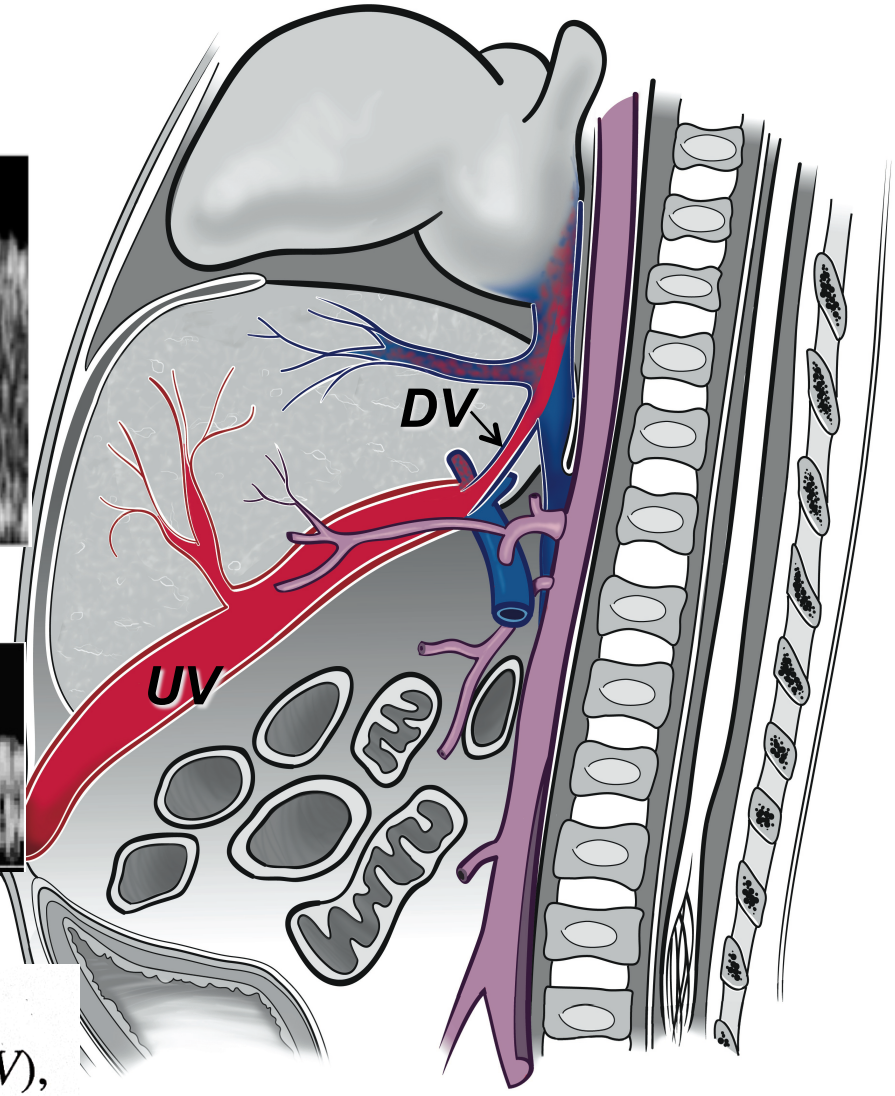
2. Fetal liver and ductus venosus represent very different hemodynamics where viscosity is important.



Kiserud T et al. Am J Obstet Gynecol 1998







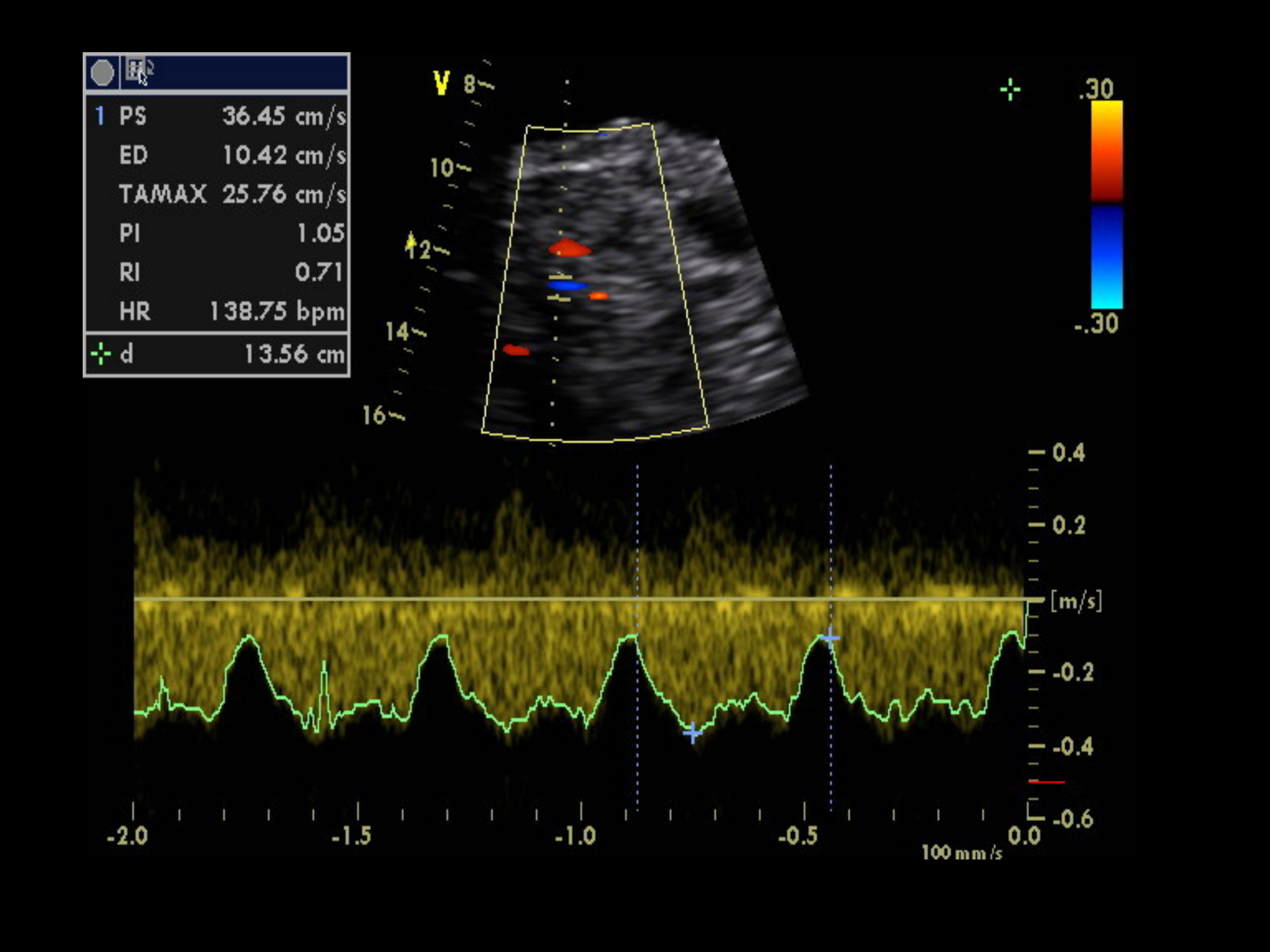
Bernoulli equation

$$\Delta p_{DV} = \frac{1}{2}\rho(V_{DV}^2 - V_{UV}^2) + \rho \int_{UV}^{DV} \frac{\partial V}{\partial t}\, dx + R(V),$$

