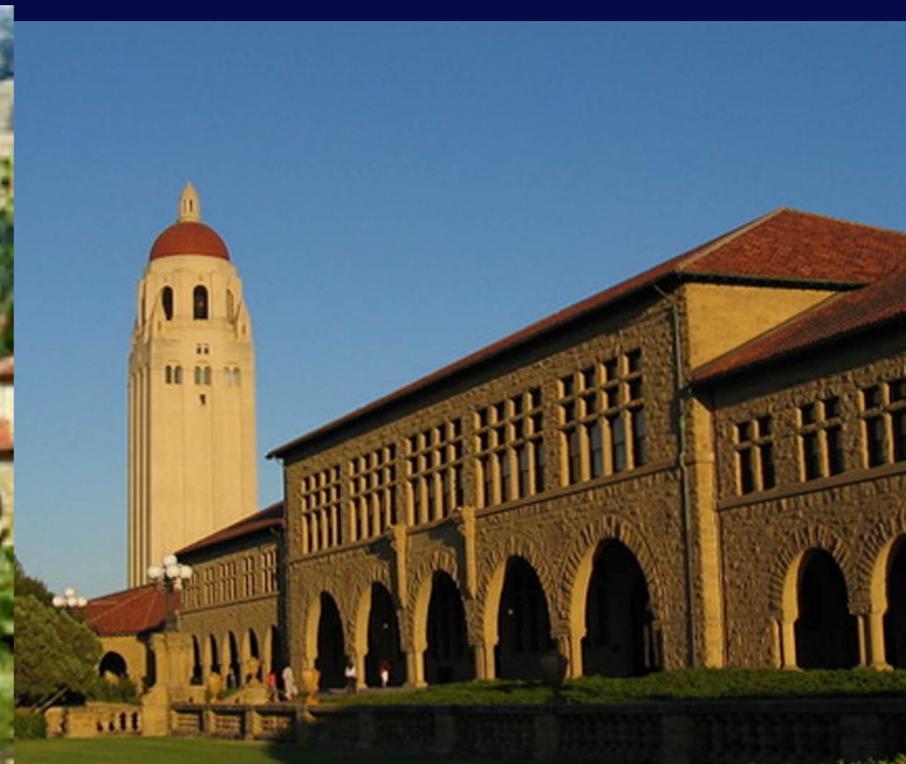


# Ductus Arteriosus: Dilemmas of Treatment vs. No Treatment in the Premature Neonate

No Disclosures.



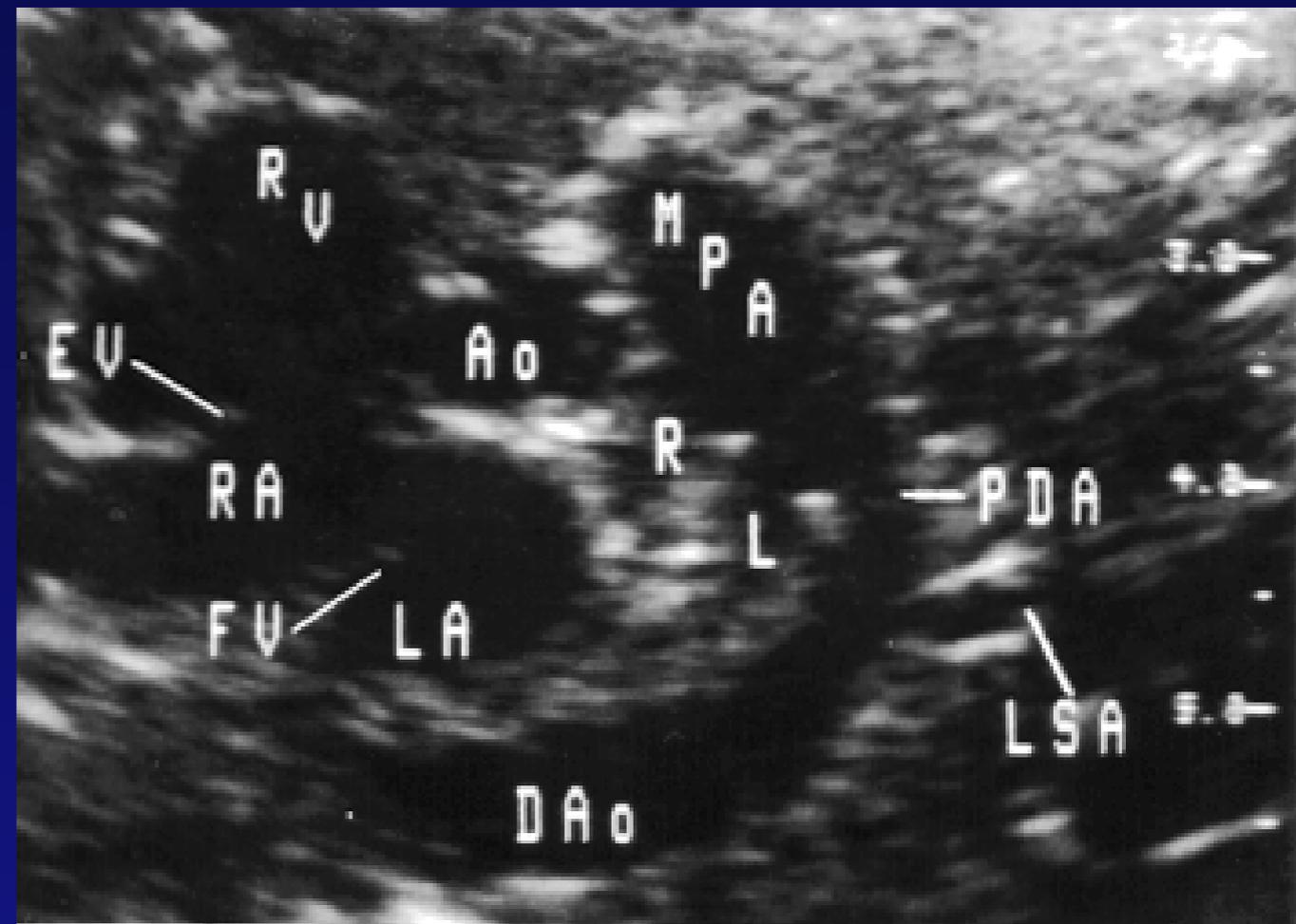
Norman H Silverman MD. D Sc (Med), FACC, FASE, FAHA.