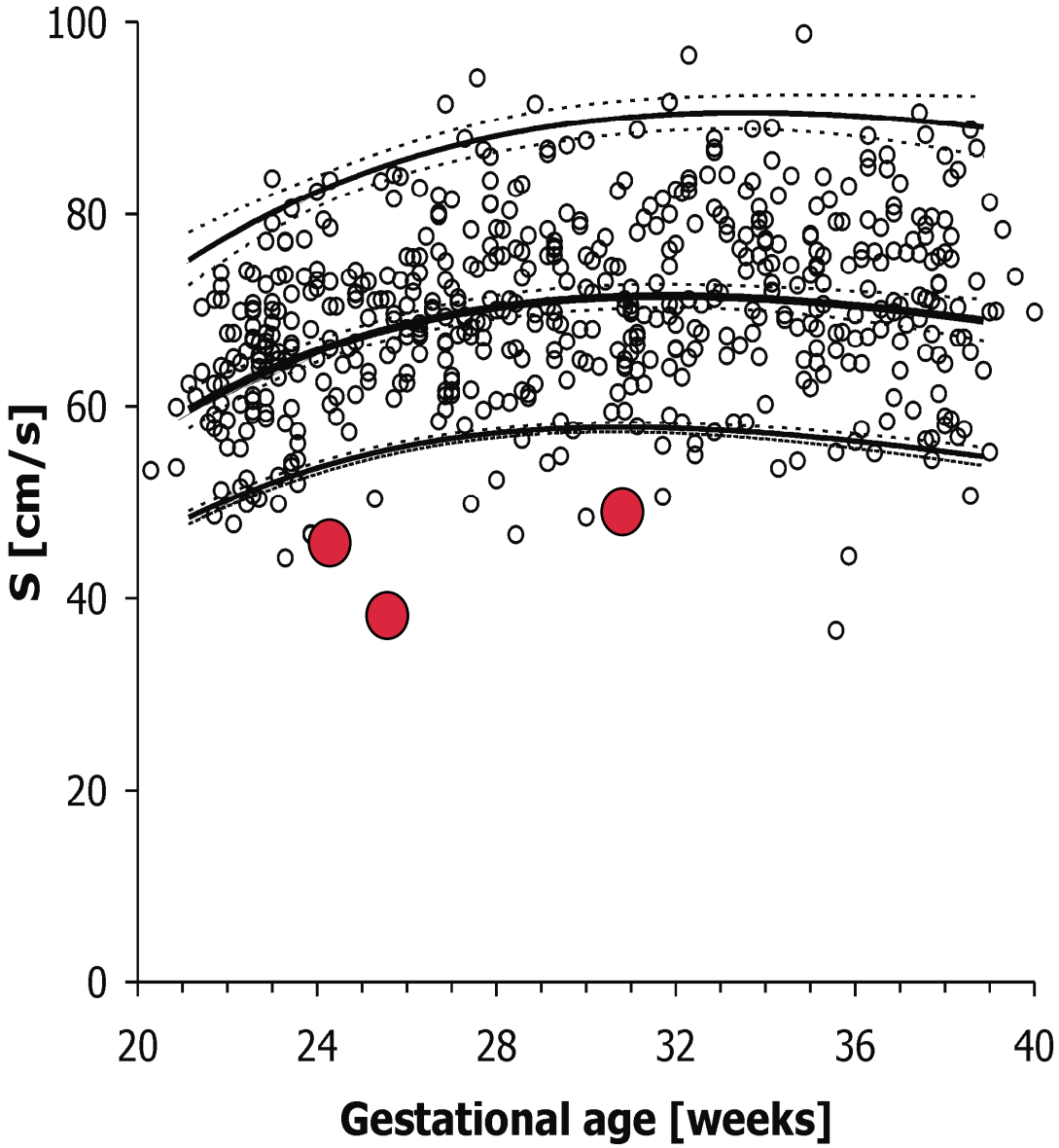
Simplified: 4 V^2 (m/s) ≈ mmHg

Portocaval pressure gradient: 0.5–3.5 mmHg

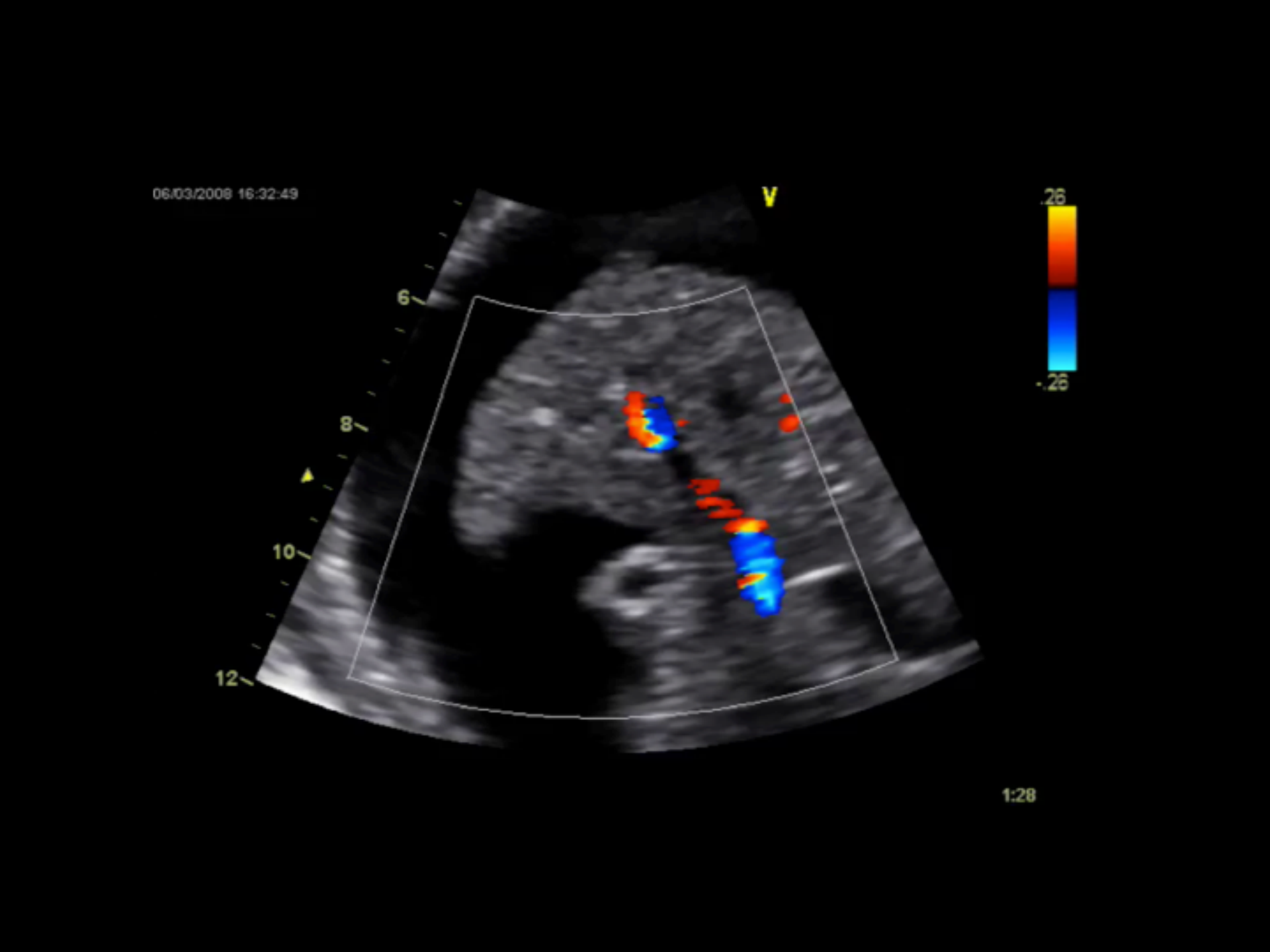
Kiserud & al.
Ultrasound Med Biol 1994

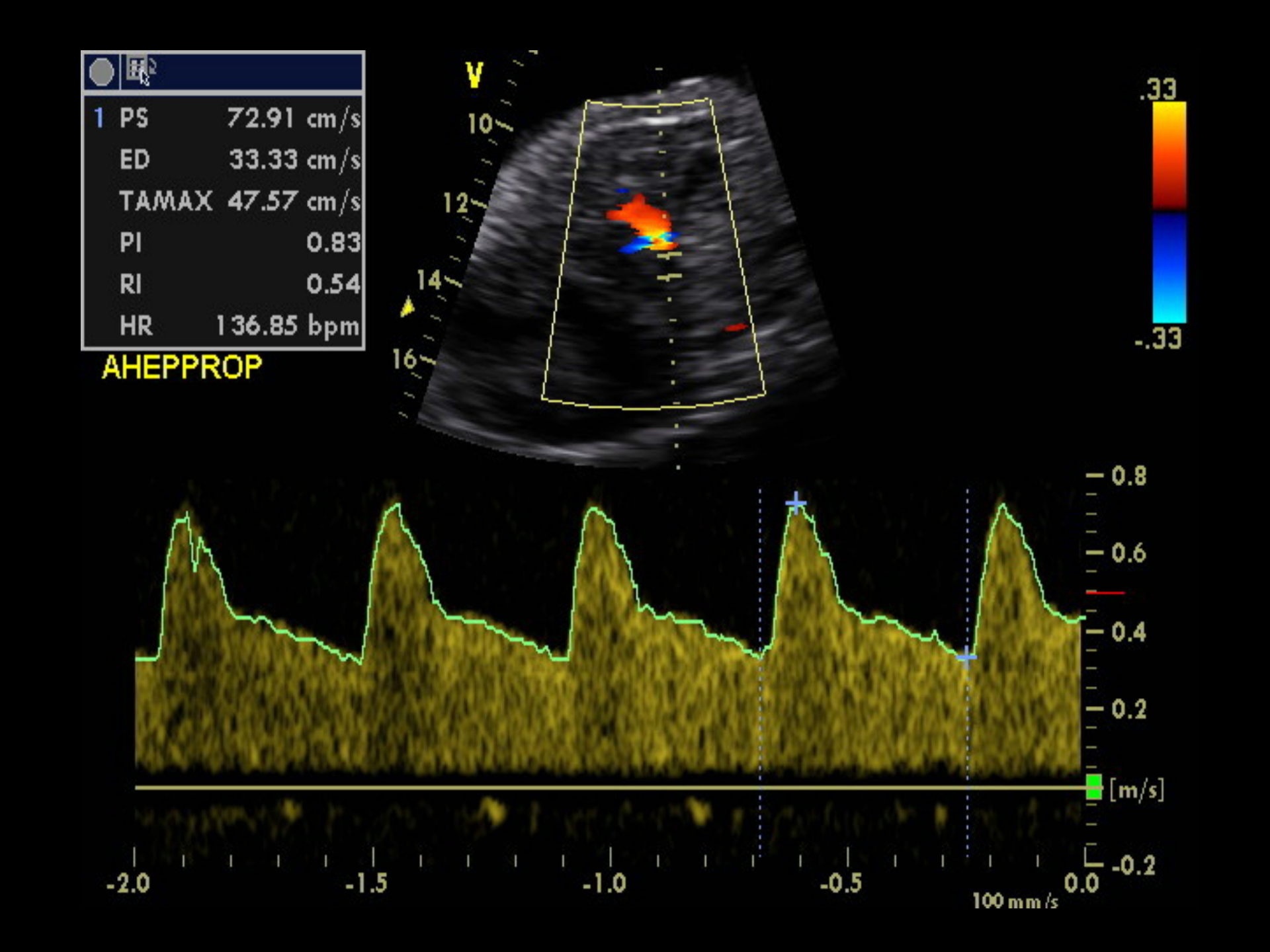

1 PS 36.45 cm/s
ED 10.42 cm/s
TAMAX 25.76 cm/s
PI 1.05
RI 0.71
HR 138.75 bpm
d 13.56 cm
V
8
10
12
14
16
.30
-.30
0.4
0.2
[m/s]
-0.2
-0.4
-0.6
-2.0
-1.5
-1.0
-0.5
0.0
100 mm/s

Ductus venosus peak velocity (S) = f(Δp)

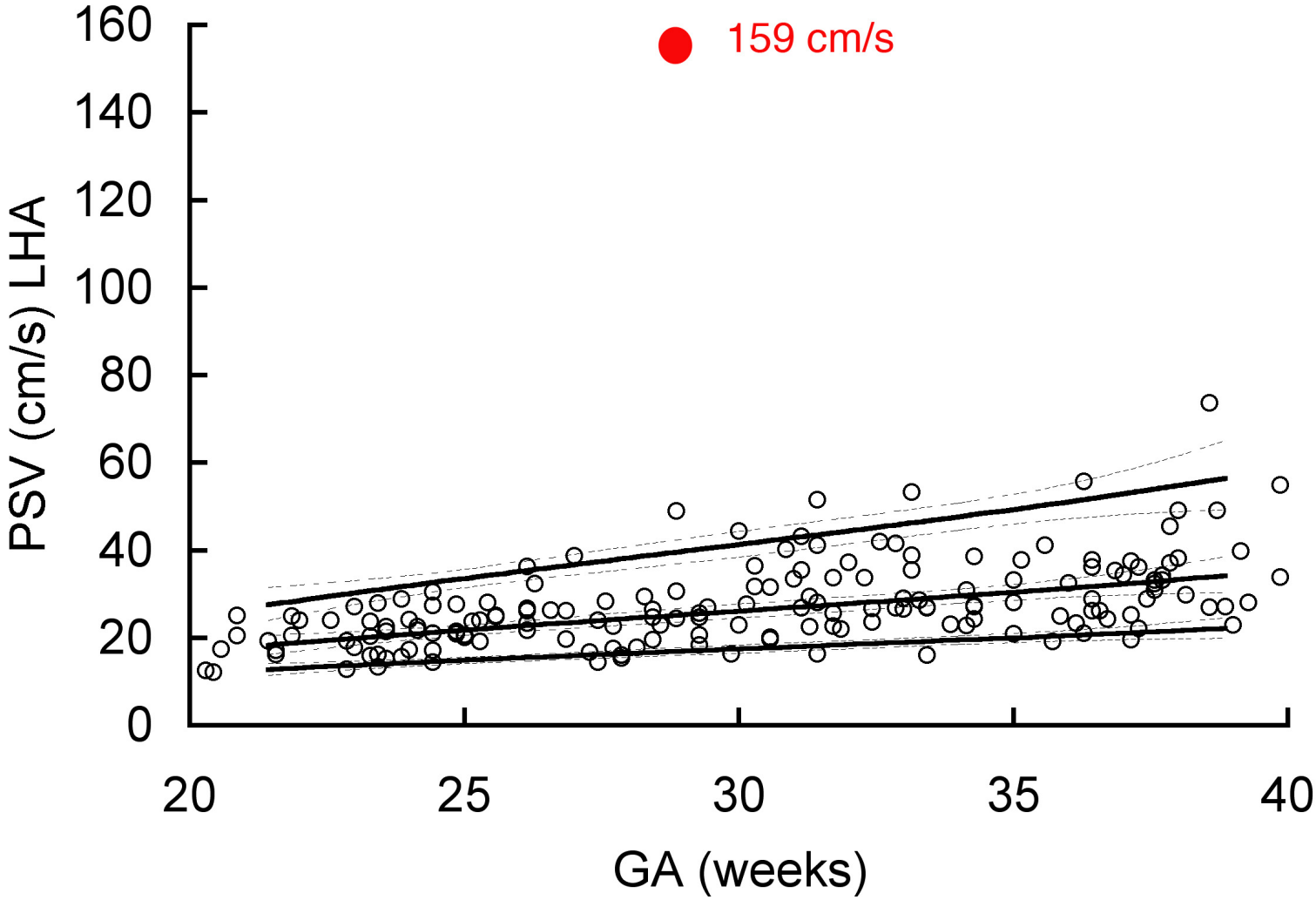


Kessler J et al UOG 200


06/03/2008 16:32:49
V
.26
-.26
6
8
10
12
1:28

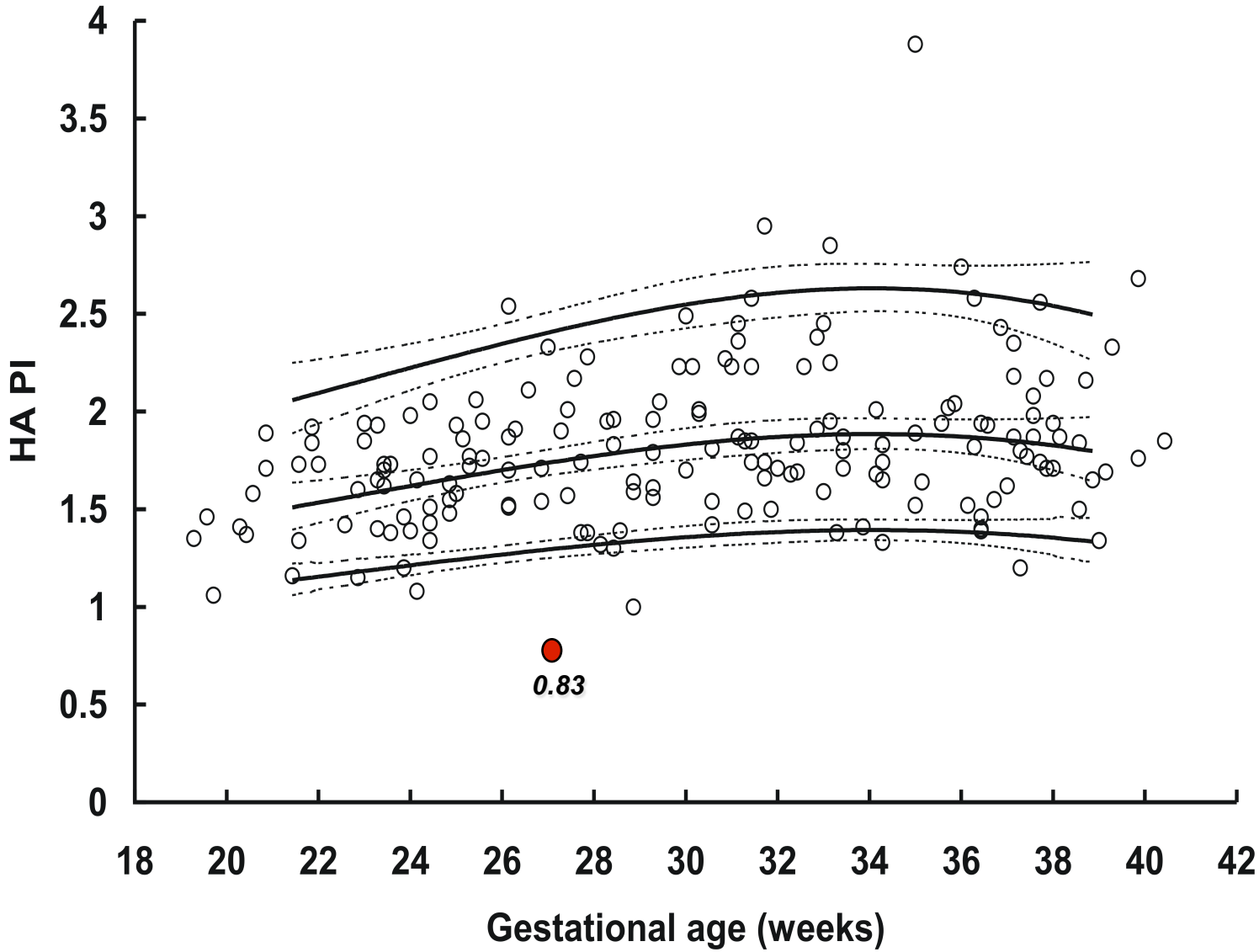

1 PS 72.91 cm/s
ED 33.33 cm/s
TAMAX 47.57 cm/s
PI 0.83
RI 0.54
HR 136.85 bpm
AHEPPROP
V
10
12
14
16
.33
-.33
0.8
0.6
0.4
0.2
[m/s]
-0.2
-2.0
-1.5
-1.0
-0.5
0.0
100 mm/s

Fetal hepatic artery peak velocity



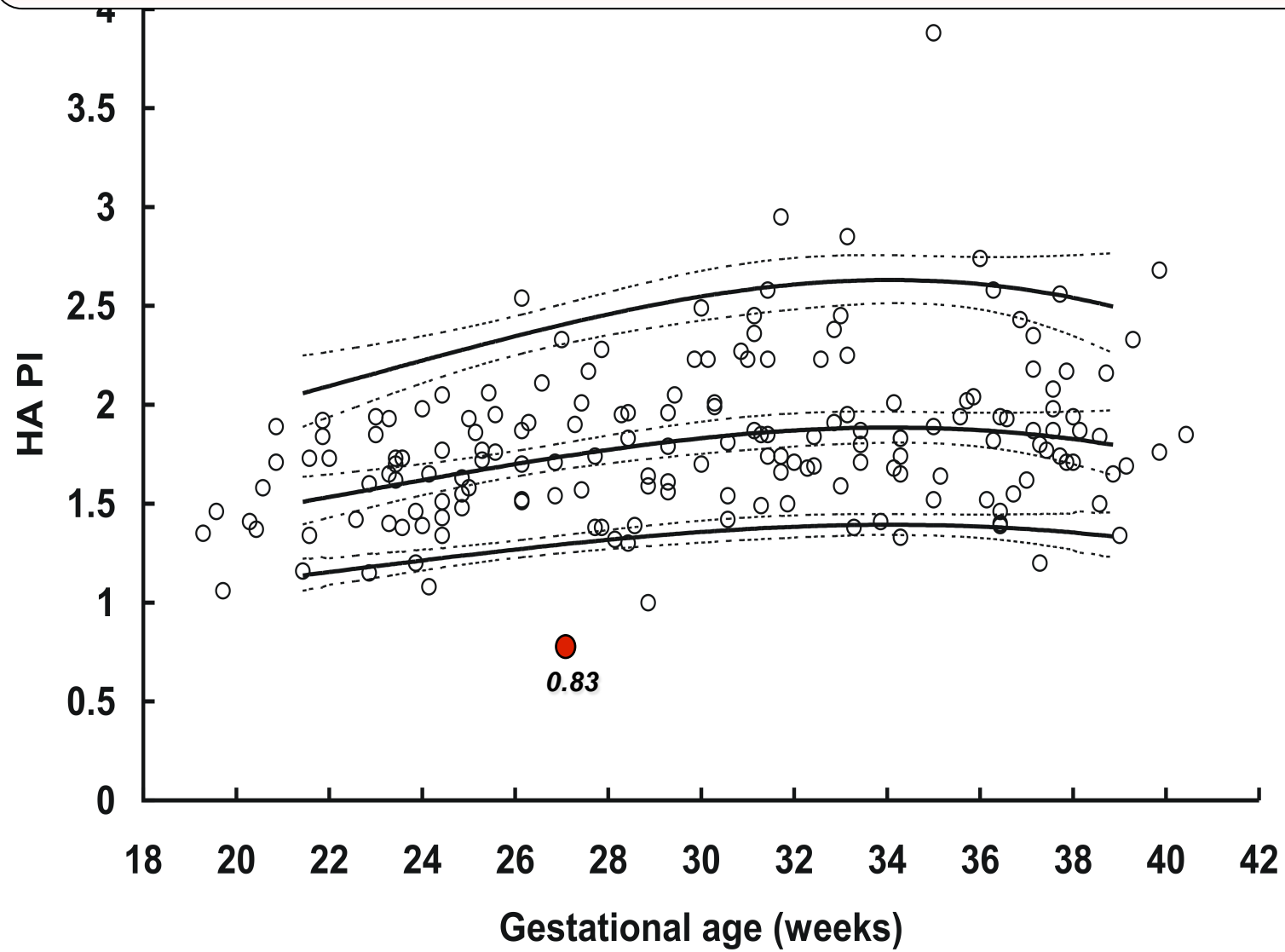
Ebbing C & al.
Reproduct Sci 2008

Fetal hepatic artery PI



Ebbing C & al.
Reproduct Sci 2008

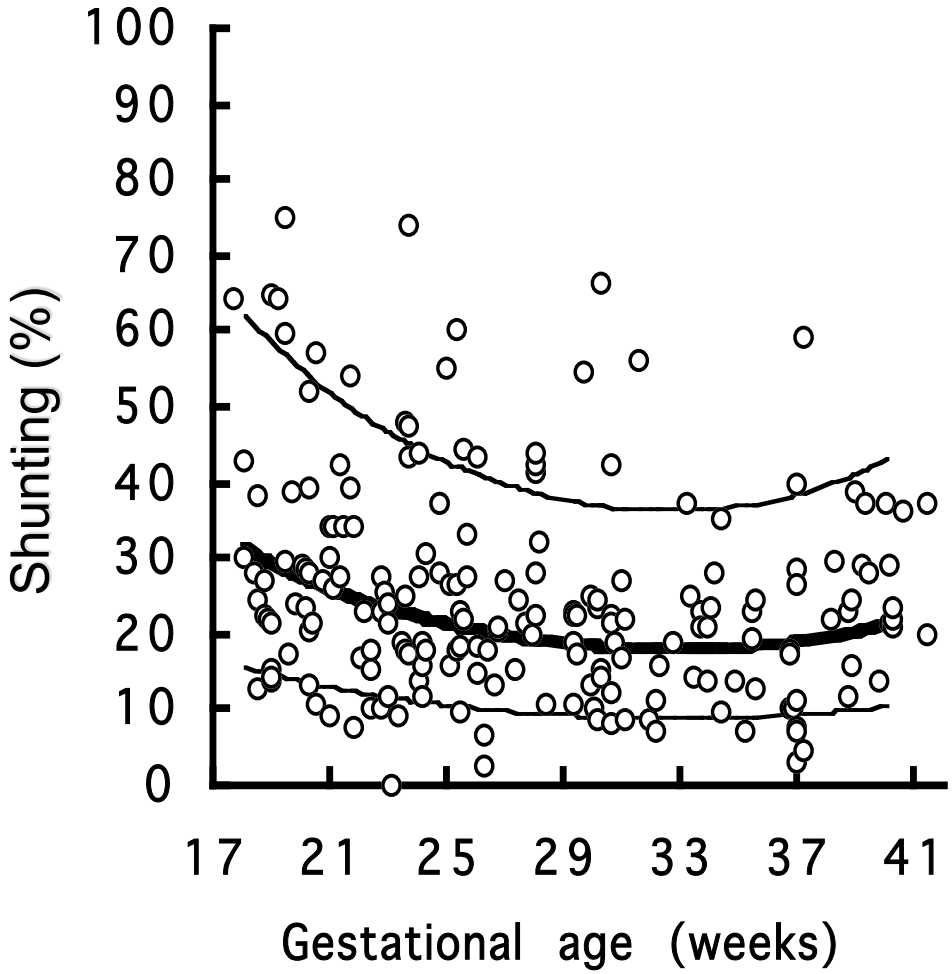
3. Gross circulatory deprivation of the fetal liver is not compatible with survival.