Professor of Pediatrics ( Cardiology) U.C. San Francisco,

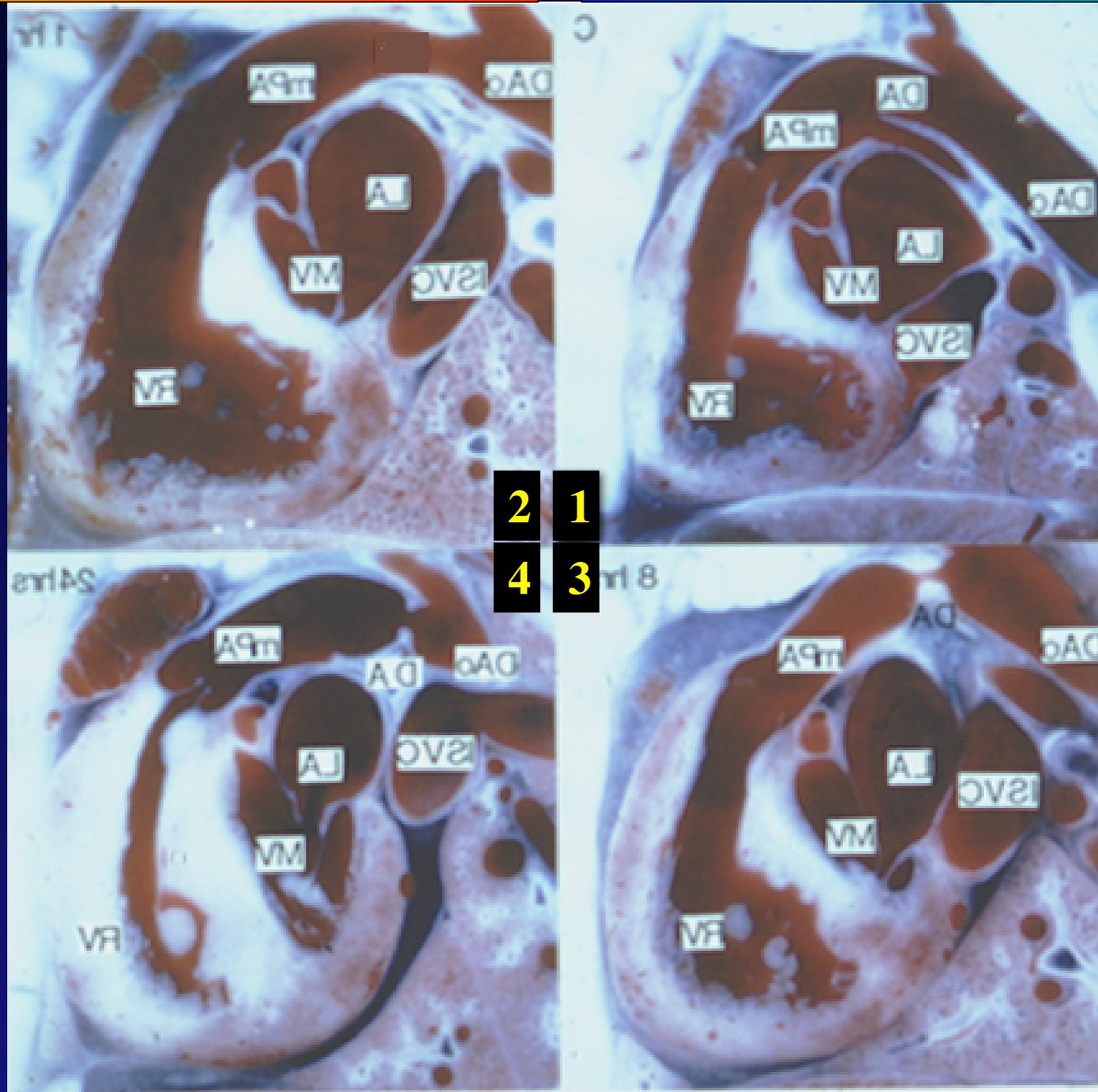
Professor Emeritus, Stanford University



# Where is the Ductus

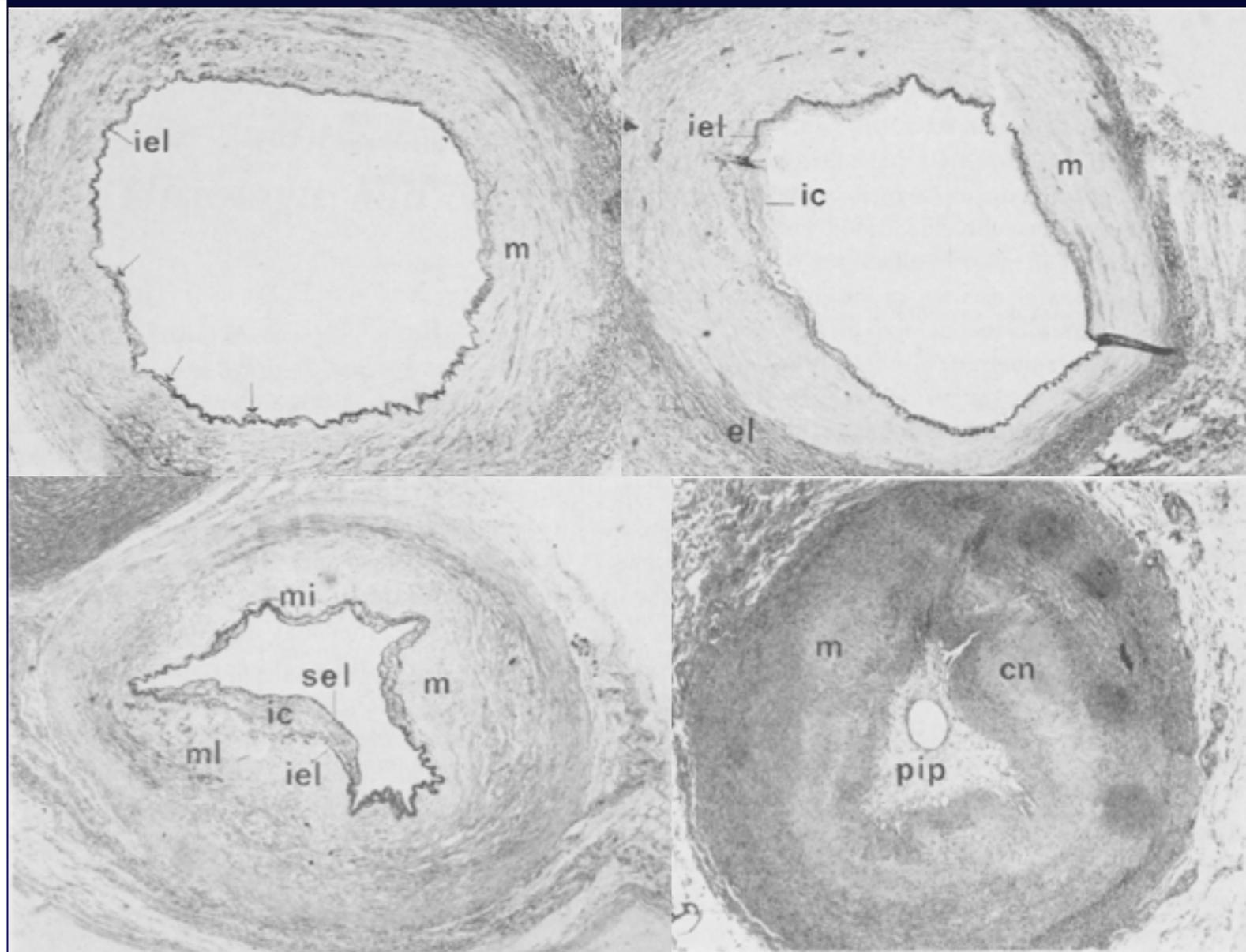
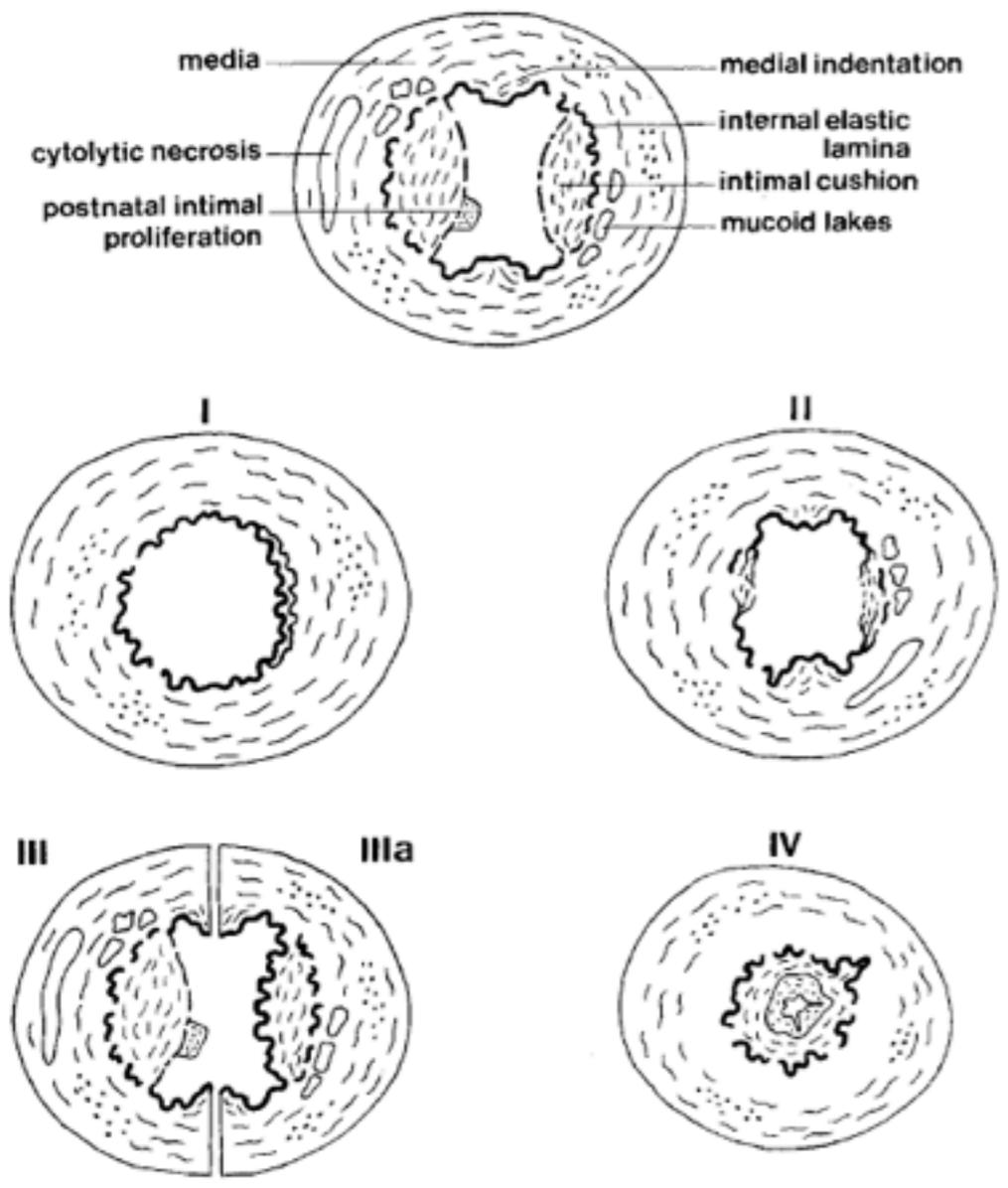


# Rat Patent Ductus



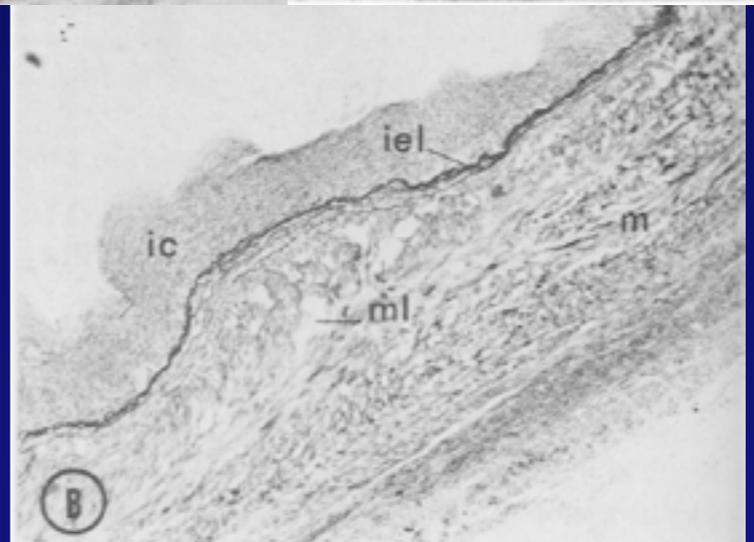
Momma

# The Course & Histology of Ductus



## ***The ductus arteriosus in the preterm infant: Histologic and clinical observations***

**Adriana C. Gittenberger-de Groot, M.D.,\* Ingrid van Ertbruggen, M.D.,  
Andr~ J.M.G. Moulart, M.D., and Eric Harinck, M.D.,**



# The Problem in Perspective

- ♥ In reality prematurity is a multisystem disorder of every organ and the consequences of immaturity in one organ may have consequences for many other organs.
- ♥ The premature infant with a patent ductus arteriosus has problems due to immaturity of most physiological processes—respiration, absorption and nutrition, central nervous system, circulation, renal function, electrolyte balance, and metabolism— all of which occur even in the absence of a patent ductus arteriosus
- ♥ As a result, it is difficult to know what contribution the patent ductus arteriosus is making to the infant's problems, and therefore difficult to decide if the ductus should be closed and if closure has made a difference to the child's course. Early experience after closure of the ductus in premature infants has shown that expectations of normality after closure of the patent ductus arteriosus are unrealistic.
- ♥ PDA may remain asymptomatic in the face of respiratory disease. Is the big ductus shunt affecting the infant? This is the hardest question to answer, because none of the findings listed above can tell us how well the left ventricle is compensating. Failure to distinguish between a large but well compensated shunt and a shunt that is causing problems is at least part of the reason why closing the ductus may not appear to be useful therapy.

# Management of Patent Ductus Arteriosus in Preterm Infants—Where Do We Stand?

*Congenit Heart Dis.* 2013

Souvik Mitra, MD,\* Arild Rønnestad, MD, PhD,<sup>†</sup> and Henrik Holmstrøm, PhD<sup>‡</sup>

- ♥ In a nutshell we can say that there has been a general shift in the management of PDA in preterm neonates from the “aggressive approach” to a more “conservative approach.”
- ♥ On the basis of available evidences, rationalization and individual emphasis on precise identification of a hemodynamically significant duct seem to be the way forward.

# Incidence of PDA in Preemies

- ♥ 1/100– Live births
- ♥ In Preemies 8/1000
- ♥ In healthy preterm neonates >30 weeks gestation, PDA closes by day 4 in 90% and by day 7 in 98%
- ♥ <24 weeks gestation babies stand at a dismal 8% and 13% by day 4 and day 7, respectively
- ♥ In 50–70% of preterm infants with birth weight <1,500 g. the ductus remains patent
- ♥ Among infants less than 1500 g who still have a PDA at the time of hospital discharge, it will spontaneously close by the end of the first year in 86% of the infants
- ♥ Among infants <27 weeks of gestation, with a PDA at the time of hospital discharge, 75% of the infants spontaneously close the duct by the end of the first year.





# William E Benitz of Stanford.



Learning to live with patency of the ductus arteriosus in  
Journal of Perinatology (2011) 31, S42–S48  
preterm infants

Five decades after the recognition of delayed closure of the ductus in preterm infants, management remains heterogeneous and controversial. Routine early treatment to close the ductus does not appear to be beneficial, but selective later treatment may still prove valuable. The timing, criteria, objectives and methods for such treatments remain to be established. Potential strategies for minimizing the adverse effects of PDA while awaiting spontaneous closure or achievement of treatment criteria need careful evaluation in clinical trials.

Elimination of ductal shunting and its consequences by surgical ligation or by induction of ductal constriction with cyclo-oxygenase (COX) inhibition promised to ameliorate the adverse outcomes associated with ductal patency. However, neither individual randomized controlled trials nor meta-analyses of those trials? have confirmed this hypothesis.



**Stanford**  
M E D I C I N E

# Evidence For and Against Treatment of Patent Ductus Arteriosus in Preterm Infants

William E. Benitz, M.D.

Philip Sunshine Professor in Neonatology

Chief, Division of Neonatal and Developmental Medicine



**Stanford**

Children's Health

Lucile Packard  
Children's Hospital  
**Stanford**

**William E. Benitz, MD, FAAP,**

# Evidence For and Against Treatment of Patent Ductus Arteriosus in Preterm Infants

## Non-Randomized Studies Since 2009

**Green:** Study supports PDA treatment    **Red:** Study does not support PDA treatment

---

Hsiao 2009	Mallya 2012	DeMauro 2013	Gudmundsdottir 2015
Madan 2009	Mirea 2012	Jawa 2013	Ibrahim 2015
Jhaveri 2010	Moore 2012	Kaempf 2013	Isayama 2015
Natarajan 2010	Olsson 2012	Ko 2013	Janz-Robinson 2015
Tefft 2010	Saldeno 2012	Fonseca 2014	Rolland 2015
Yoshimoto 2010	Sirc 2012	Mondal 2014	Roze 2015
Badalyan 2011	Tantraworasin 2012	Sadeck 2014	Schena 2015
Letshwiti 2011	Tauzin 2012	Sung 2014	Lainwala 2016
Pelausa 2011	Wickremasinghe 2012	Youn 2014	Resende 2016
Dani 2012	Candel-Pau 2013	Chen 2015	Tashiro 2016

---

**William E. Benitz, MD, FAAP,**

Benitz 2016 (unpublished analysis)

# Evidence For and Against Treatment of Patent Ductus Arteriosus in Preterm Infants

Persistent patency of the ductus arteriosus is associated with a variety of untoward outcomes in preterm infants.