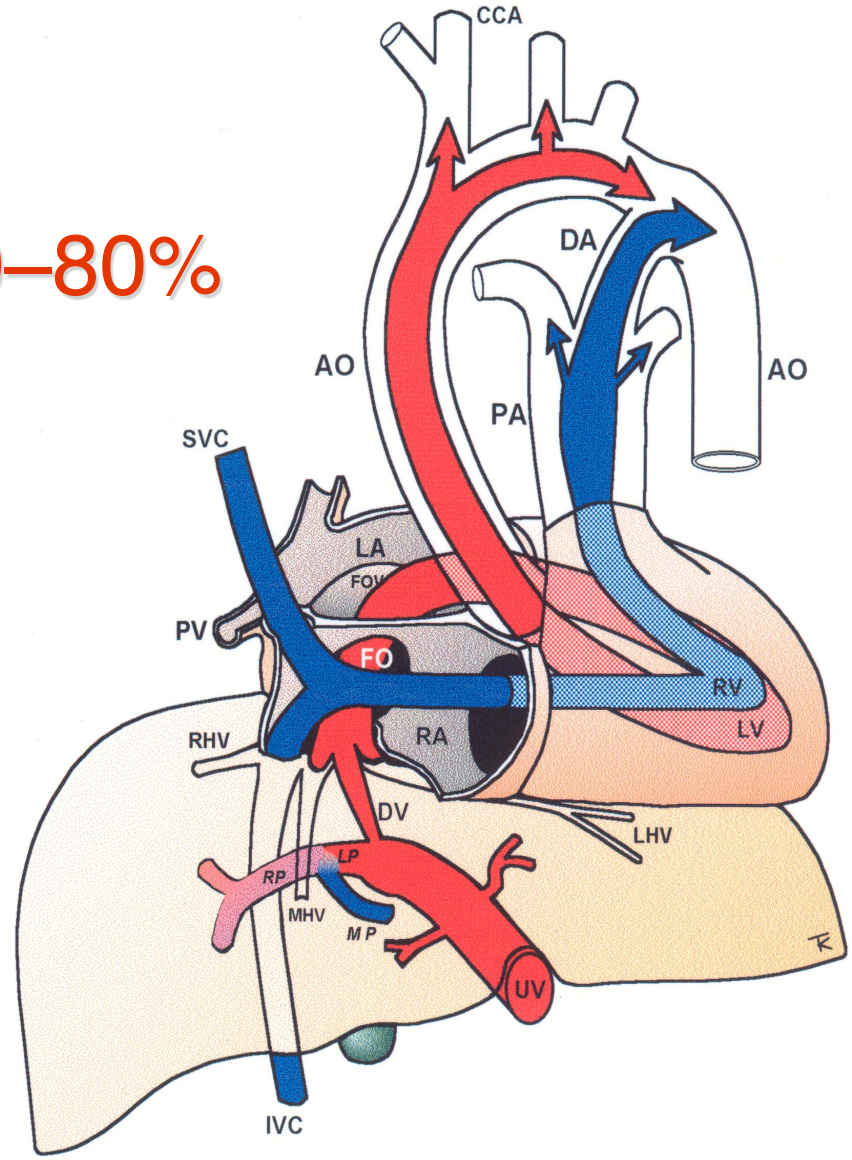


Ebbing C & al.
Reproduct Sci 2008

Ductus venosus shunting

Umbilical flow to the liver: 70–80%

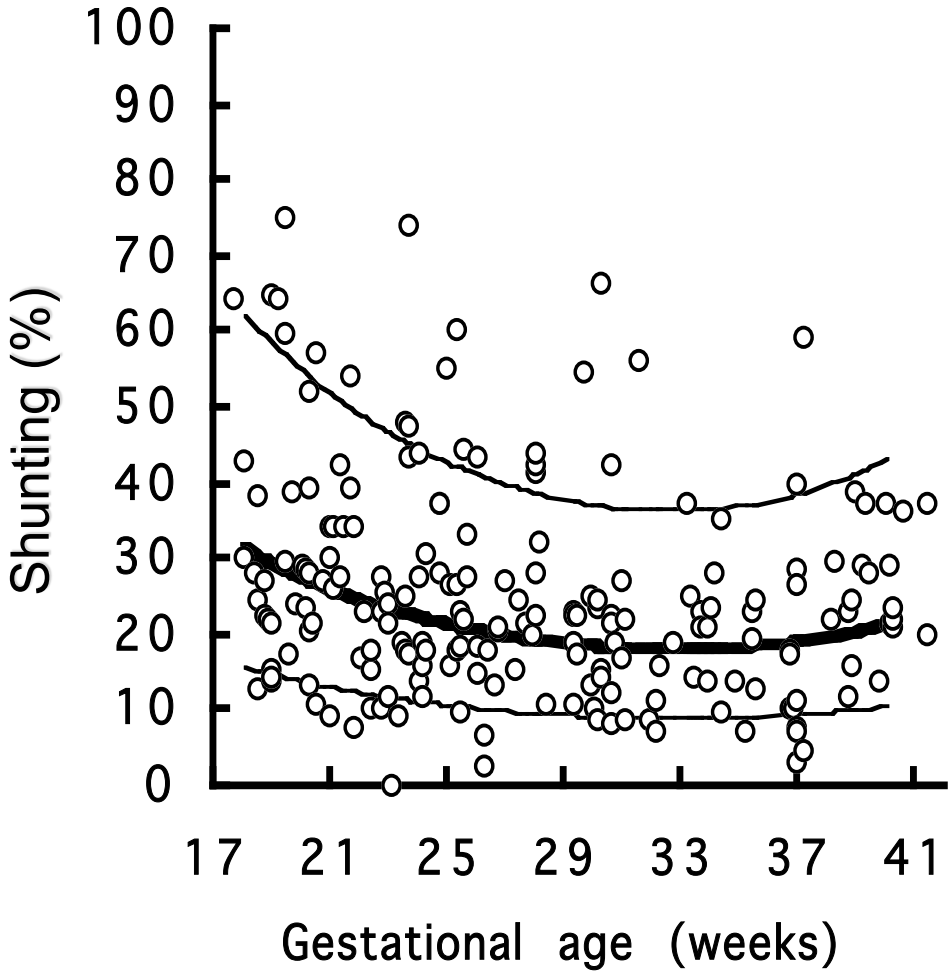


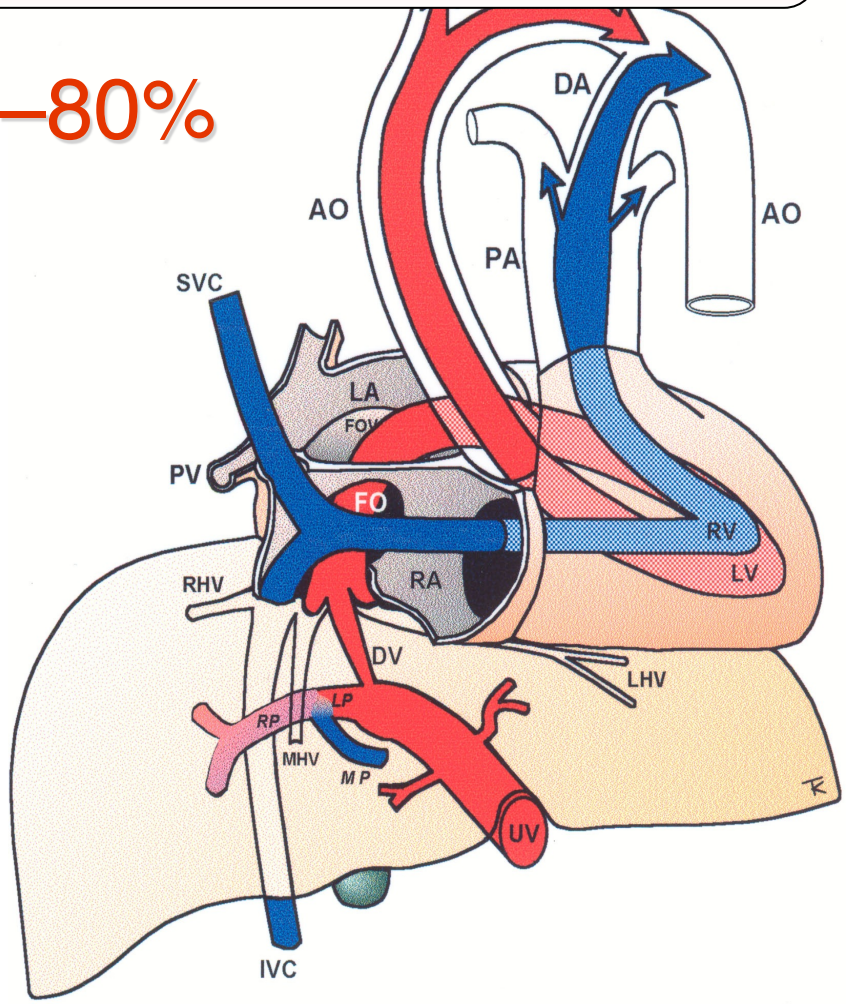


Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

4. Fetal liver is prioritised by anatomic position, flow volume and vascular supply

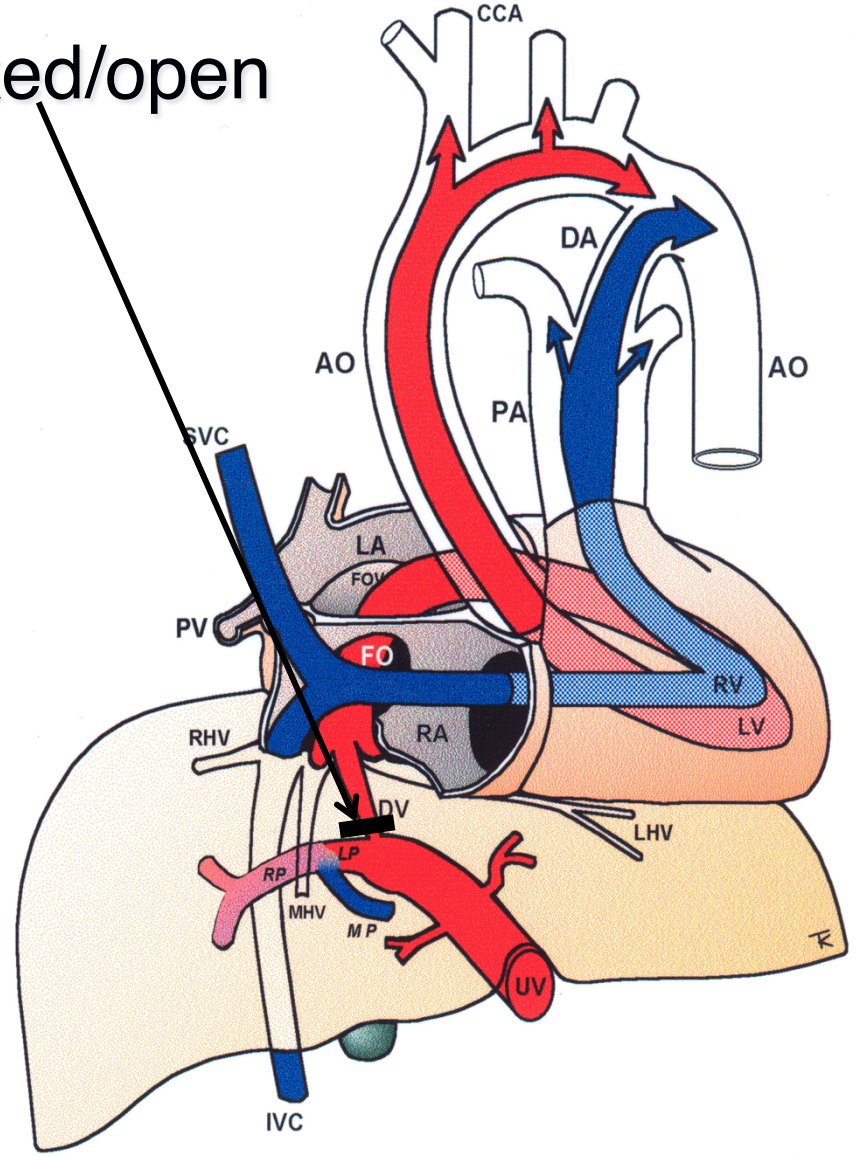
Umbilical flow to the liver: 70–80%



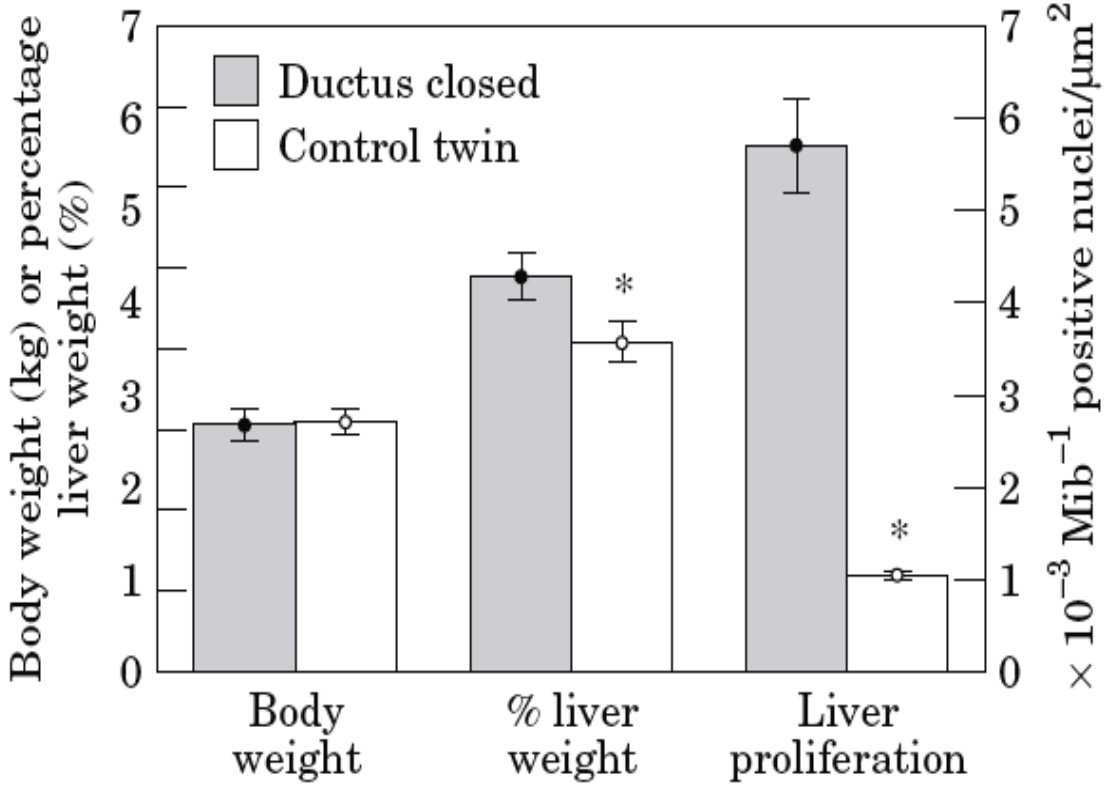


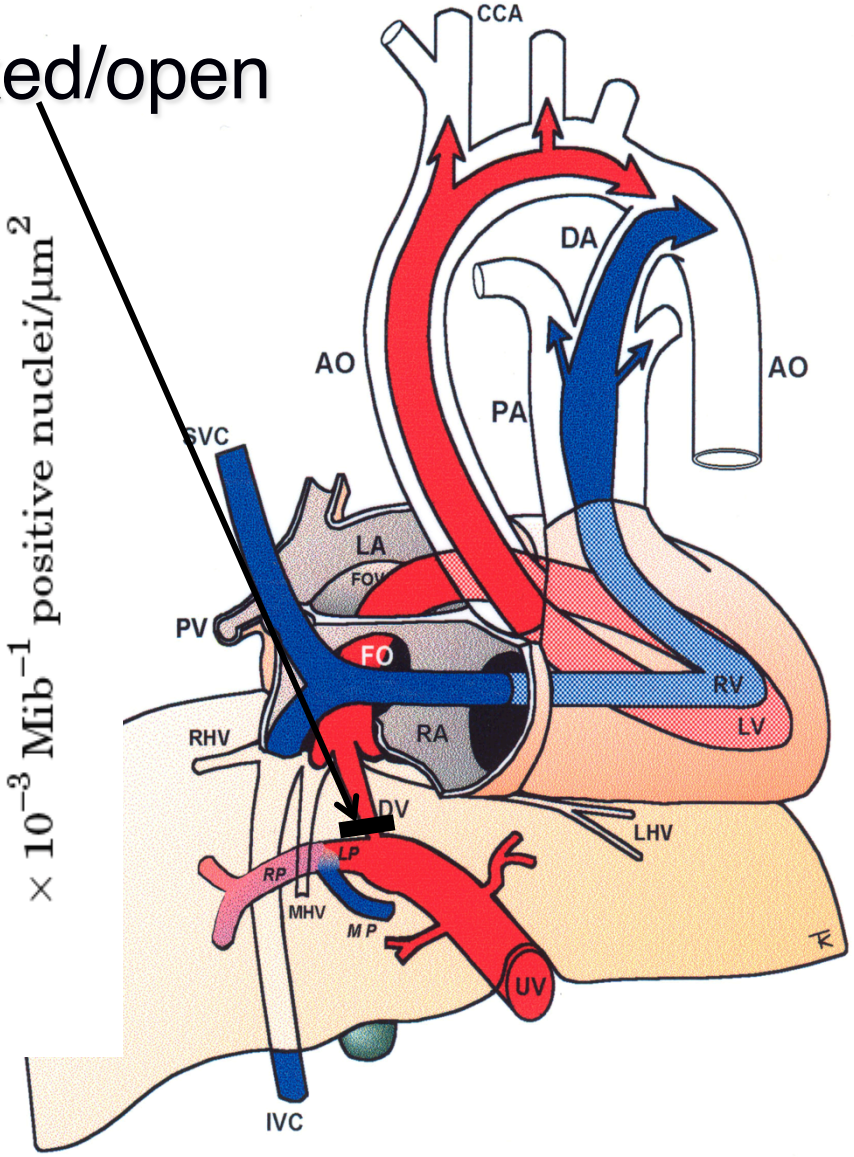
Kiserud T et al. Am J Obstet Gynecol 2000;182:147-153

Ductus venosus shunting blocked/open



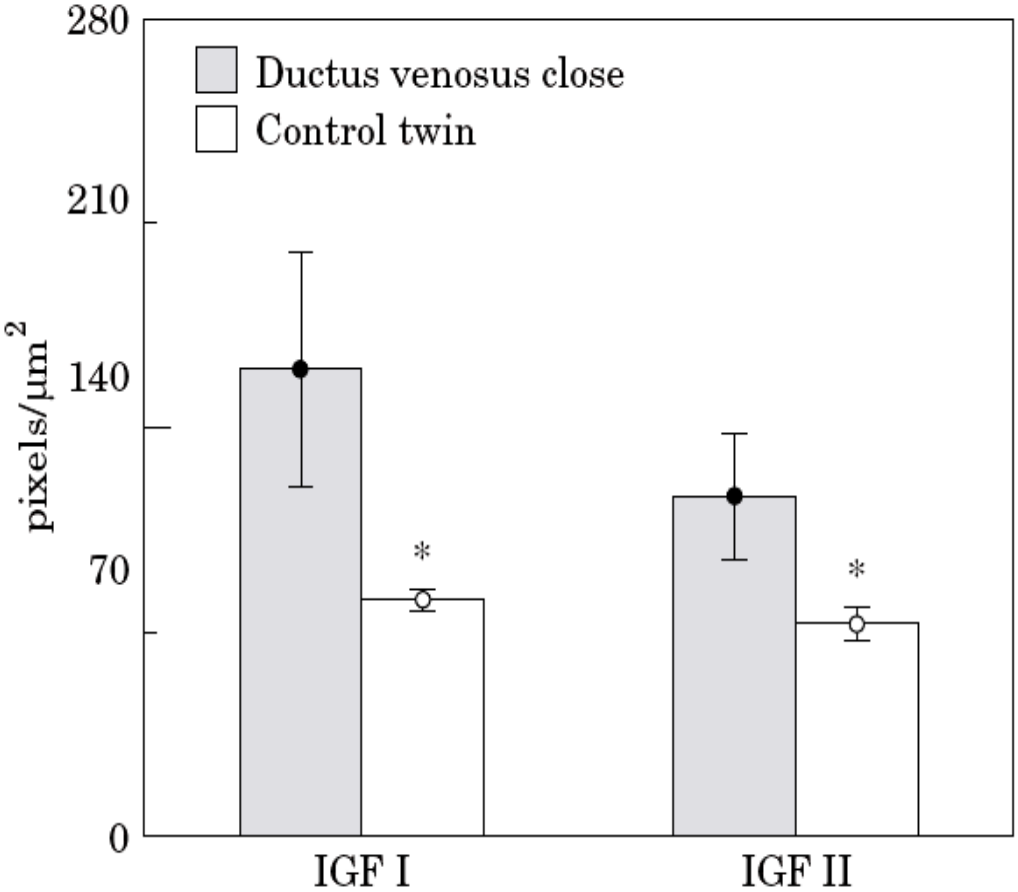
Ductus venosus shunting blocked/open

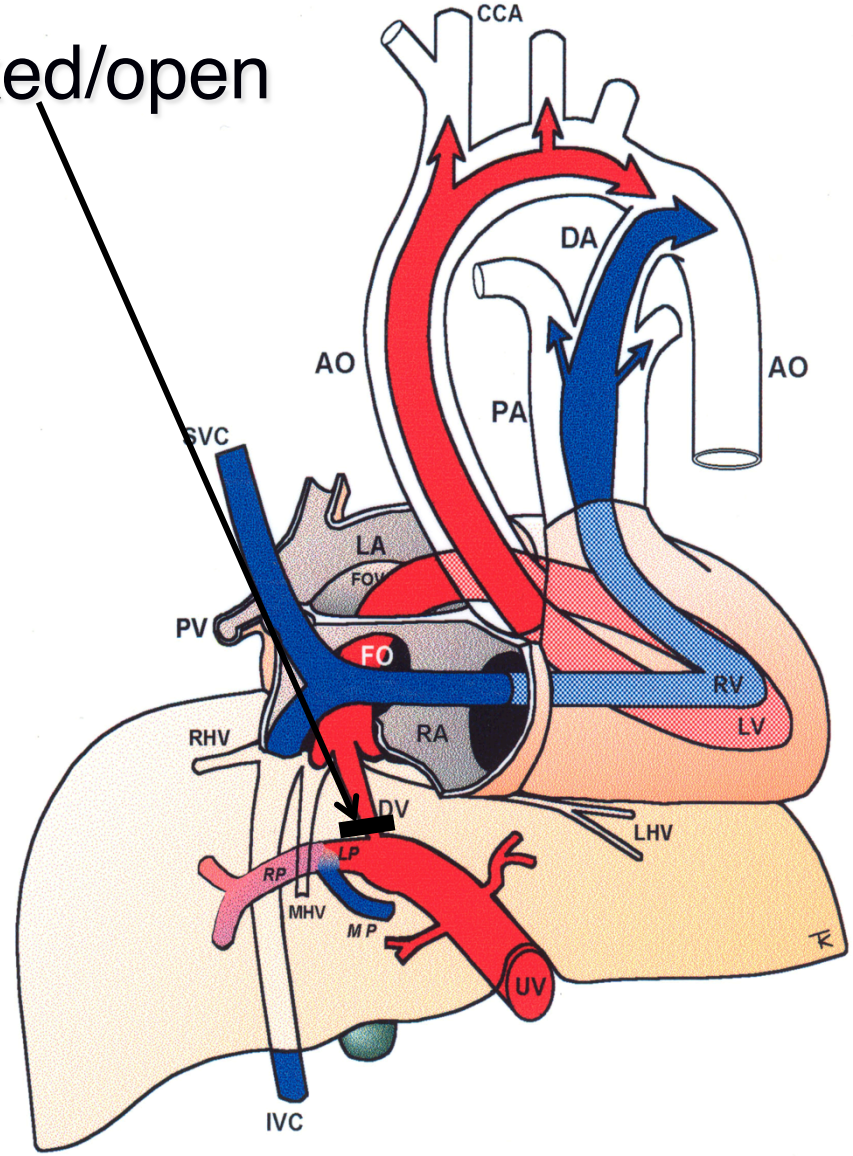




Tchirikov M et al.
Placenta 2002; 23: S153-8

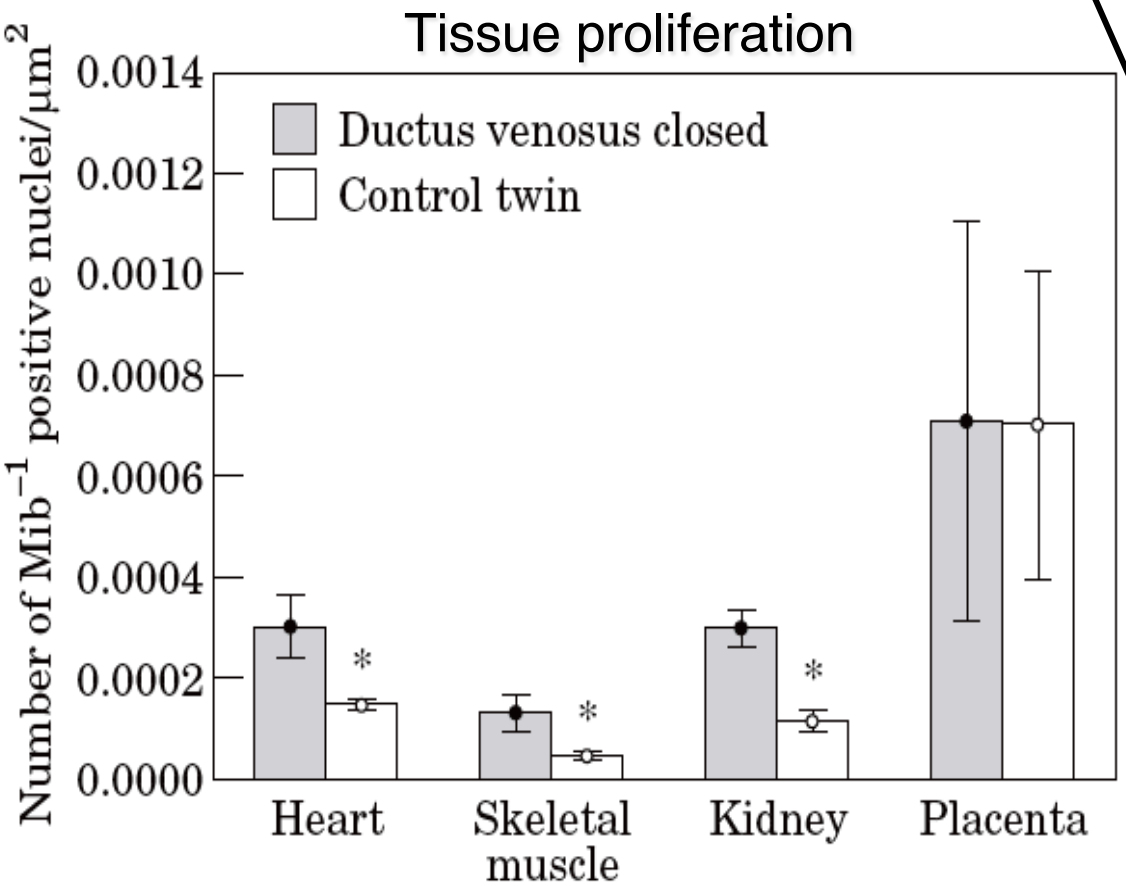
Ductus venosus shunting blocked/open

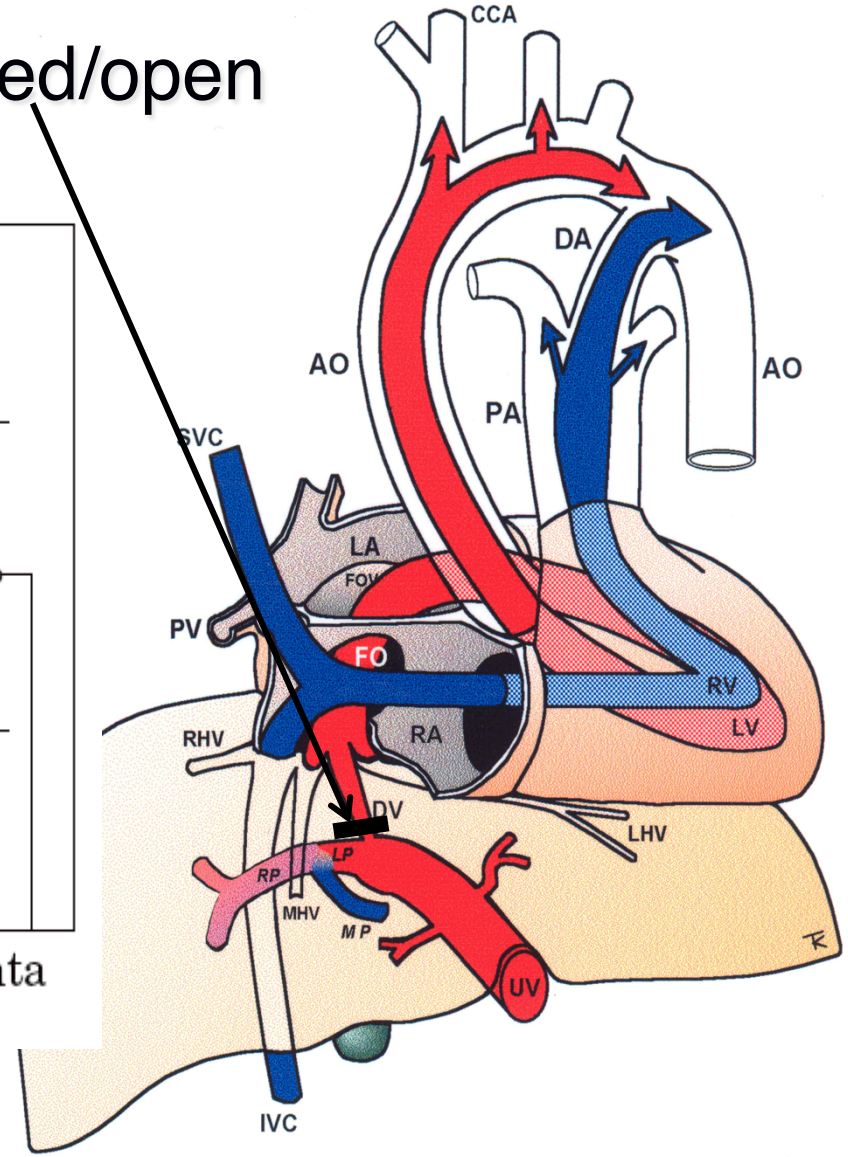




Tchirikov M et al.
Placenta 2002; 23: S153-8

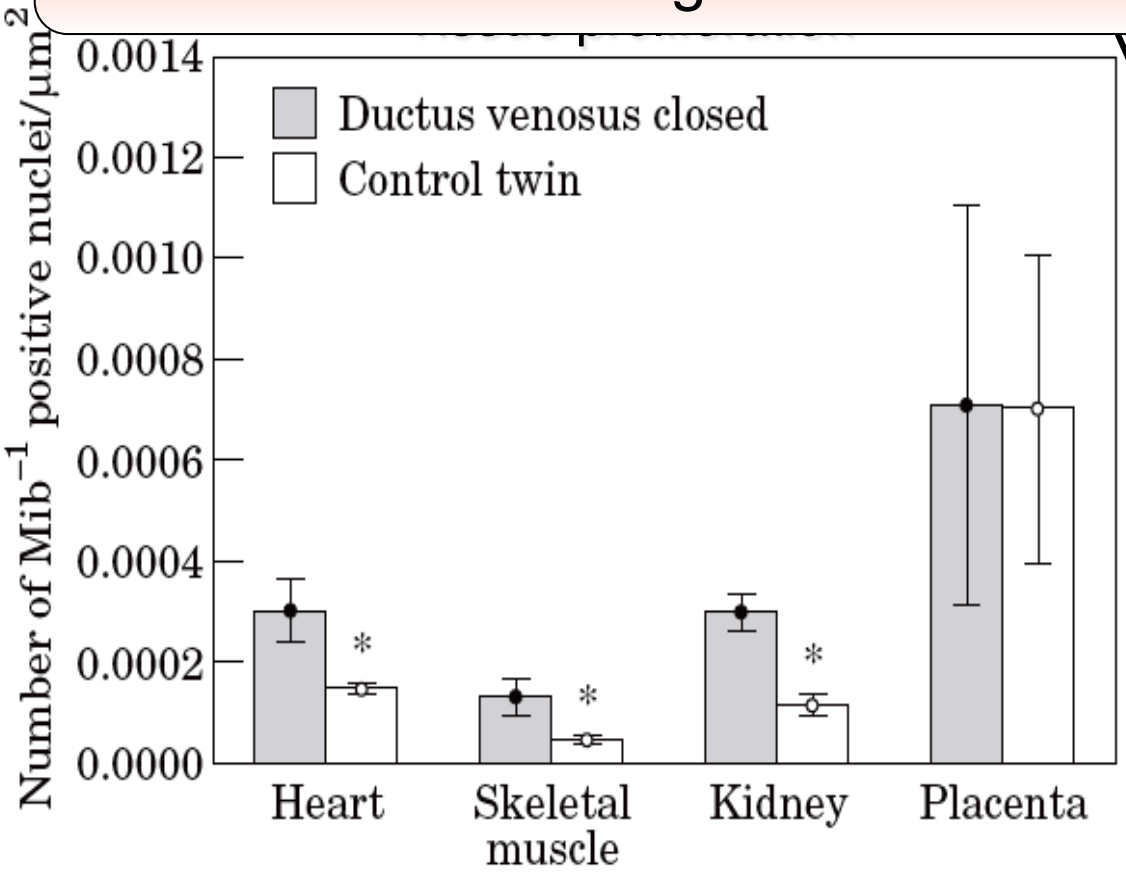
Ductus venosus shunting blocked/open

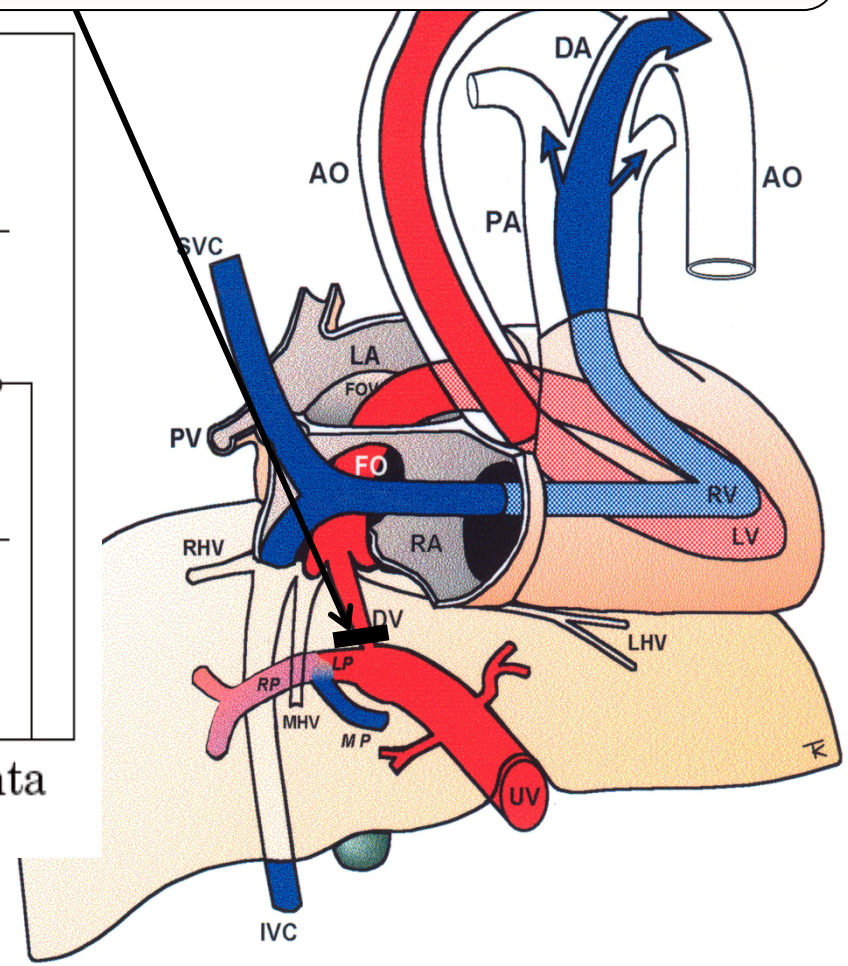




Tchirikov M et al.
Placenta 2002; 23: S153-8

5. No growth without a fetal liver that senses placental resources and assigns individual organ growth





Tchirikov M et al.
Placenta 2002; 23: S153-8

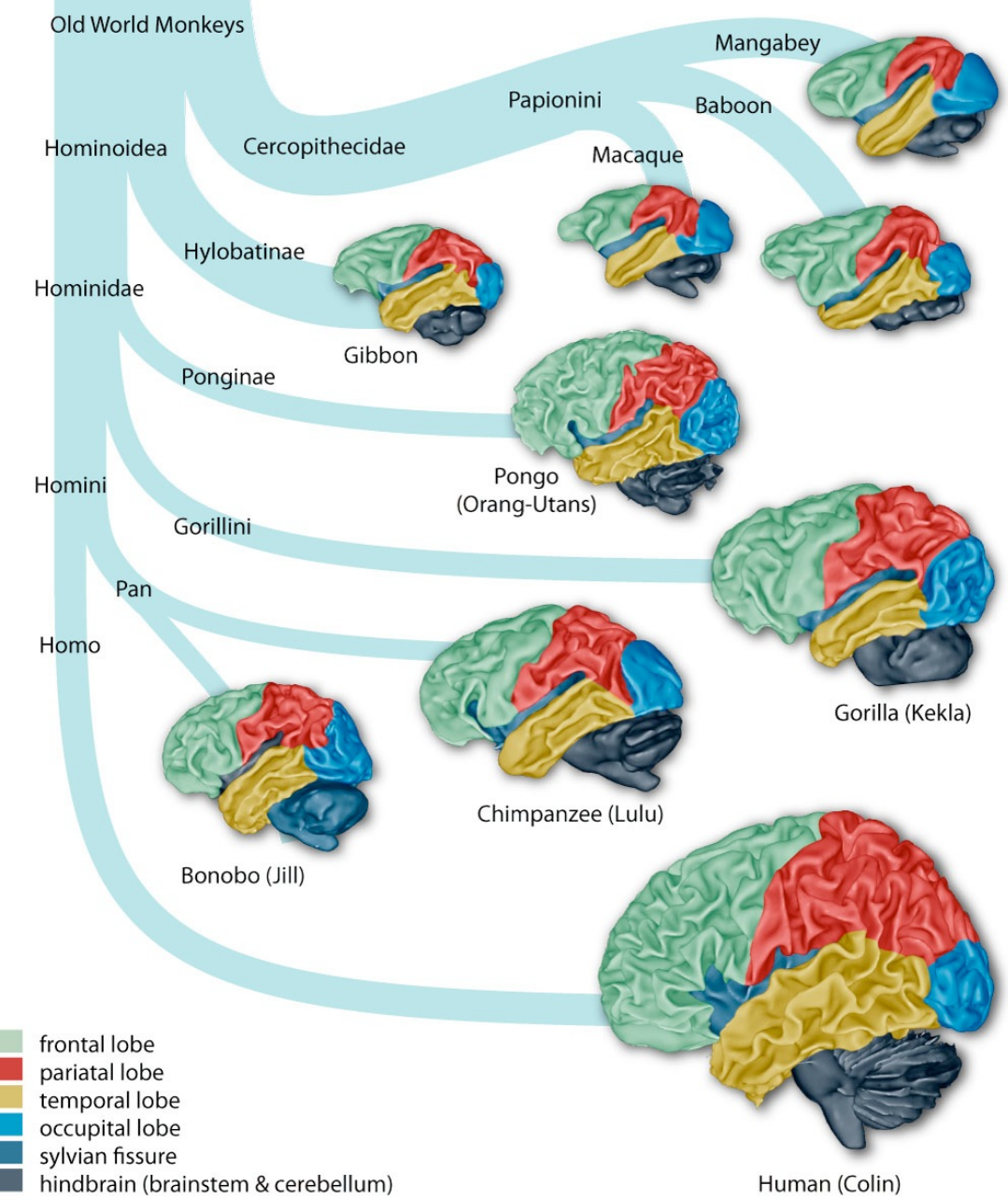
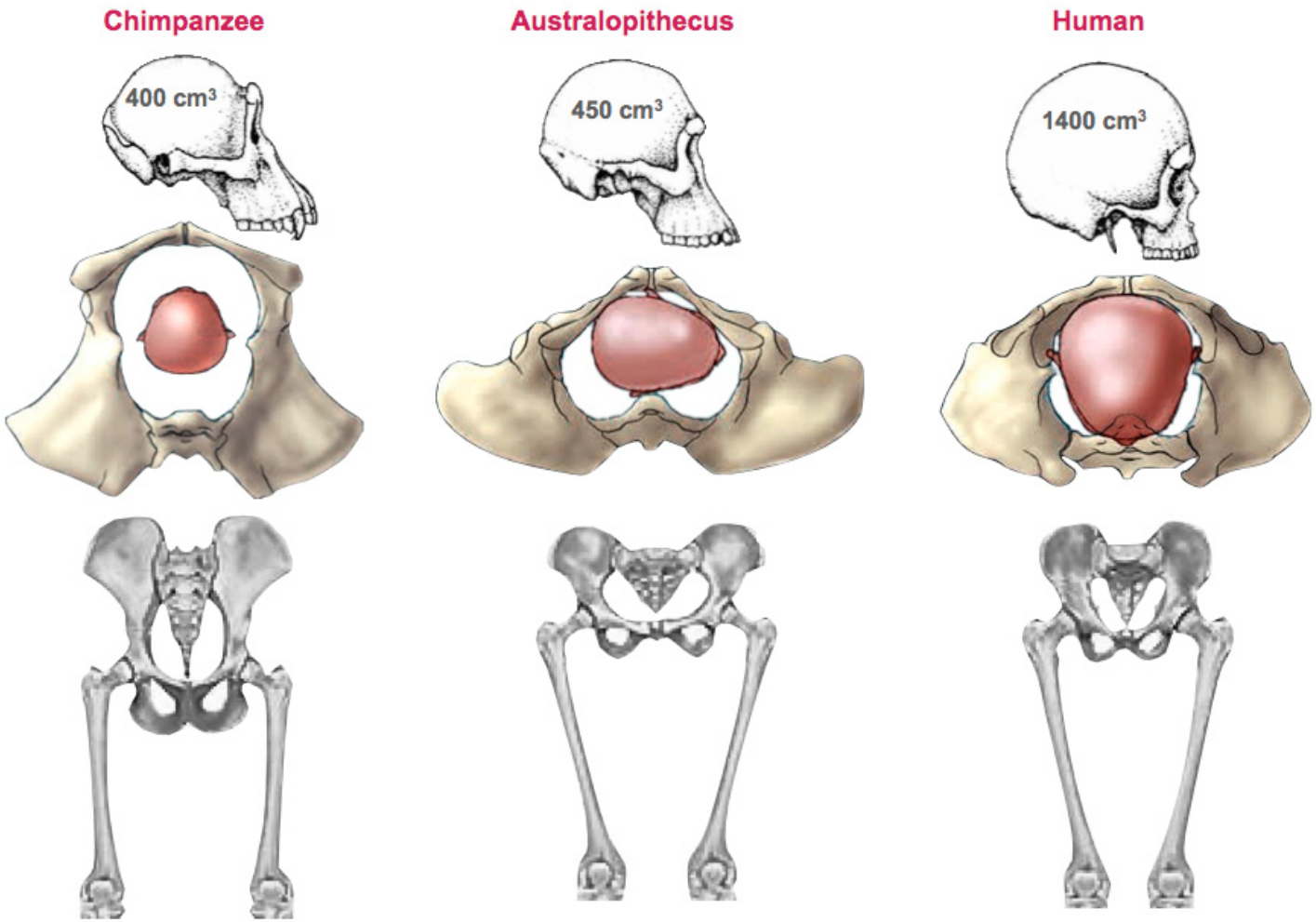
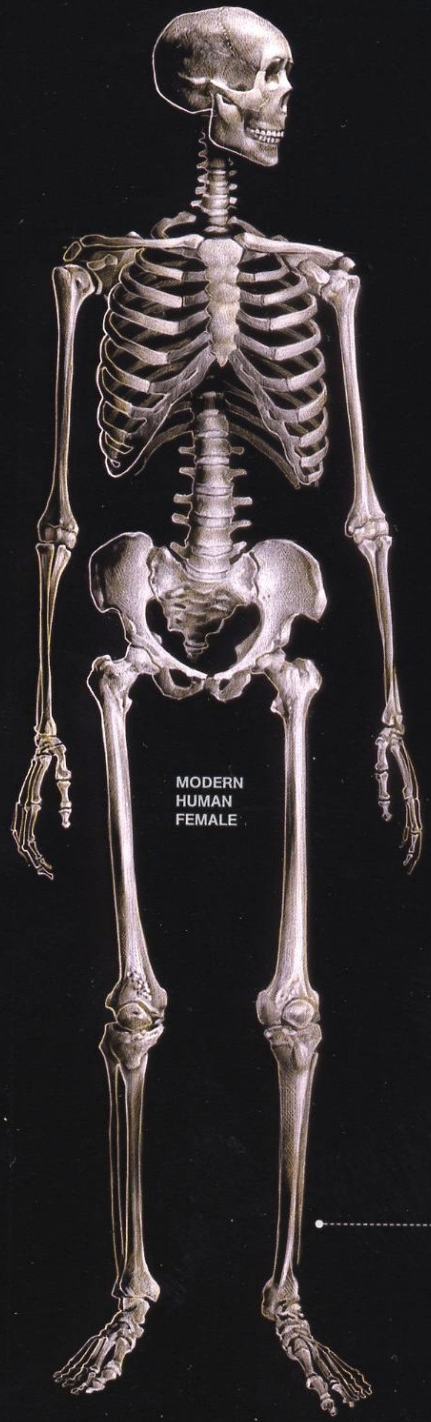