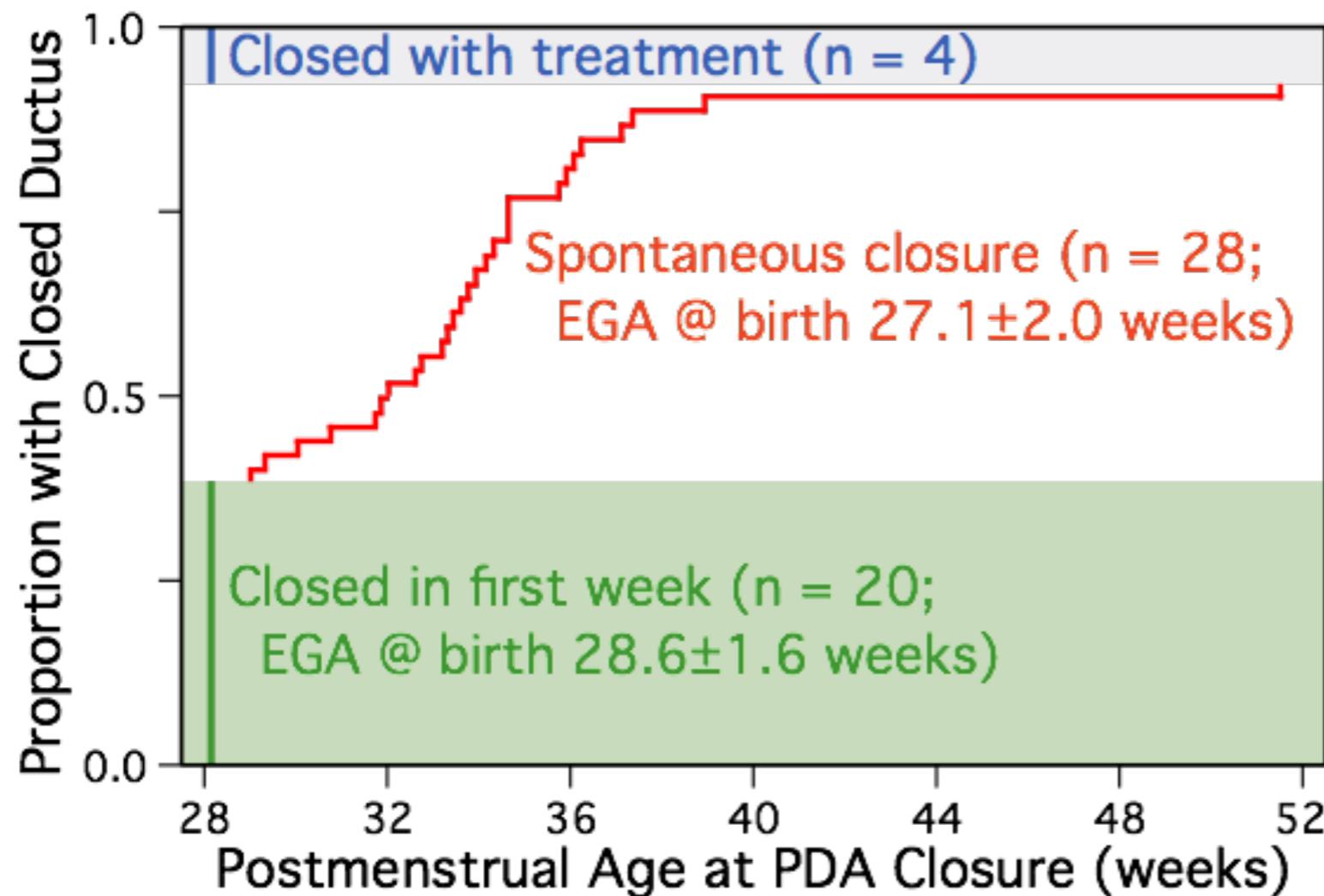
Medical and surgical treatments are effective in achievement of ductal closure.

The critical question is whether medical or surgical PDA closure mitigates any untoward outcome.

# Evidence For and Against Treatment of Patent Ductus Arteriosus in Preterm Infants

## Natural History of Ductal Closure in Preterm Infants

Timing of Closure in 52 Infants < 1500 g\*



### PDA Closure\*\*

Vanhaesebrouck 2007 (n=109):  
Spontaneous 94%, Rx 6%

Nemerofsky 2008 (n=65)  
Spontaneous 64%, Rx 28%

Sirc 2012 (n=198):  
Spontaneous 89%, Rx 7%

Chen 2015 (n=52):  
Spontaneous 92%, Rx 8%

Rolland 2015 (n=103):  
Spontaneous 77%, Rx 1%

\* Not representative of complete birth cohort

\*\* proportion of survivors

# Evidence For and Against Treatment of Patent Ductus Arteriosus in Preterm Infants

## Conclusions

- Neither randomized trials nor meta-analysis of randomized trials have demonstrated any reproducible short- or long-term benefits from treatment to close the patent ductus arteriosus.
- There is substantial evidence that PDA treatment *is not* beneficial, *not* simply an absence of evidence that it *is*.
- Absence of effects of treatment cannot reasonably be attributed to open-label treatment of control subjects in those studies, nor can they be discounted as including too few ELBW/ELGAN infants.
- Nonrandomized clinical studies provide only scant, weak evidence to suggest a benefit that is not evident in randomized trials.
- Any treatment intended to close PDA constitutes an unproven therapy, which is not supported by empiric evidence.

William E. Benitz, MD, FAAP, COMMITTEE ON FETUS AND NEWBORN

**To cite:** Benitz WE and COMMITTEE ON FETUS AND NEWBORN.

Patent Ductus Arteriosus in Preterm Infants. *Pediatrics*.

2016;137(1):e20153730

American Academy  
of Pediatrics



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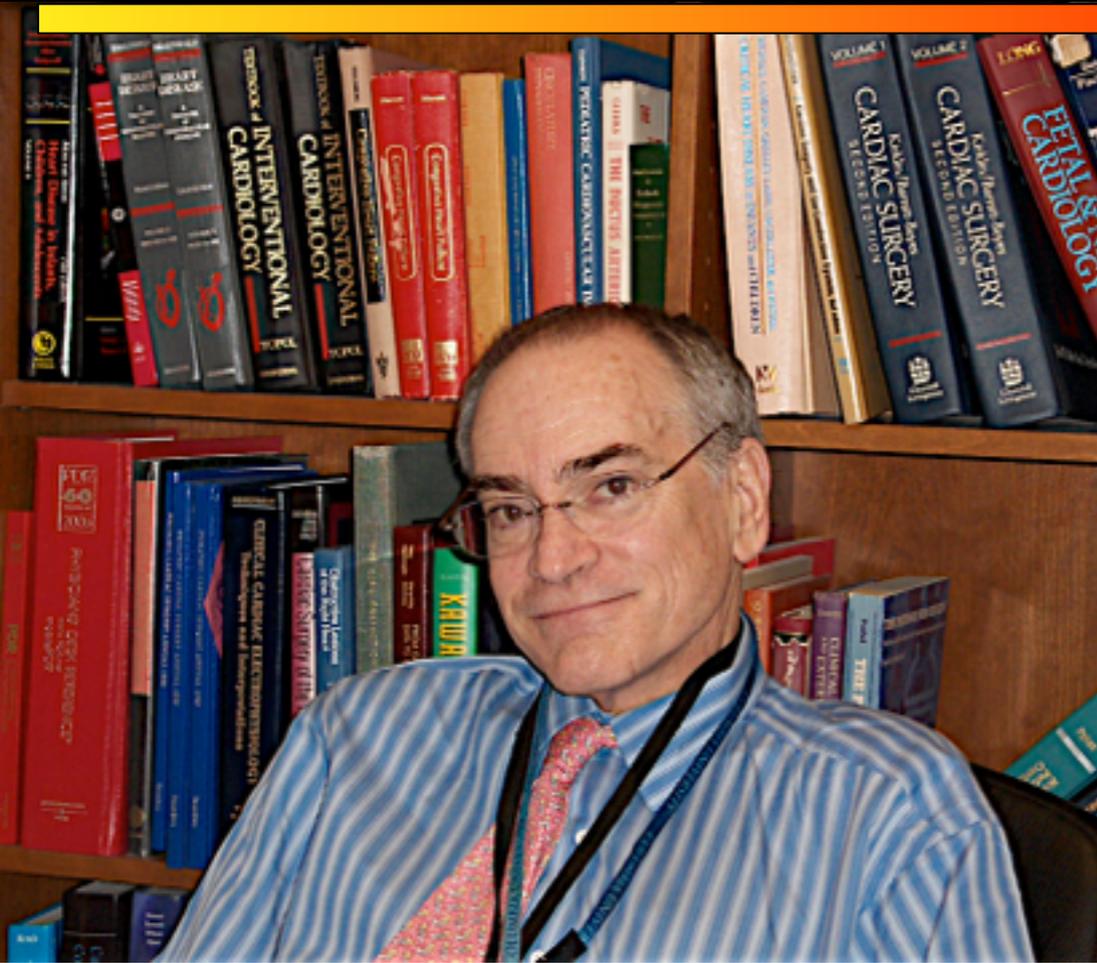
**A large body of evidence now exists demonstrating that early, routine treatment to induce closure of the ductus in preterm infants, either medically or surgically, in the first 2 weeks after birth does not improve long-term outcomes**

**The role of more selective use of medical methods for induction of ductal closure, either for defined high-risk infants in the first 2 postnatal weeks, or more generally, for older infants in whom the ductus remains patent, remains uncertain and requires further study.**

**Prophylactic use of indomethacin may be appropriate in settings where rates of IVH are high or if early, severe pulmonary hemorrhage is common, but may not be justified by expected effects on PDA or by an expectation of better long-term outcomes.**

**There is a lack of evidence to guide management of PDA, necessitating equipoise regarding treatment options and support for parents to permit enrollment of their infants in trials that can expand the available body of evidence.**

# What did Charlie Say?

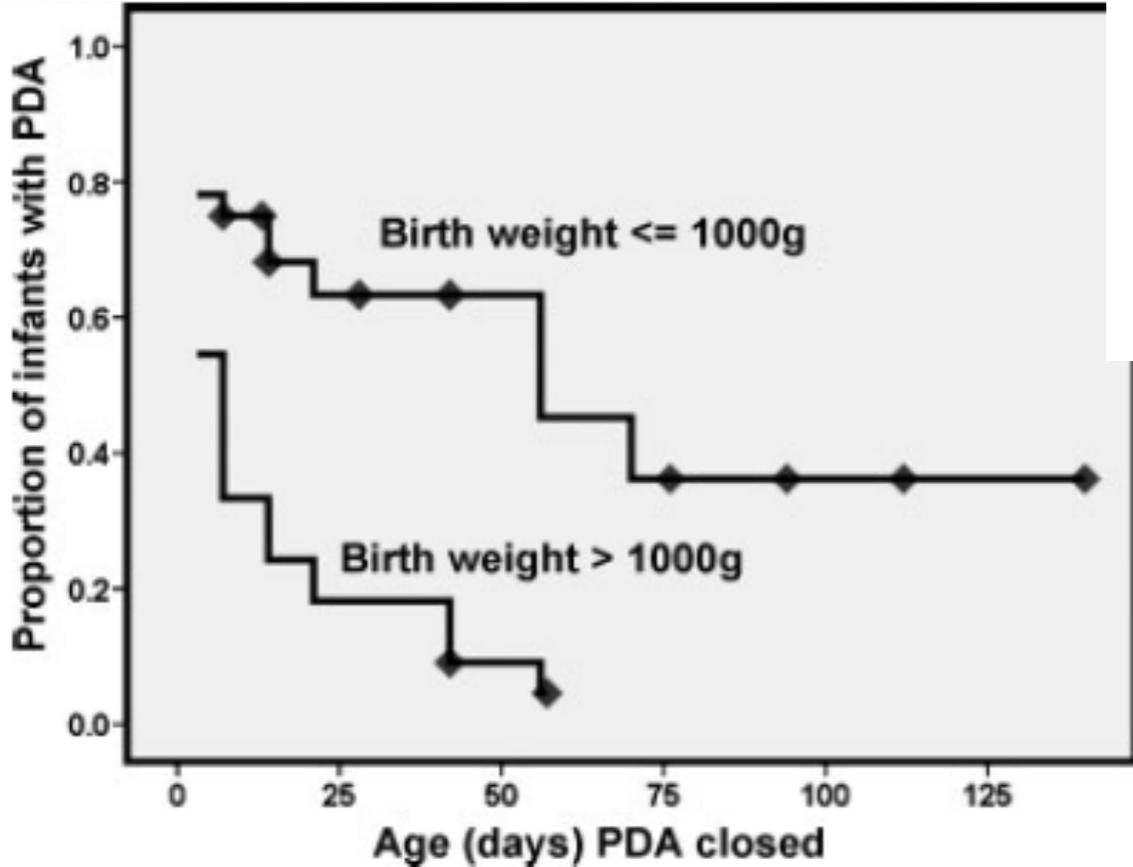


## The Ductus Arteriosus Rarely Requires Treatment in Infants $> 1000$ Grams

Sheri L. Nemerofsky, M.D.,<sup>1</sup> Elvira Parravicini, M.D.,<sup>2</sup> David Bateman, M.D.,<sup>2</sup> Charles Kleinman, M.D.,<sup>3</sup> Richard A. Polin, M.D.,<sup>2</sup> and John M. Lorenz, M.D.<sup>2</sup>

We sought to determine the rate of spontaneous closure of the ductus arteriosus (DA) in very-low-birth-weight infants. This prospective observational study included 65 infants whose birth weight (BW)  $< 1500$  g. Echocardiograms were done on day of life (DOL) 3 and 7, weekly for the first month, and bimonthly until ligation, discharge, or death. Treatment was reserved for infants with heart failure, acute renal impairment, or those with significant persistent or escalating respiratory support. Chi-square tests, Student  $t$  tests, and logistic regression models were used to identify possible associations between spontaneous ductal closure by DOL 7 and predictor variables. Patterns of spontaneous DA closure over time were examined using Kaplan-Meier survival analysis. The DA closed spontaneously in 49% infants by DOL 7. Rates of spontaneous closure by DOL 7 differed significantly by BW strata: 67% for BW  $> 1000$  g, 31% for BW  $\leq 1000$  g ( $p < 0.01$ ). Ninety-seven percent of infants  $> 1000$  g did not require intervention, and the DA closed spontaneously prior to discharge in 94%. In a logistic regression model, only BW  $> 1000$  g and male gender were significantly associated with spontaneous closure by 1 week of life. The median time to spontaneous closure differed significantly between infants in the two BW strata: 7 days for  $> 1000$  g versus 56 days for  $\leq 1000$  g ( $p < 0.001$ ). Intervention for the patent DA in infants  $> 1000$  g BW is rarely indicated. In infants  $\leq 1000$  g BW, deferring treatment decisions until at least 1 week of life may avoid unnecessary treatment exposure.

AMERICAN JOURNAL OF PERINATOLOGY/VOLUME 25, NUMBER 10 2008 PP 661-6



Treatment of the PDA in infants  $> 1000$  g BW is rarely warranted, as nearly all (94%) will spontaneously close and the rate of complications in this population are low. However, among infants  $< 1000$  g BW, the PDA is far less likely to close spontaneously.

# Predictors of bronchopulmonary dysplasia or death in premature infants with a patent ductus arteriosus

Valerie Y. Chock<sup>1</sup>, Rajesh Punn<sup>2</sup>, Anushri Oza<sup>1</sup>, William E. Benitz<sup>1</sup>, Krisa P. Van Meurs<sup>1</sup>, Alice S. Whittemore<sup>2</sup>, Fariborz Behzadian<sup>3</sup> and Norman H. Silverman<sup>3</sup>

Pediatric RESEARCH

Volume 75 | Number 4 | April 2014

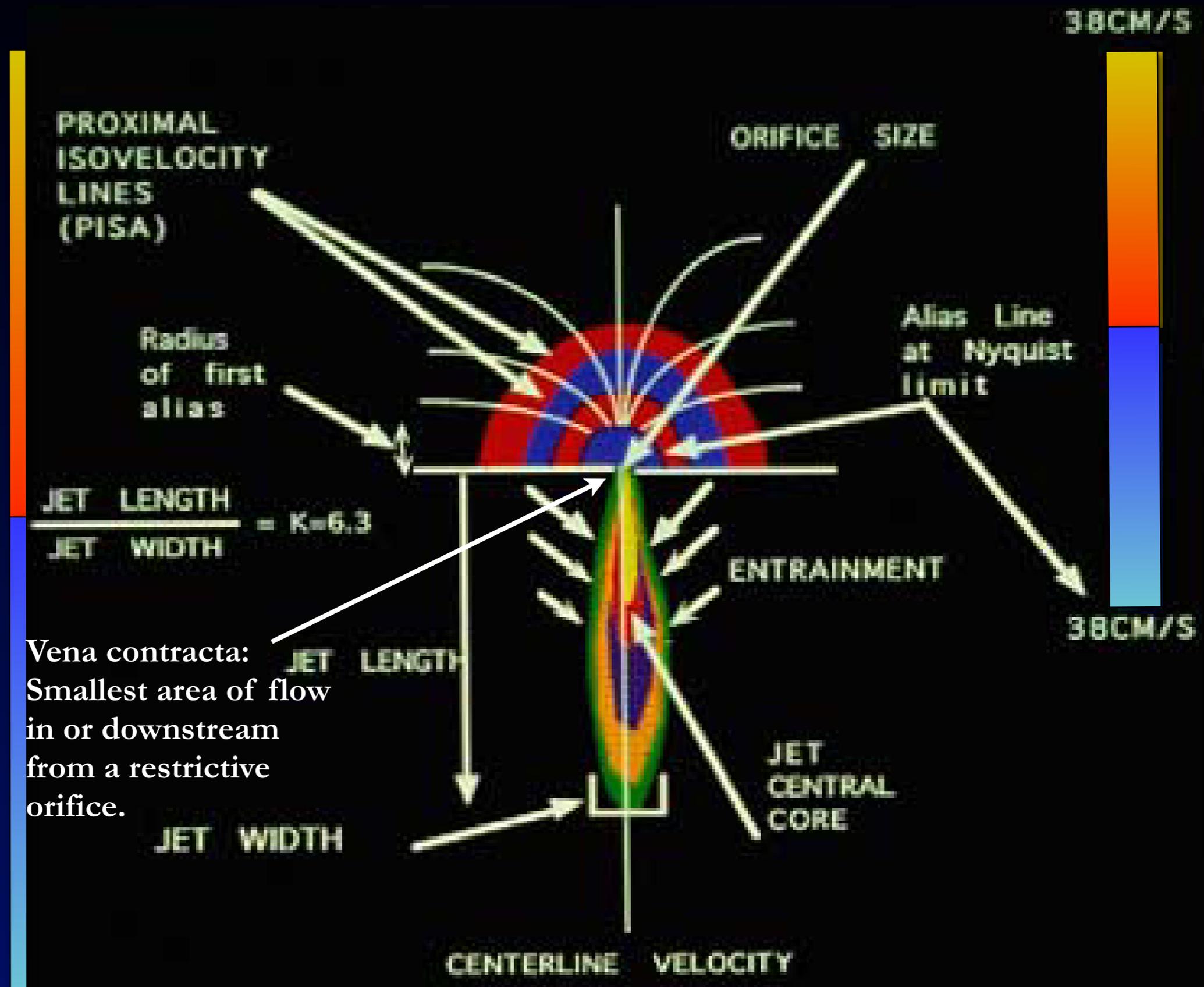
- ♥ In 50–70% of preterm infants with birth weight <1,500 g, the ductus remains patent
- ♥ An open ductus may contribute to the development of BPD by shunting blood into the lungs, resulting in pulmonary edema and the persistent need for ventilatory support. This population of preterm infants with a PDA would benefit from strategies to reduce complications and optimize outcomes.
- ♥ 615 preterm infants with birth weight <1,500 g admitted to the Neonatal Intensive Care Unit, of whom 209 (34%) were found to have a PDA by ECHO. Twenty-two patients were excluded and 187 remaining subjects had their PDA either treated (75%) or conservatively managed.
- ♥ The mean gestational age of the 187 subjects was  $27.6 \pm 2$  wk and the mean age at PDA treatment was  $4 \pm 4$  d among those treated. Mean ductal diameter at the time of treatment was  $1.7 \pm 0.6$  mm.
- ♥ Only lower gestational age and not PDA treatment or ECHO score was associated with the adverse outcome of death or BPD. Further investigation of PDA management strategies and effects on adverse outcomes of prematurity is needed.



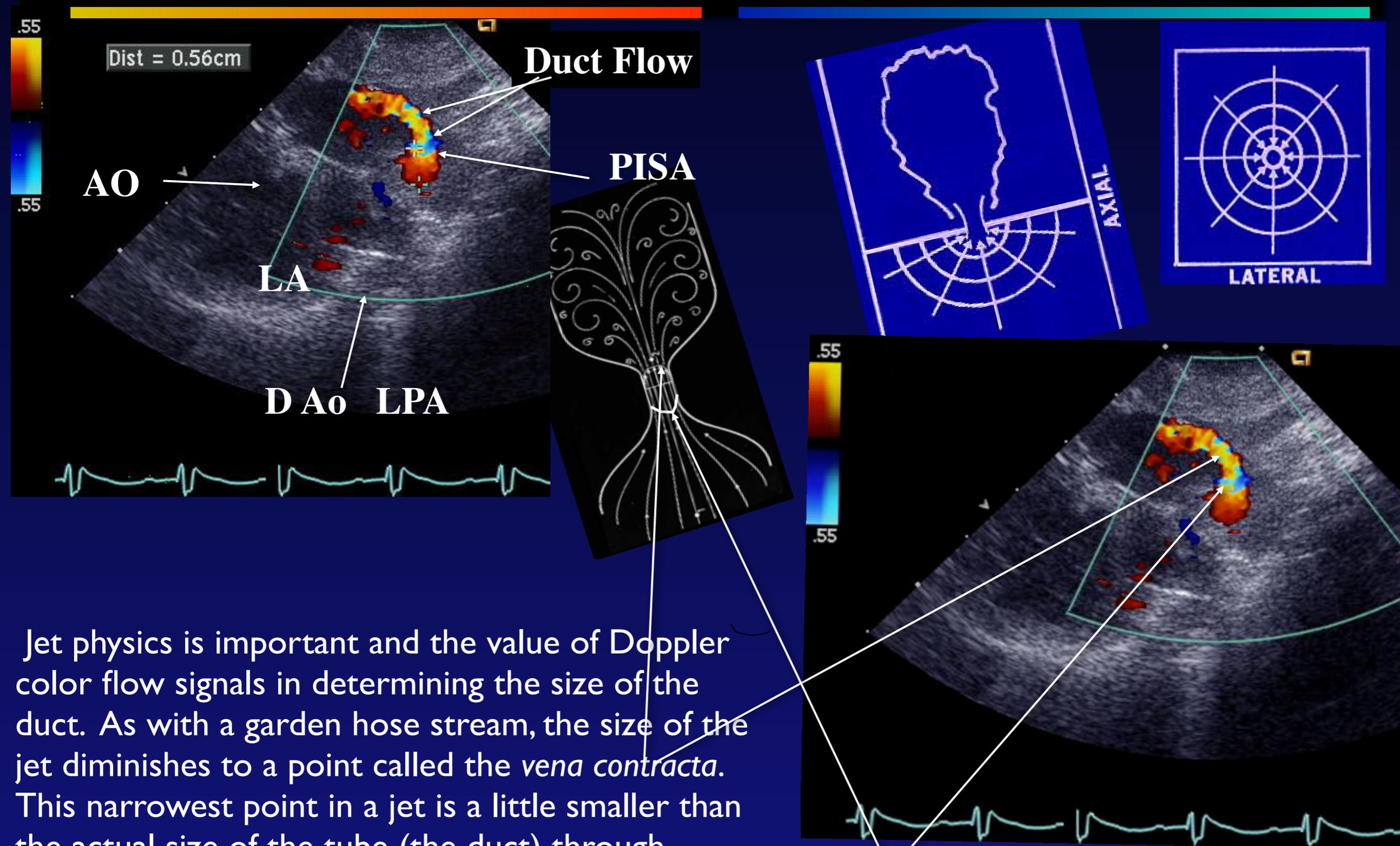
**Table 1. Comparison of Echocardiographic Markers of HSDA** where LVO = left ventricular output, SVC = superior vena cava, LVSTI = left ventricular stroke volume index, IVRT = isovolumic relaxation time, PWD = pulse wave Doppler, CWD = continuous wave Doppler, PA = pulmonary artery. (empty boxes implies data not available)

Feature quantified	Modality / Position of sample gate	No PDA	Small	Moderate	Large
Transductal diameter (mm)	Two-dimensional, short axis view	0	< 1.5	1.5-3	> 3
Left atrial: aortic ratio	M-mode, long axis view	1.13 ± 0.23	< 1.4:1	1.4 -1.6:1	> 1.6:1
Left ventricular: aortic ratio	M-mode, long axis view	1.86 ± 0.29	-	2.15 ± 0.39	2.27 ± 0.37
Ductal velocity $V_{max}$ (cm/s)	PWD at pulmonary end of duct	0	> 2	1.5-2	< 1.5
Antegrade PA diastolic flow (cm/s)	PWD within main pulmonary artery	0	0-20	> 20	-
Antegrade PA diastolic flow (cm/s)	PWD within left pulmonary artery	0	>30	30-50	> 50
Retrograde diastolic flow (cm/s)	CWD within descending Ao (% of forward flow)	10	< 30	30-50	> 50
Aortic stroke volume (ml/kg)	PWD of LV outflow tract	≤ 2.25	-	-	≥ 2.34
Left ventricular output (ml/kg/min)	PWD of LV outflow tract	190-310	-	-	> 314
LVO / SVC flow ratio	PWD of flow in superior vena cava	2.4 ± 0.3	-	-	4.5 ± 0.6
LVSTI ratio	M-mode of aortic valve	0.34 ± 0.09	-	0.26 ± 0.03	0.24 ± 0.07
E wave / A wave ratio	Transmitral Doppler	< 1	< 1	1-1.5	> 1.5
IVRT (ms)	Between mitral & aortic valves	> 55	46-54	36-45	< 35

# Jet Physics



# Proximal Flow Convergence in PDA



Jet physics is important and the value of Doppler color flow signals in determining the size of the duct. As with a garden hose stream, the size of the jet diminishes to a point called the *vena contracta*. This narrowest point in a jet is a little smaller than the actual size of the tube (the duct) through which it is traveling, but provides a reasonable estimate of its true size.