Fig. HE: Visualization of evolution of brains in primates based on the inner surface. The lobes, the sylvian fissure and the hindbrain (brainstem and cerebellum) are colorized for better orientation.

© 2009 Dahnke@http://dbm.neuro.uni-jena.de



Mesiano S & Welsh T: Progesterone and control of human pregnancy and parturition. Fetal Matern Med Rev 2009; 20: 97-118.



NEANDERTHAL SKELETON

Neanderthal skulls were long and low, but held brains slightly larger on average than those of living humans.

Wide bodies conserved heat in cold climates, while large, conical rib cages housed big lungs needed for high levels of activity.

Sturdy, heavily muscled limb bones evolved in response to a demanding lifestyle.

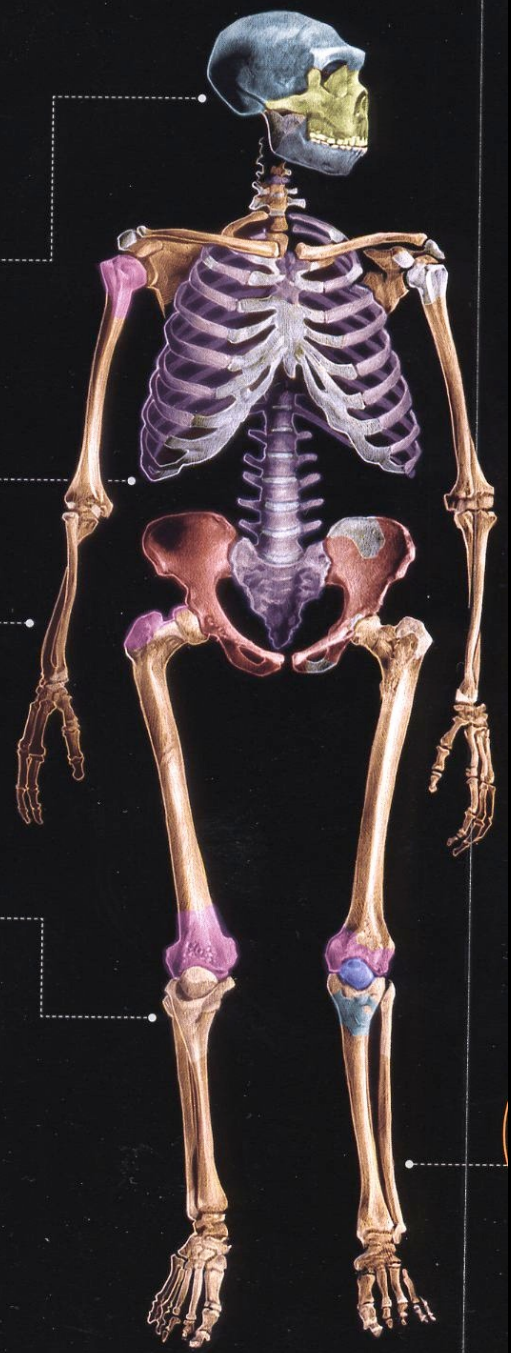
Large muscles positioned to maximize leverage resulted in exceptional strength.

Short limbs helped reduce surface area to retain body heat.

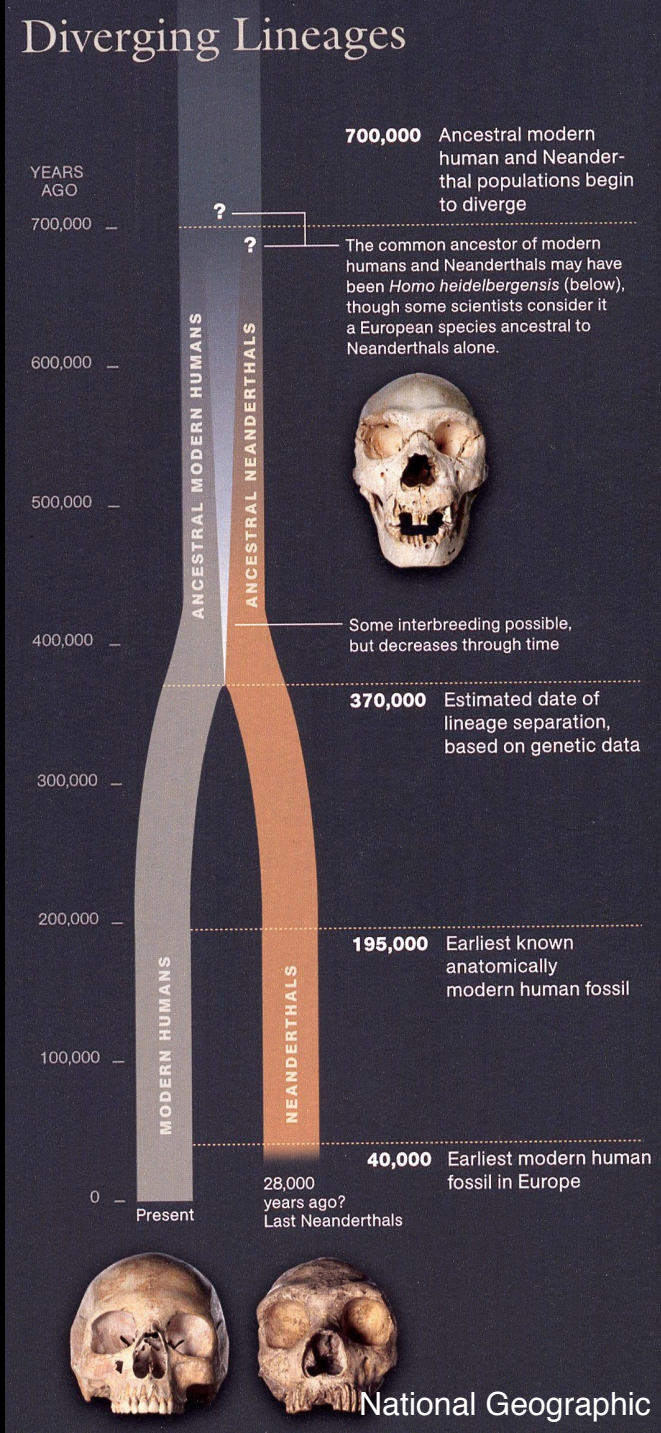
DAILY CALORIC NEEDS

2,200 cal/day

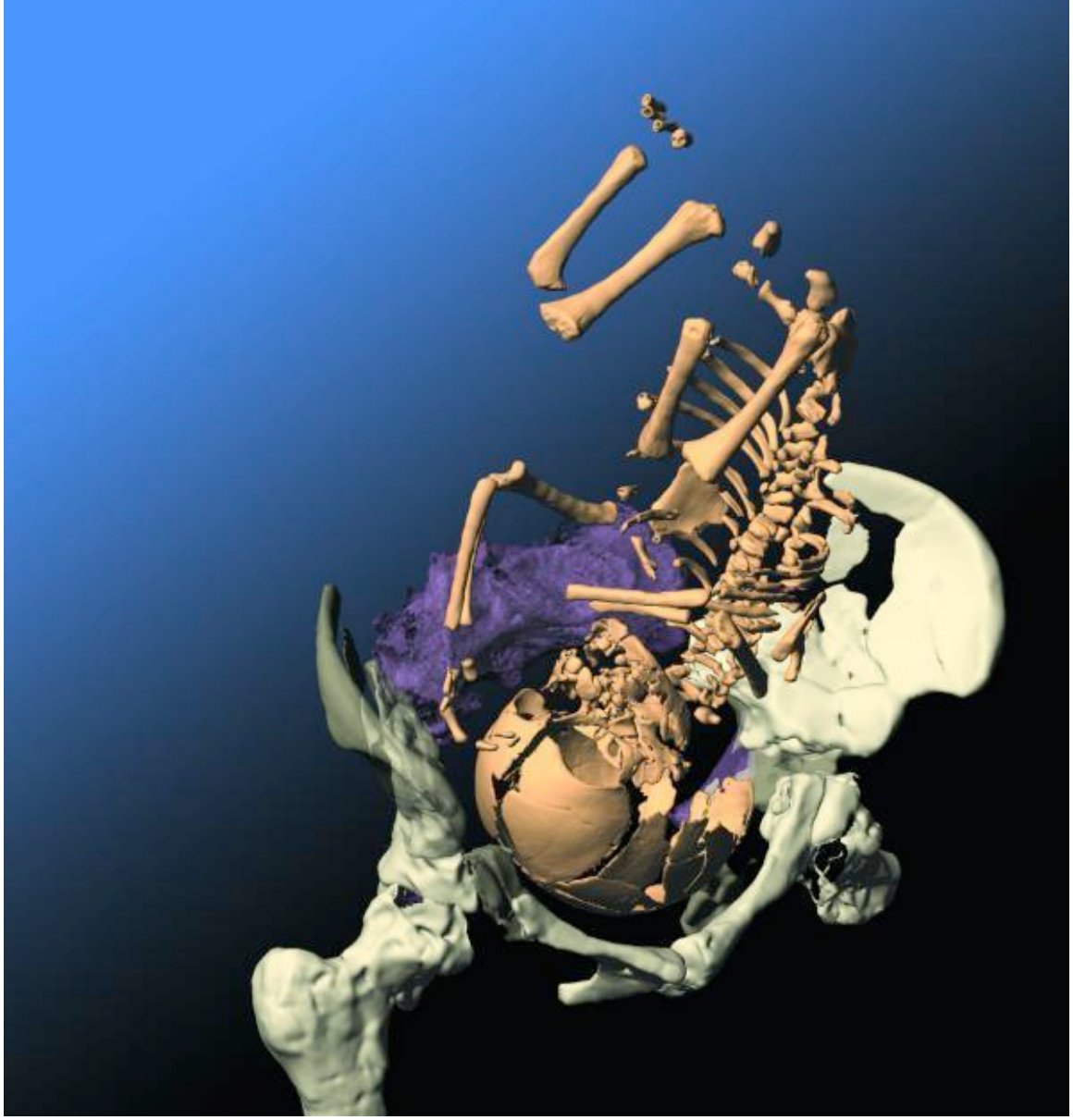
** USDA recommendation for female of average size (5'4" tall, 138 pounds) who engages in light-to-moderate activity*



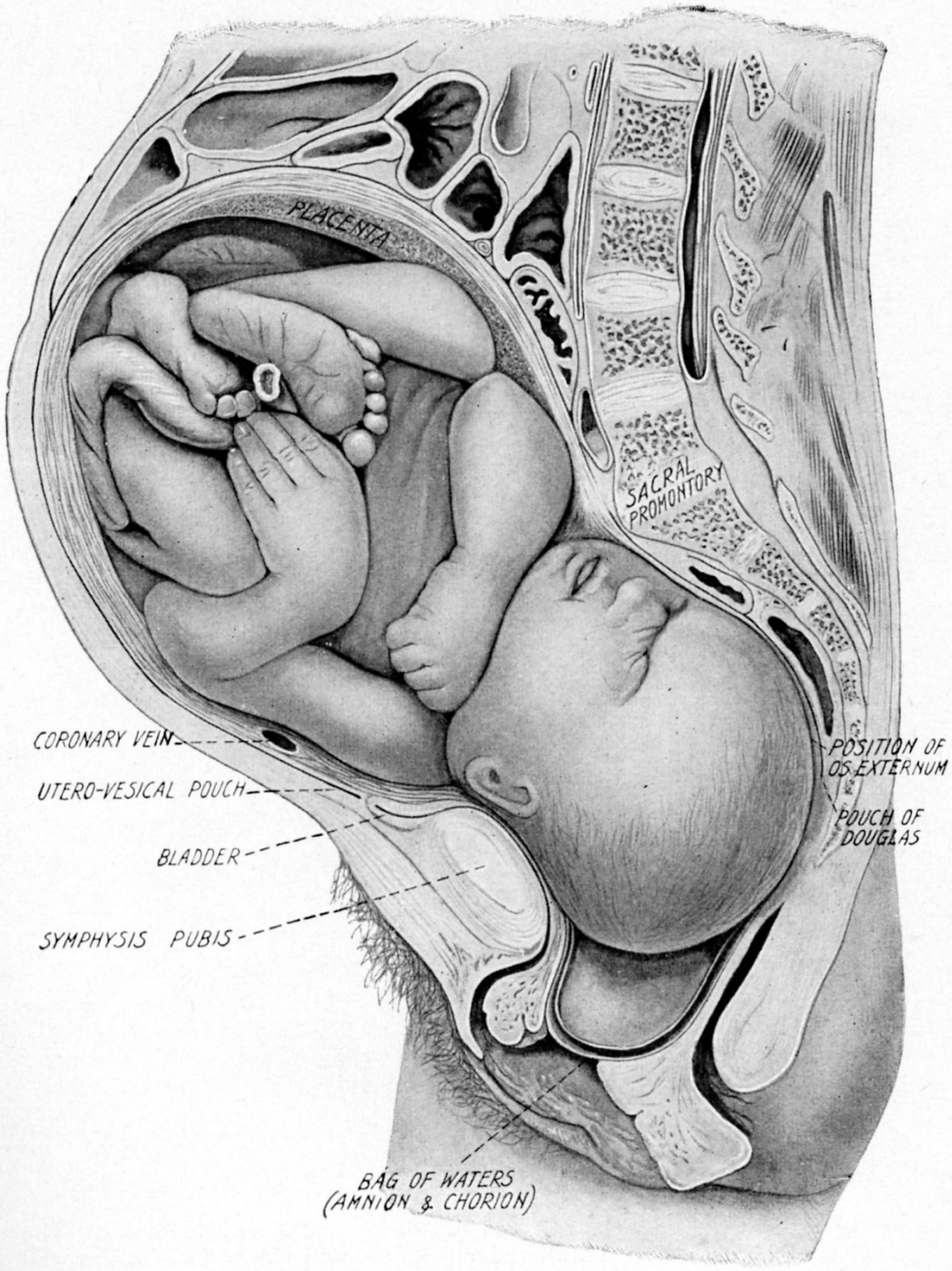
Diverging Lineages



National Geographic



Dr. Marcia Ponce de León and Prof. Christoph Zollikofer. Zurich
www.sciencedaily.com/releases/2008/09/080908203013.htm



Holland & Brewer
Manual of Obstetrics, 1969

Sex of the neonate involved in the obstructed labour and the previous

Boys in obstructed labour: 77% (95%CI 73.3-80.1)

Boys in previous labour: 44.6% (95%CI 38.6-50.6)

Stillbirth rate (obstructed labour)

Boys 91.9% (89.3-94.5) vs. girls 78.9% (75.1-82.7)

Muleta M et al. Acta Scand Obstet Gynecol 2010

6. Still a high evolutionary pressure for a larger brain

Boys in obstructed labour: 77% (95%CI 73.3-80.1)

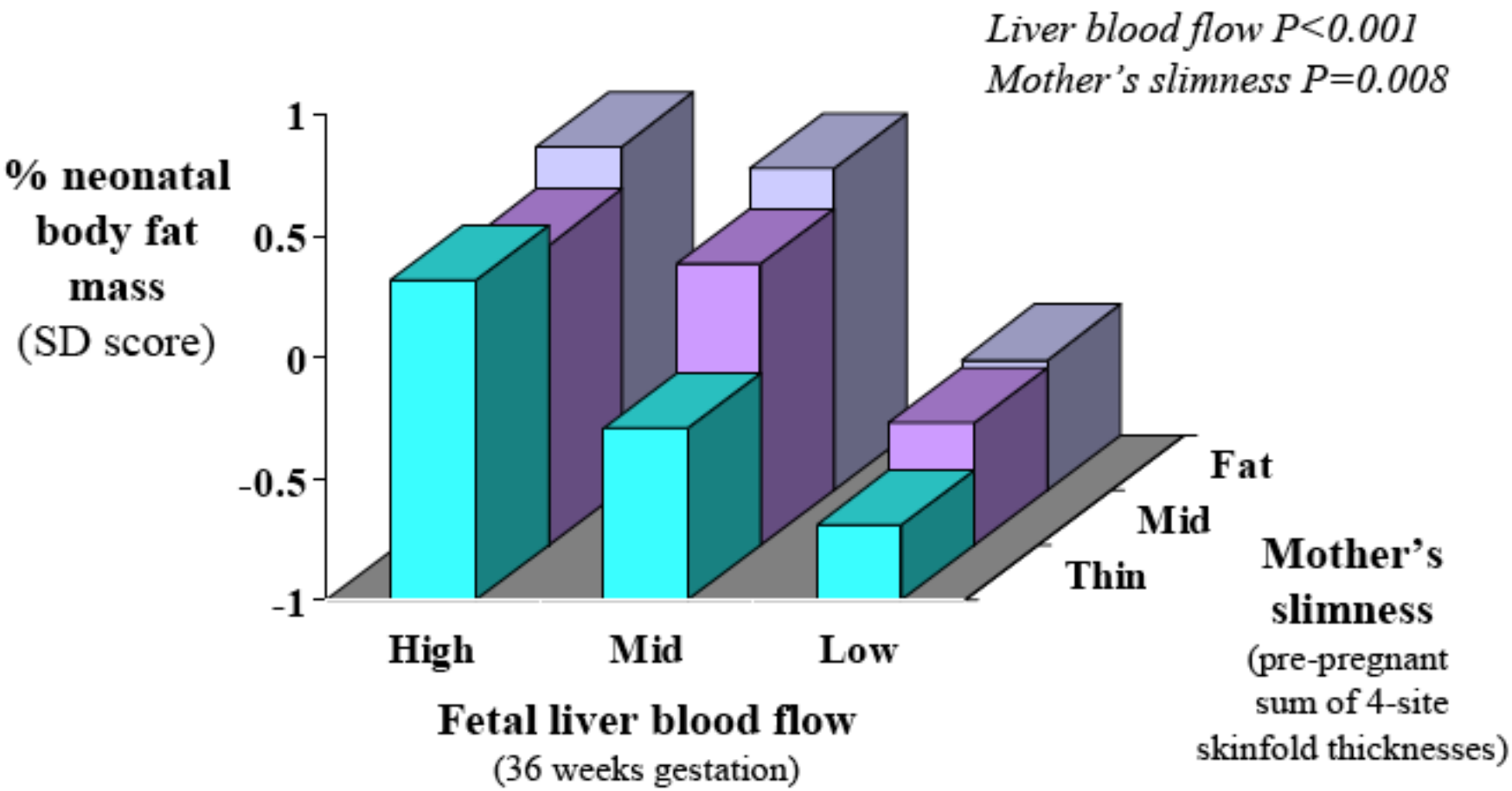
Boys in previous labour: 44.6% (95%CI 38.6-50.6)

Stillbirth rate (obstructed labour)

Boys 91.9% (89.3-94.5) vs. girls 78.9% (75.1-82.7)

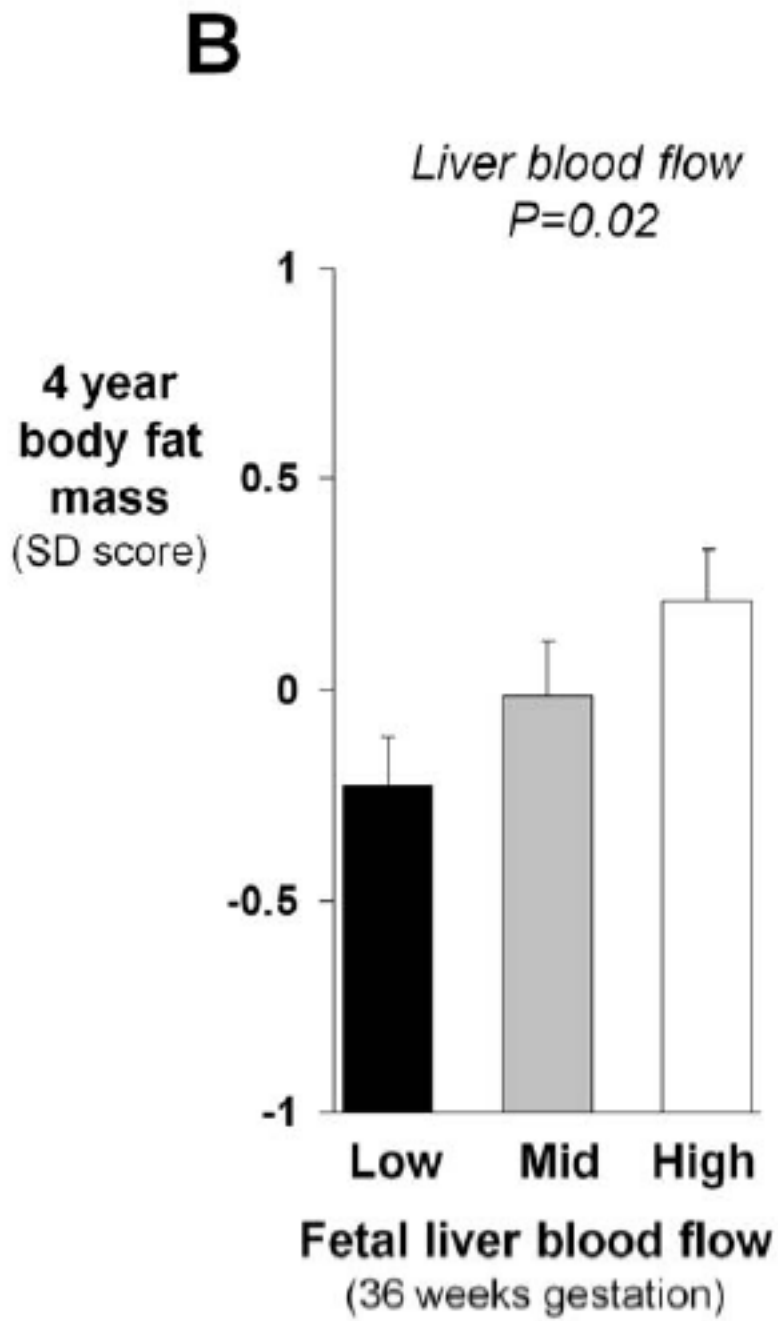
Muleta M et al. Acta Scand Obstet Gynecol 2010