The PISA stands for Proximal Isovelocity Surface Acceleration.

# The Other PISA



# Quantitation of Patent Ductus Size.

- ♥ Documentation of size of ductus by imaging, color & *Vena Contracta*
- ♥ Ductus diameter as a % of the of the left pulmonary artery:
  - ♥  $>1$  indicated a large PDA,  $<1$  but  $>0.5$  moderate and  $<0.5$  a small duct
- ♥ LA/Ao Ratio ( $>1.3:1$ ) and Left Ventricular hyperdynamic contractions
- ♥ Retrograde abdominal aortic flow
  - ♥ If Prograde Flow--> Mild; If Retrograde flow---> large
    - (VTI of Reverse vs. Forward Flow)
- ♥ Ductus Doppler --> Restrictive if velocity is  $>2$  msec and continuous Non-restrictive, if goes to baseline
- ♥ PISA
  - ♥ Small-- small shunt
  - ♥ Pisa Moderate- moderate sized shunt
  - ♥ No Pisa Large Shunt

Apgar-like score

# Echocardiographic Scoring System for Patent Ductus Arteriosus

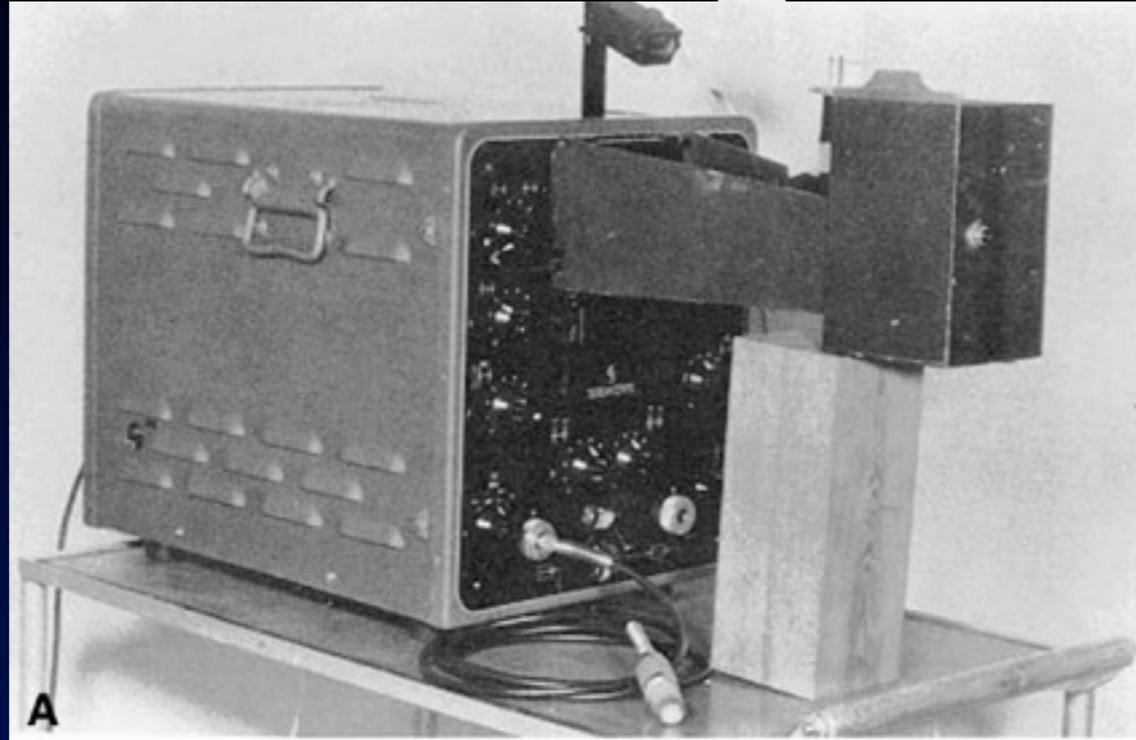
Start with 10 points

Parameter	0	-1	-2
LA:Ao ratio	<1	1-1.3	>1.3
Retrograde aortic flow (reverse:forward flow)	None	0-0.4	>0.4
PISA	No ductus	Some	None when ductus
Ductus:LPA ratio	<0.25	0.25-0.5	>0.5
Doppler of PDA	Continuous flow	Left-right and stops at baseline	Bidirectional

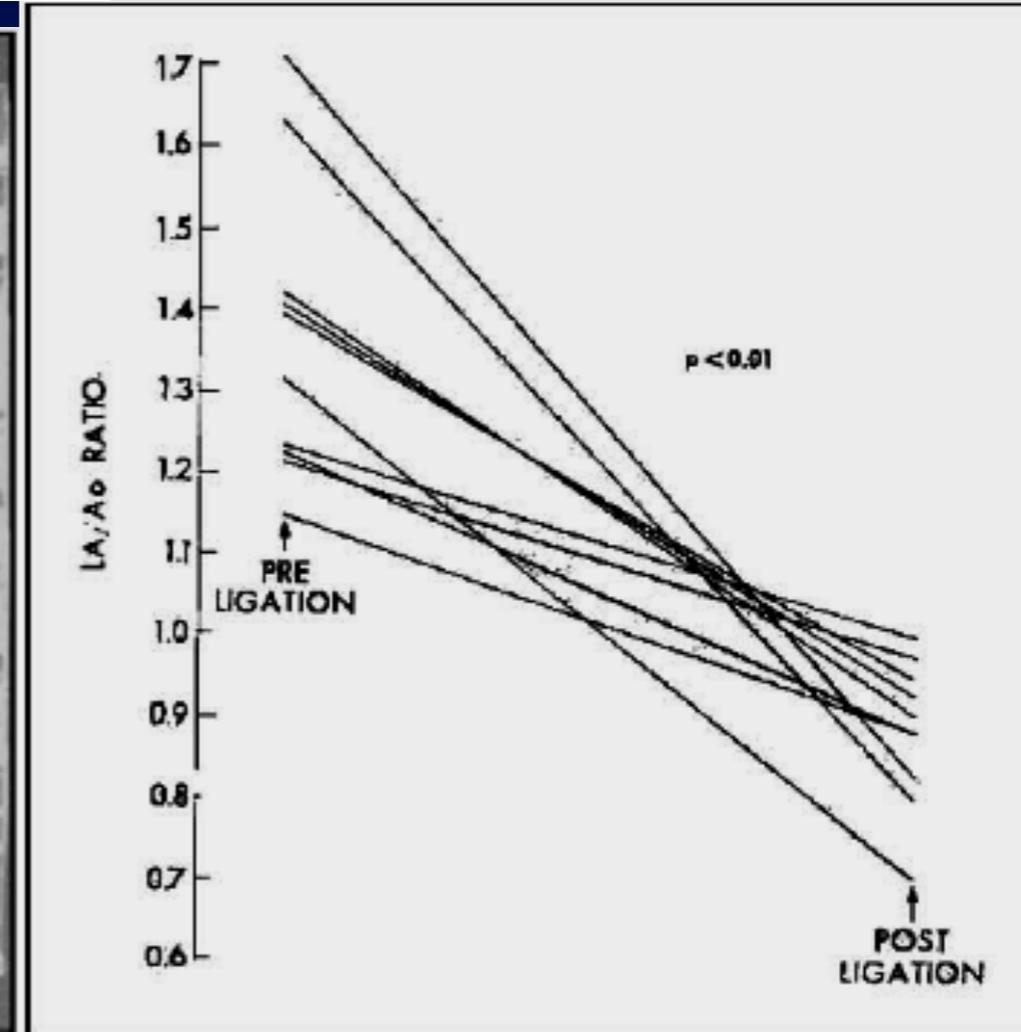
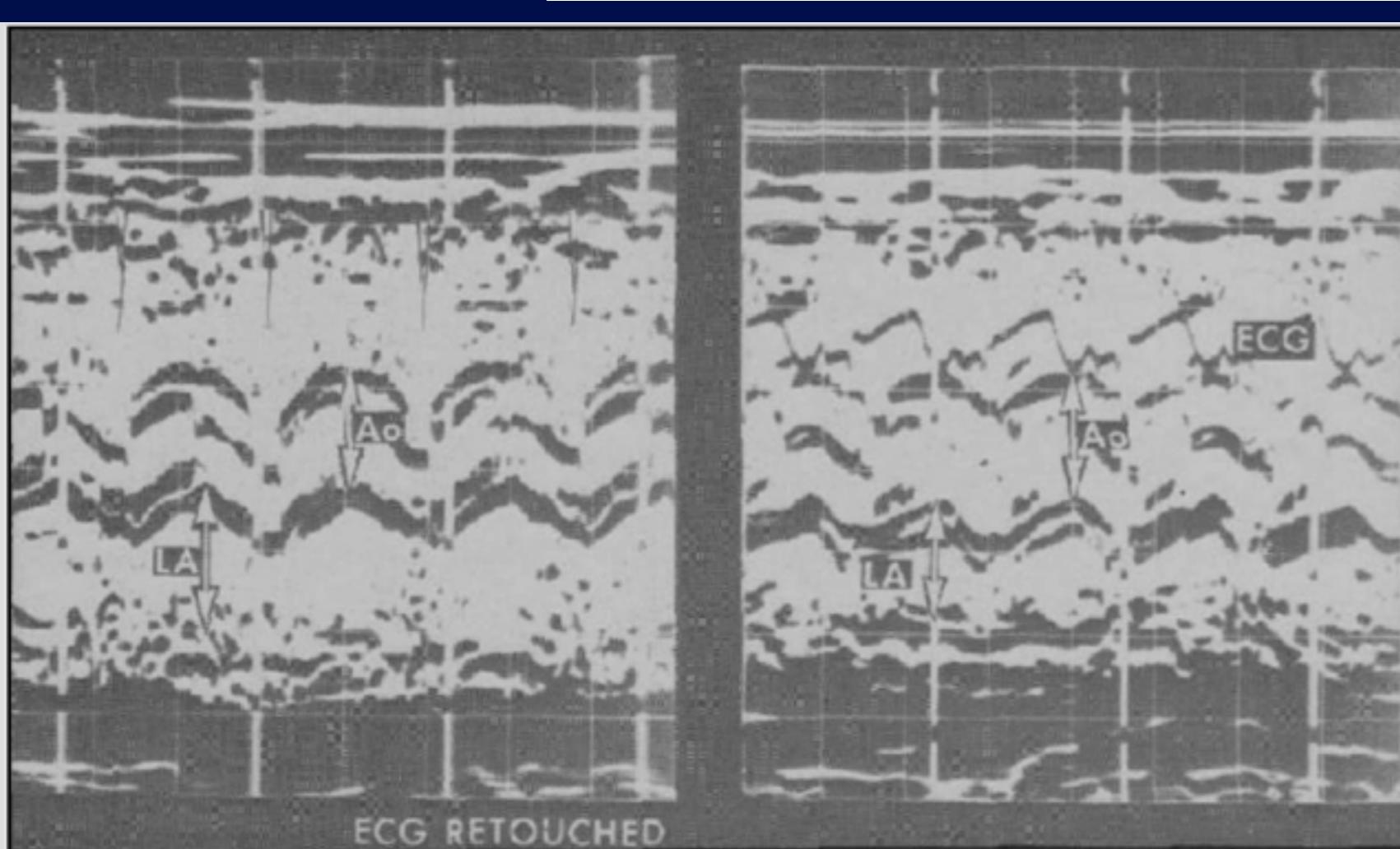
Hemodynamically significant ductus if score <5

# THE LA:A0 RATIO

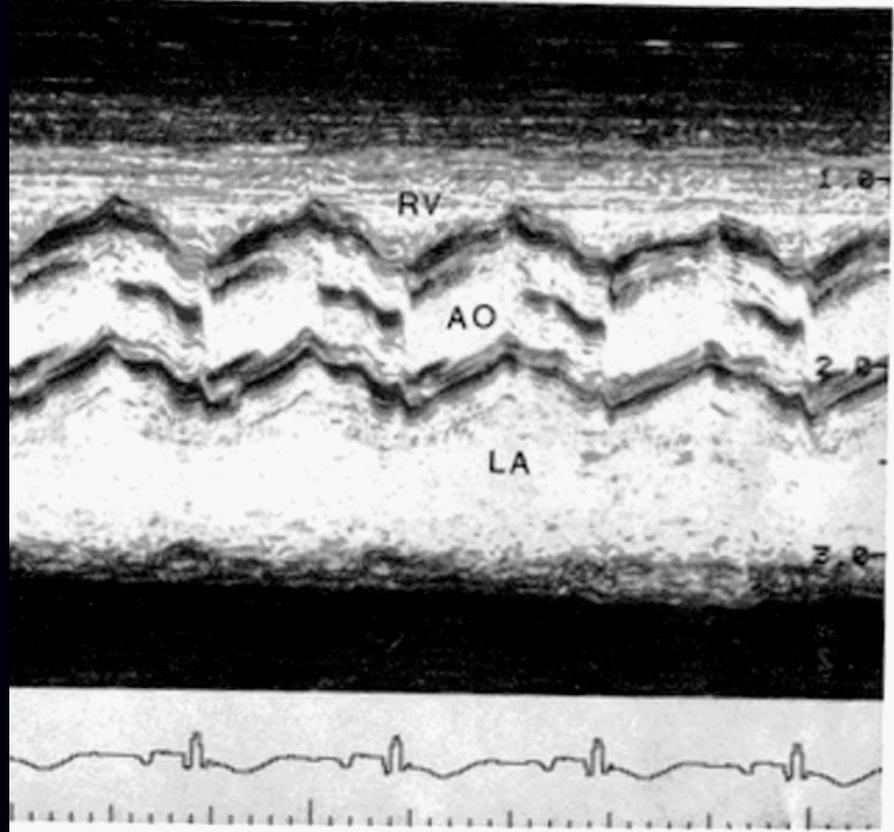
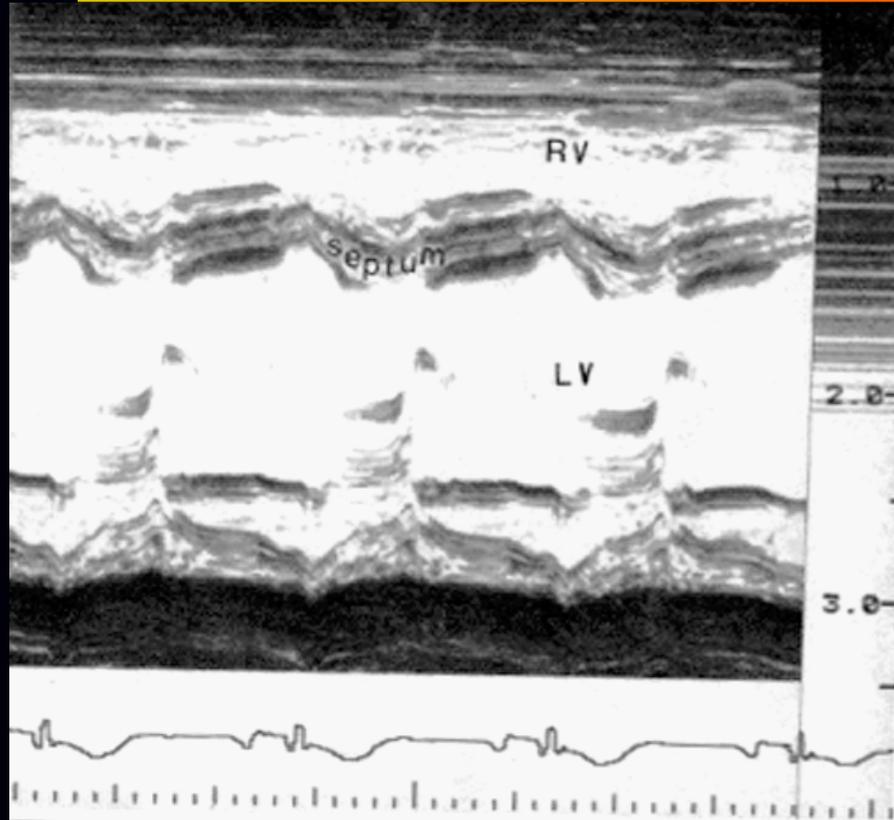
**Strength:** This is simple measurement made by the technologist usually fairly accurate. Can be made of Two-dimensional Echo as well.



**Weakness:** This technique was a surrogate for measuring left atrial size. Now Z scores are available. Confounding associations on the cardiac basis, Premature infants have a PFO



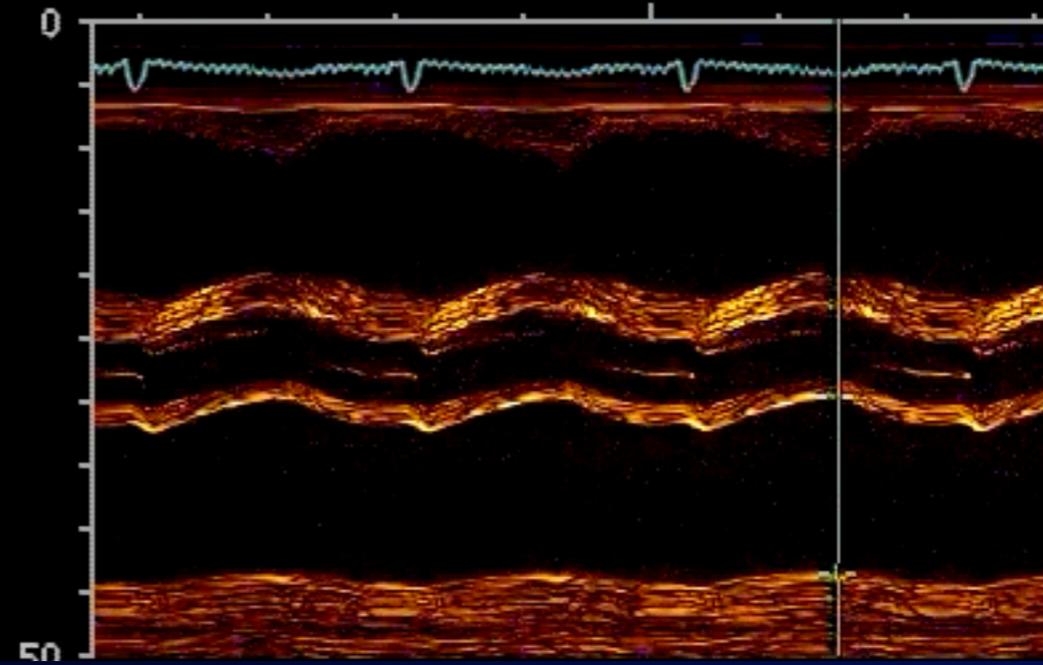
# The LA:AO Ratio (> 1.3:1)