Fetal liver blood flow, maternal slimness and neonatal body fat



Godfrey KM & al.
PLoS One 2012; 7(8): e41759

Fetal liver blood flow, maternal adiposity and neonatal body fat



Godfrey K et al. PLoSONE 2013

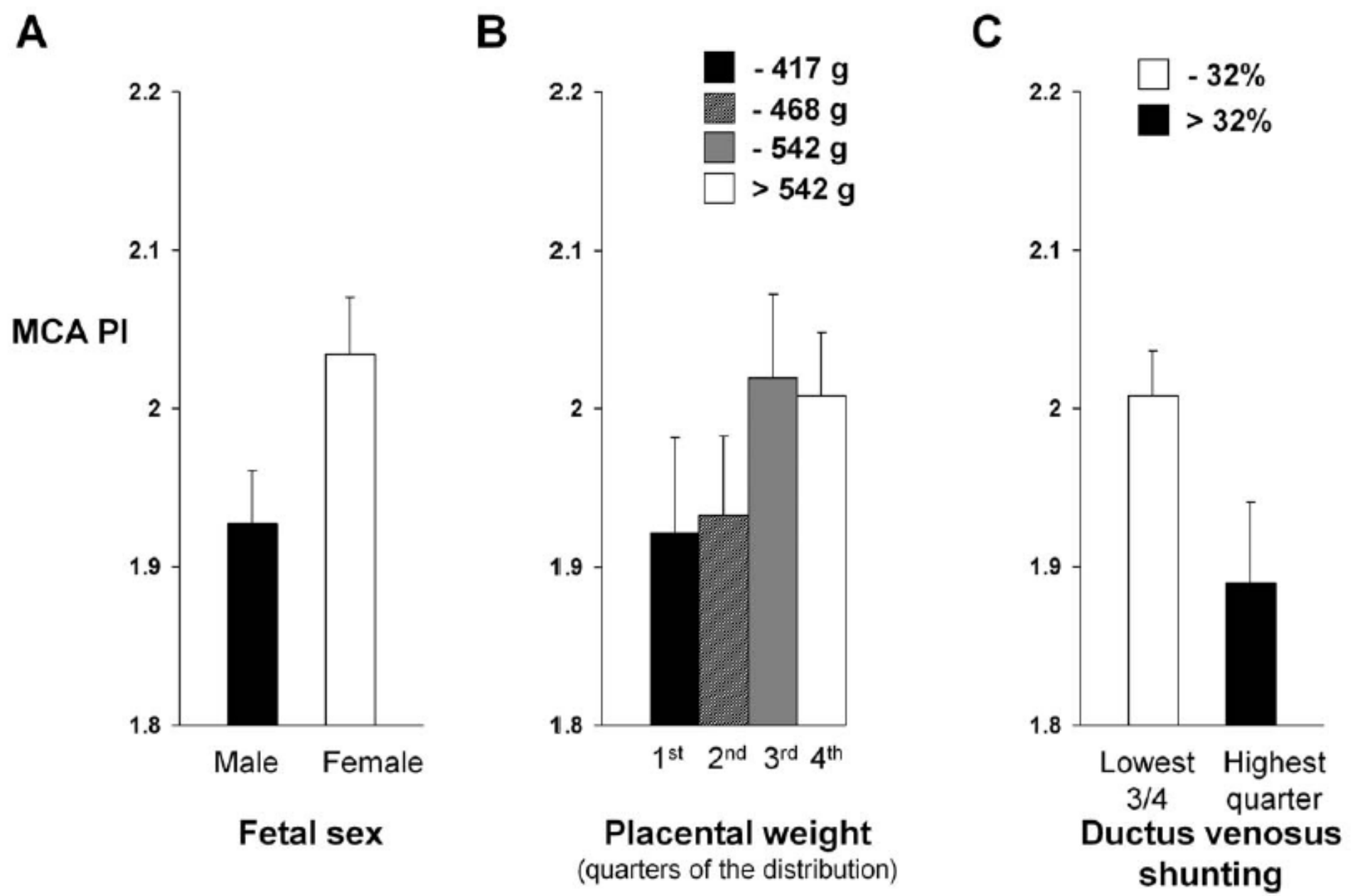
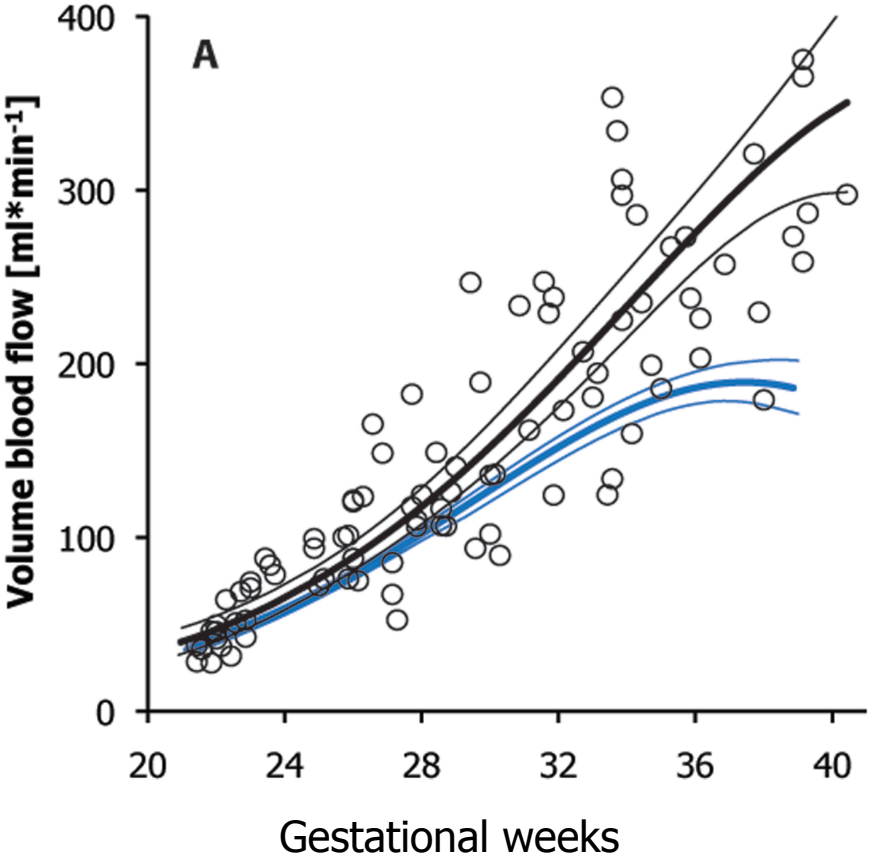


Figure 2. Brain-sparing blood flow pattern in relation to fetal sex, placental weight and liver shunting.

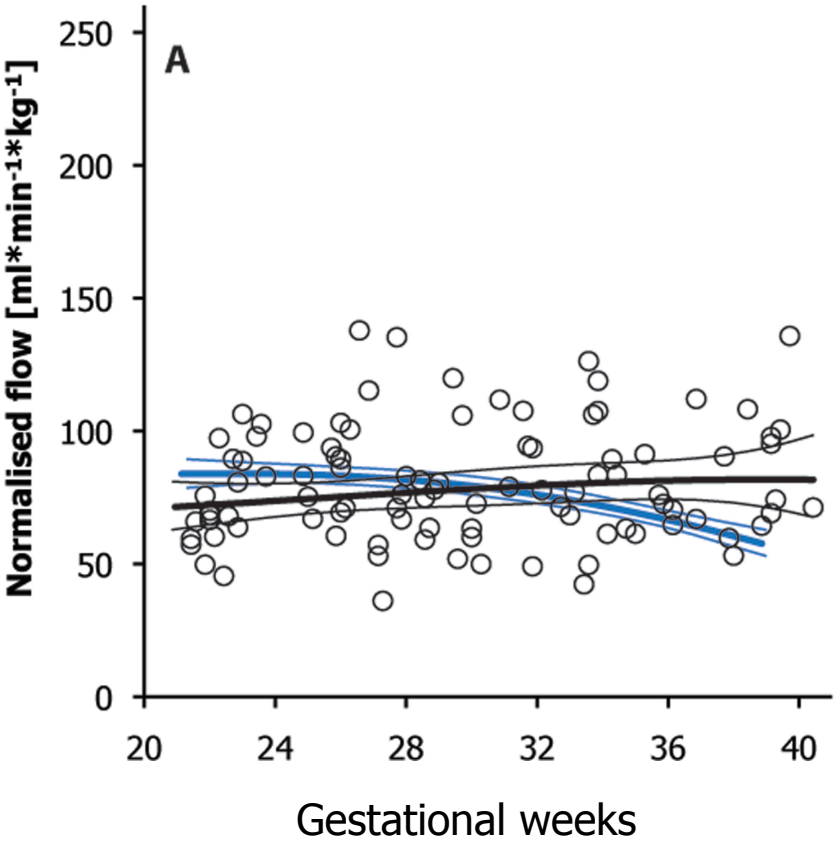
Godfrey K et al. PLoSONE 2013

Venous liver flow in macrosomic (black) vs reference fetuses (blue)

Venous liver flow

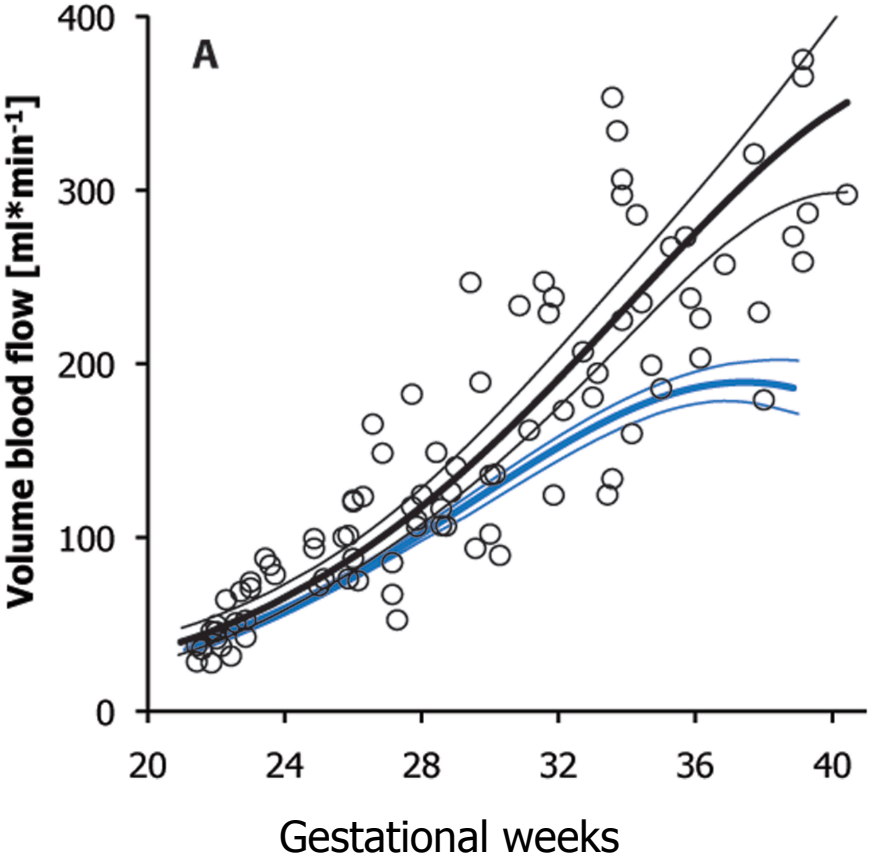


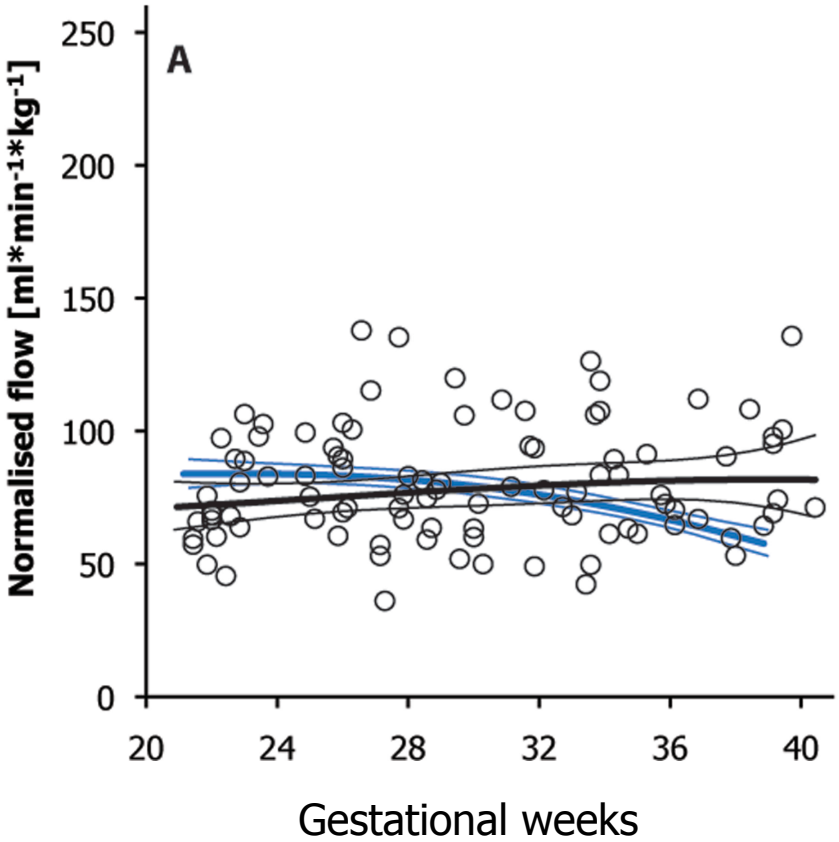
Venous liver flow
normalised for fetal weight



Kessler J et al. 2010

7. There is a delicate equilibrium between brain and liver circulation graded across the entire normal population.





Kessler J et al. 2010

Conclusion

Brain is prioritised during placental compromise/hypoxia.

Fetal liver is also a prioritised organ that monitors nutritional availability and regulates organ growth.

Both liver and brain are downregulated during compromise.

There is a careful interplay between liver and brain graded across the entire population to adapt to maximum fitness, survival and a large brain.

Thank you!