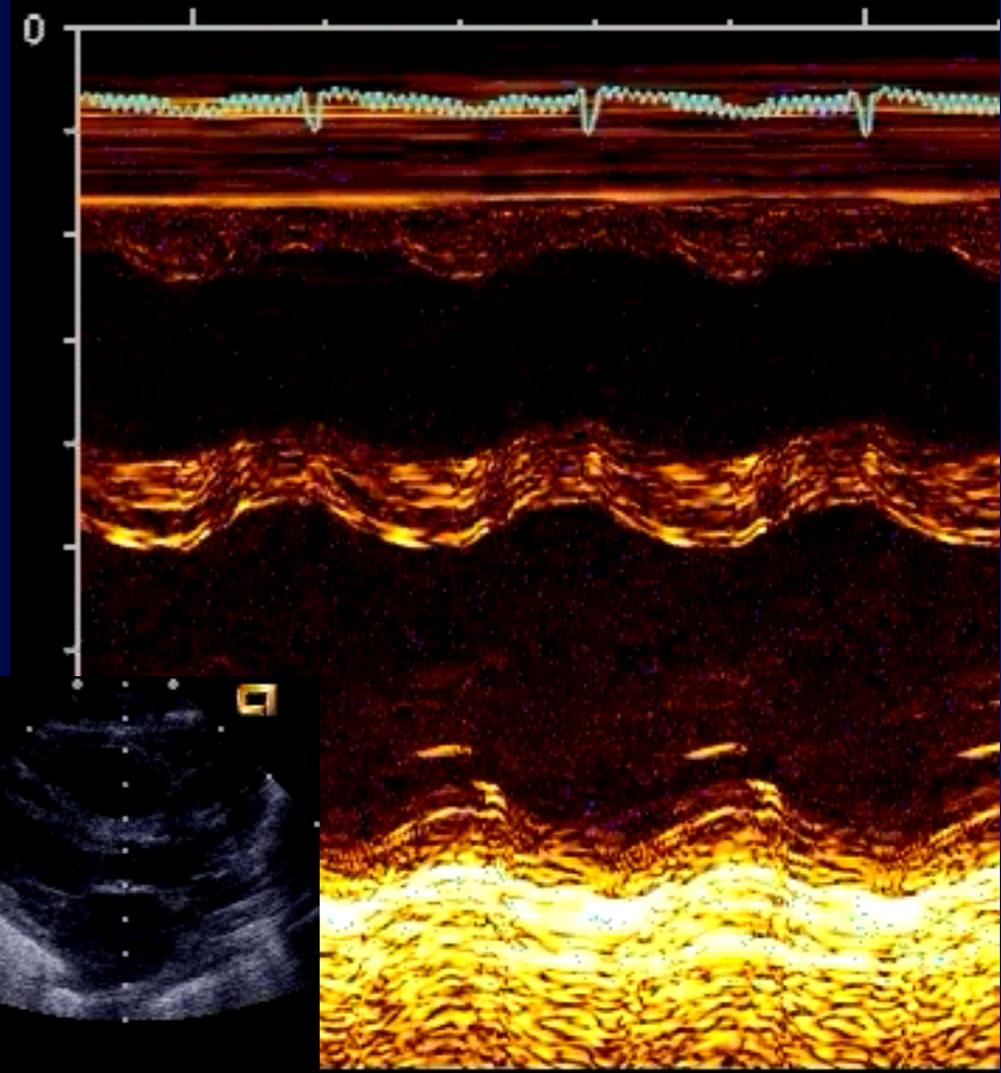
45dB +/-1/ +/-2  
M Gain= 0dB

LA Diam, s = 1.40 cm

Cal= 5mm



Cal= 5mm



# Flow Dynamics in the Juxtaductus Aorta.

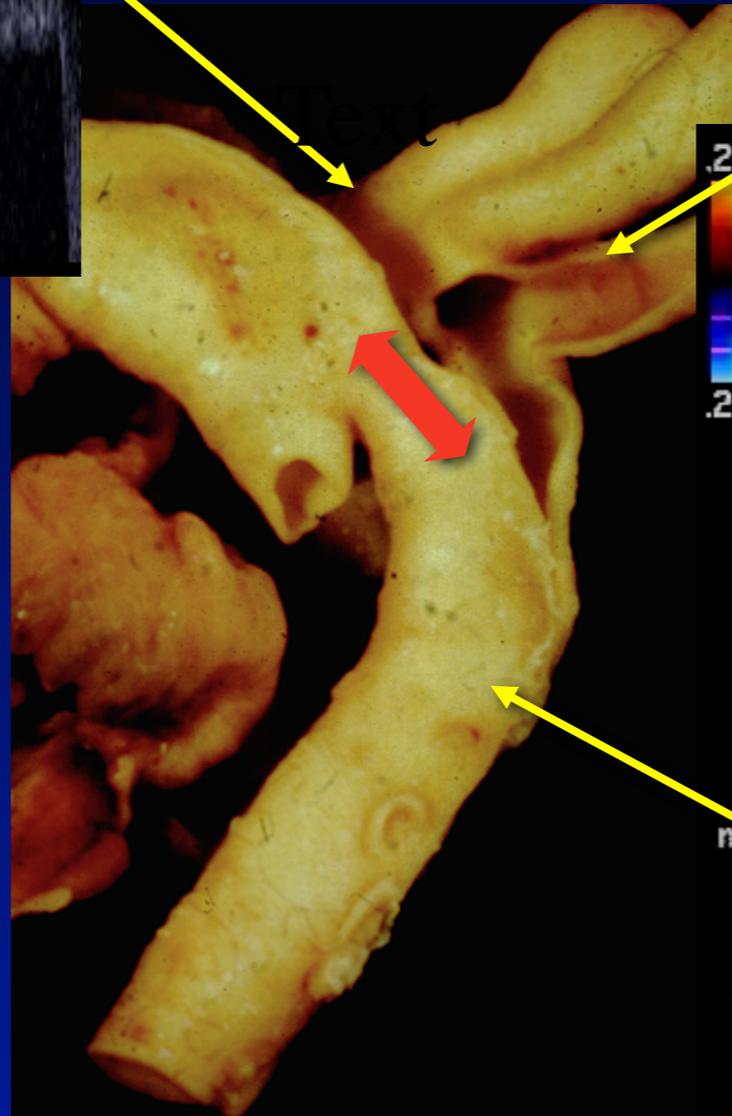
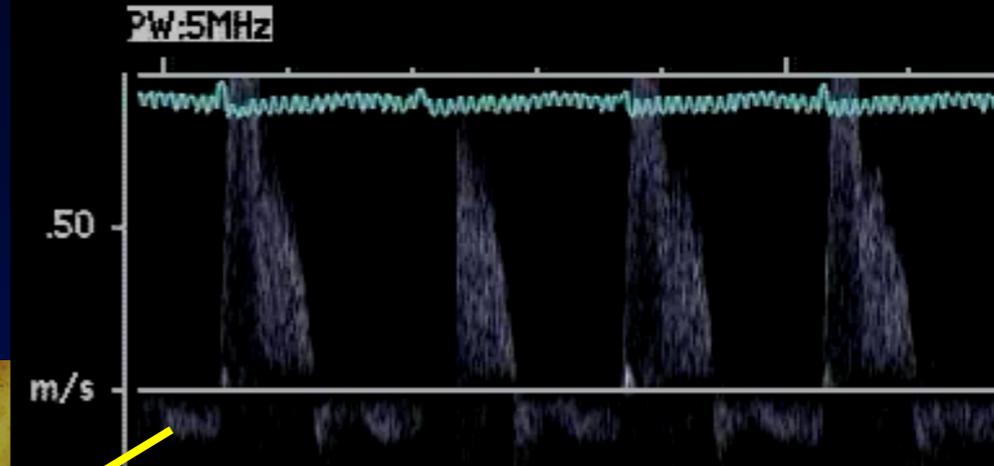
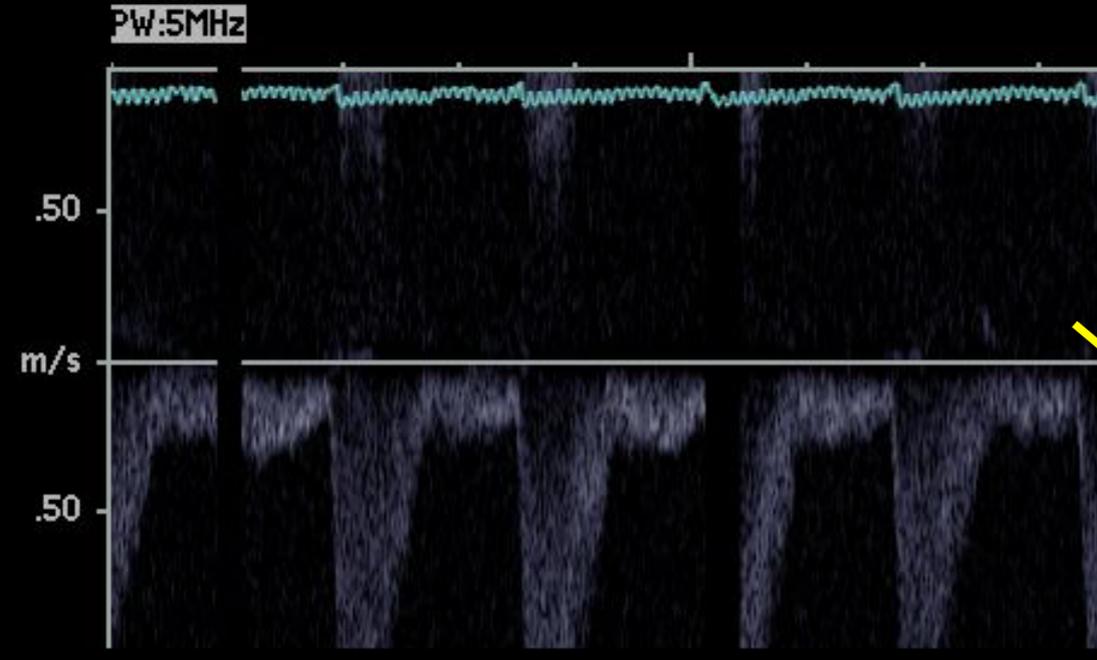
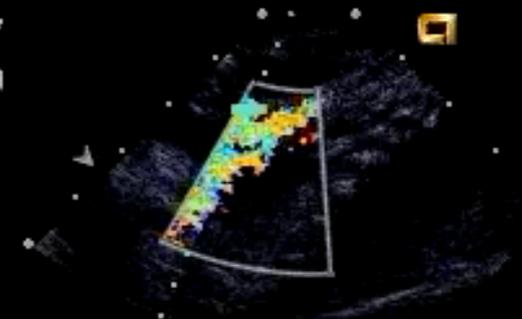
.28 50dB 3 +/-1/0/2  
PW Depth= 24mm  
PW Gate= 1.0mm  
PW Gain= -8dB



Ao Prox  
to Duct

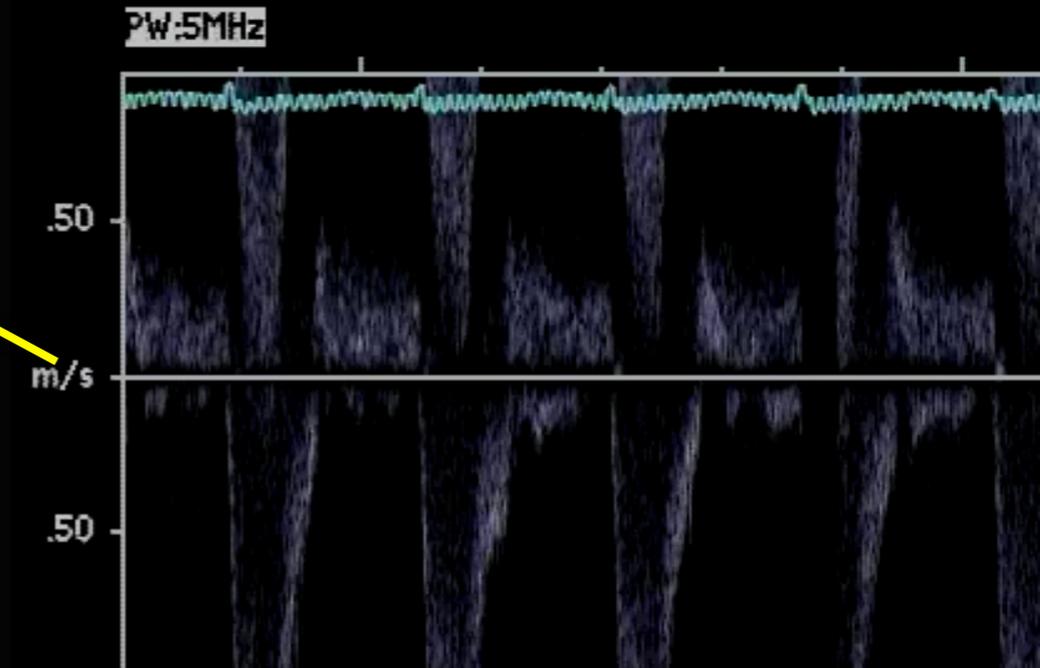
Ao  
Distal  
to Duct

.28 50dB 3 +/-1/0/2  
PW Depth= 16mm  
PW Gate= 1.0mm  
PW Gain= -8dB



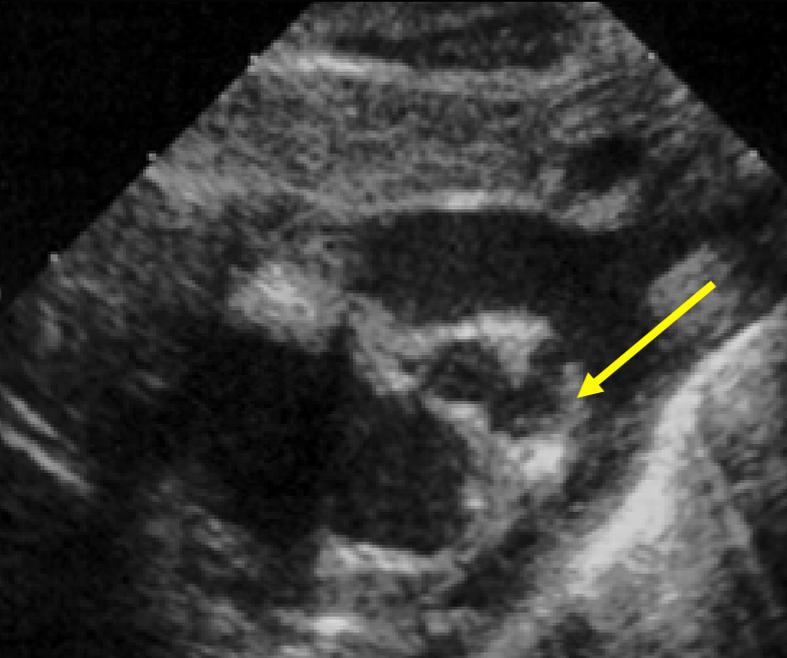
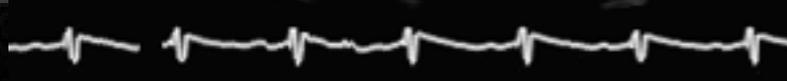
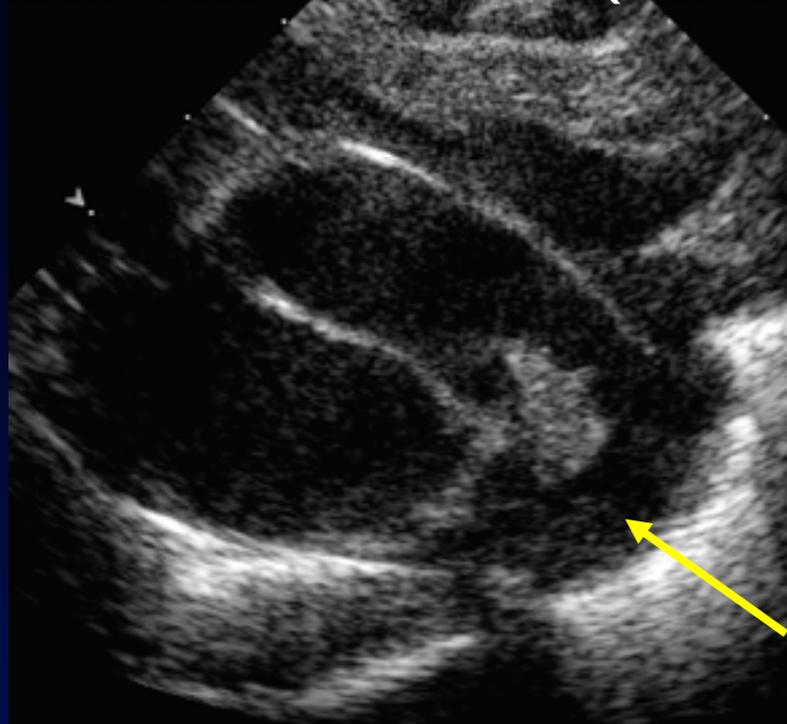
.28 50dB 3 +/-1/0/2  
PW Depth= 32mm  
PW Gate= 1.0mm  
PW Gain= -8dB

Ductus Flow

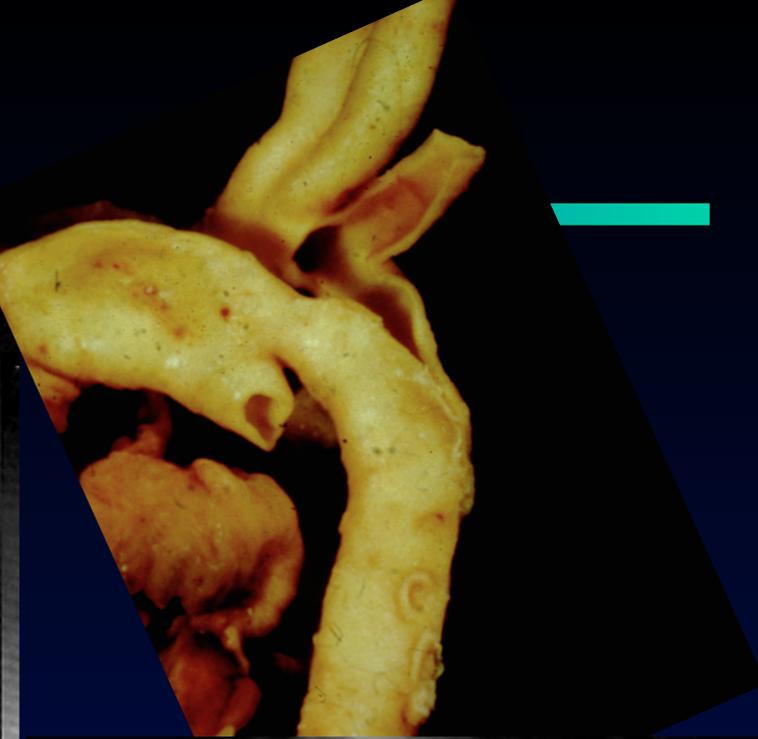
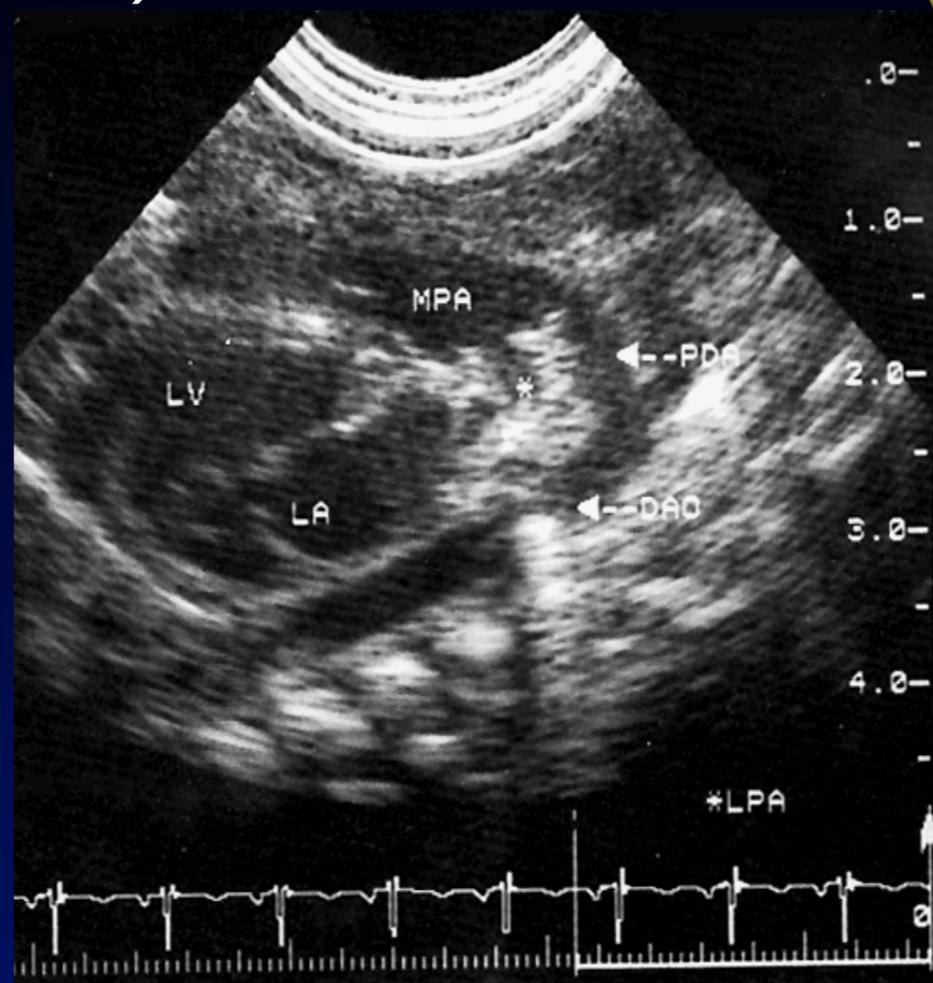


# Ductus Size

## Horizontal Ductus (Transposition)



## Vertical Ductus ( Pulmonary Under- circulation )

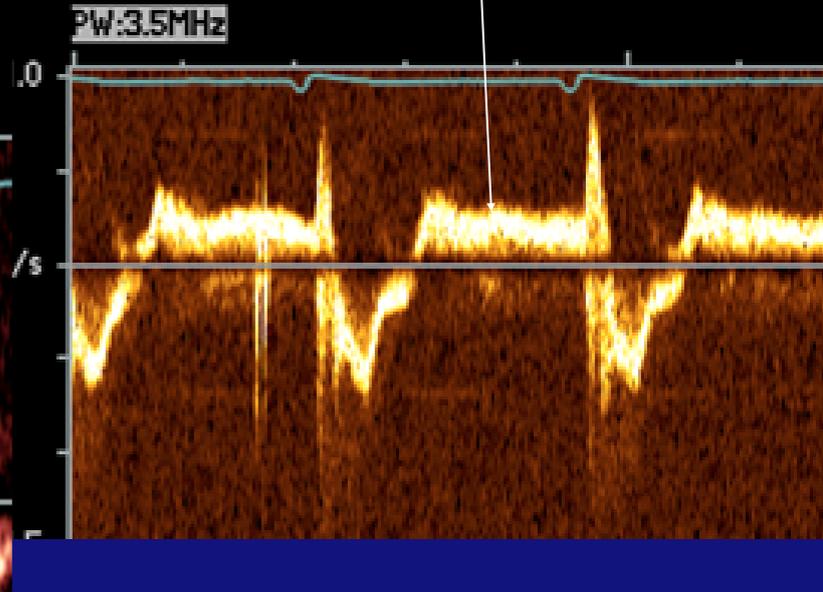
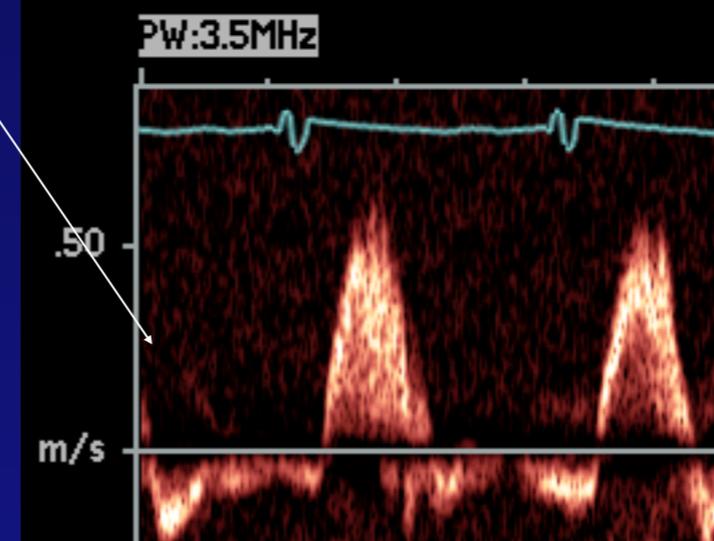
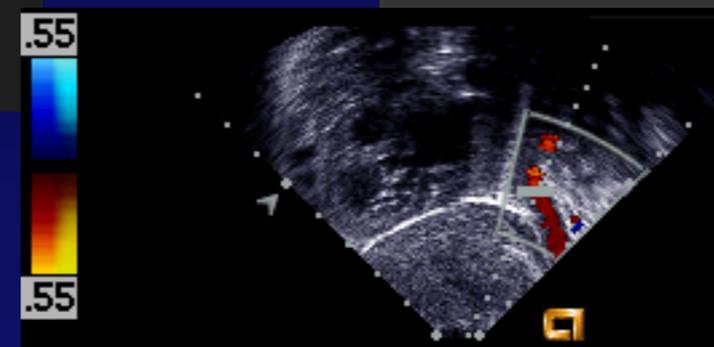
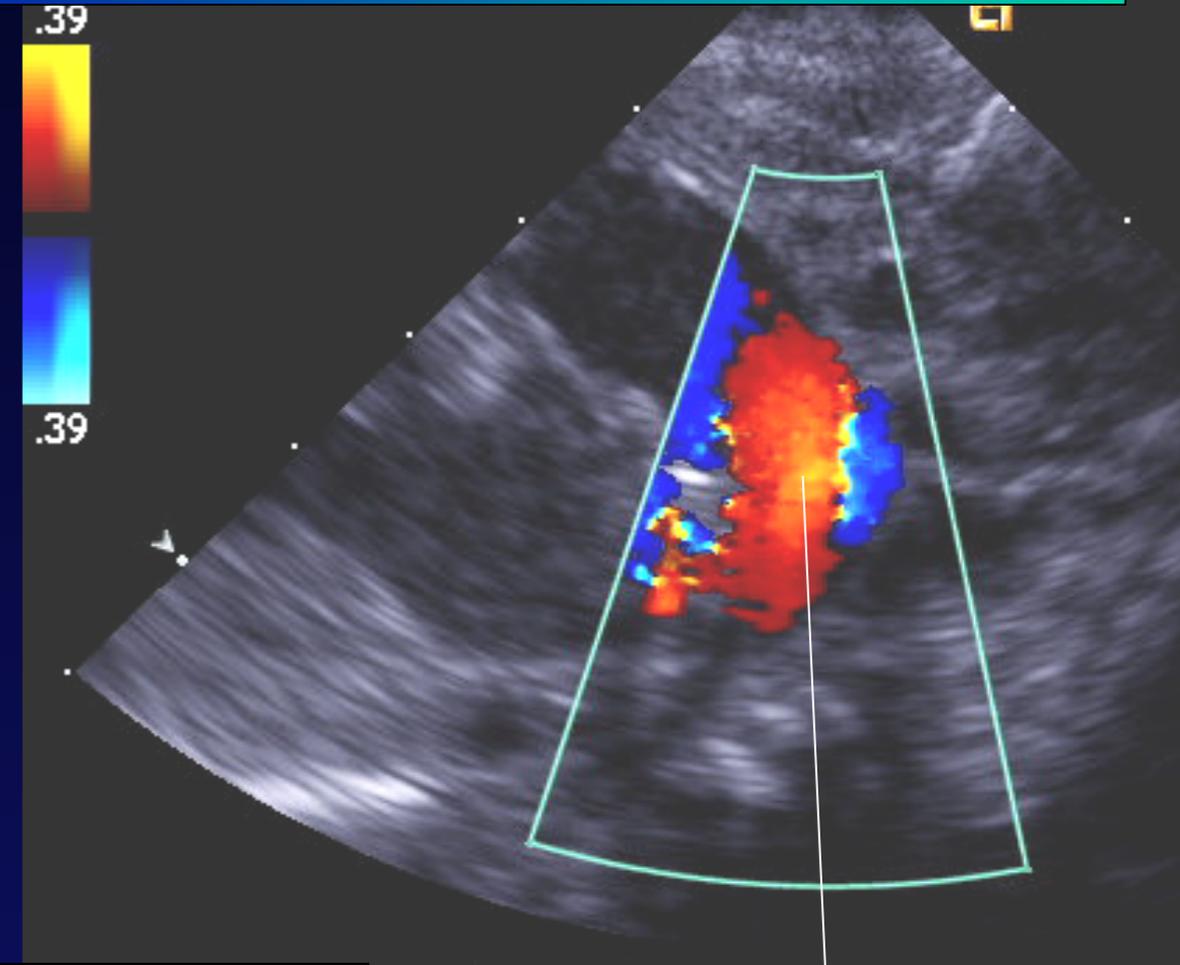
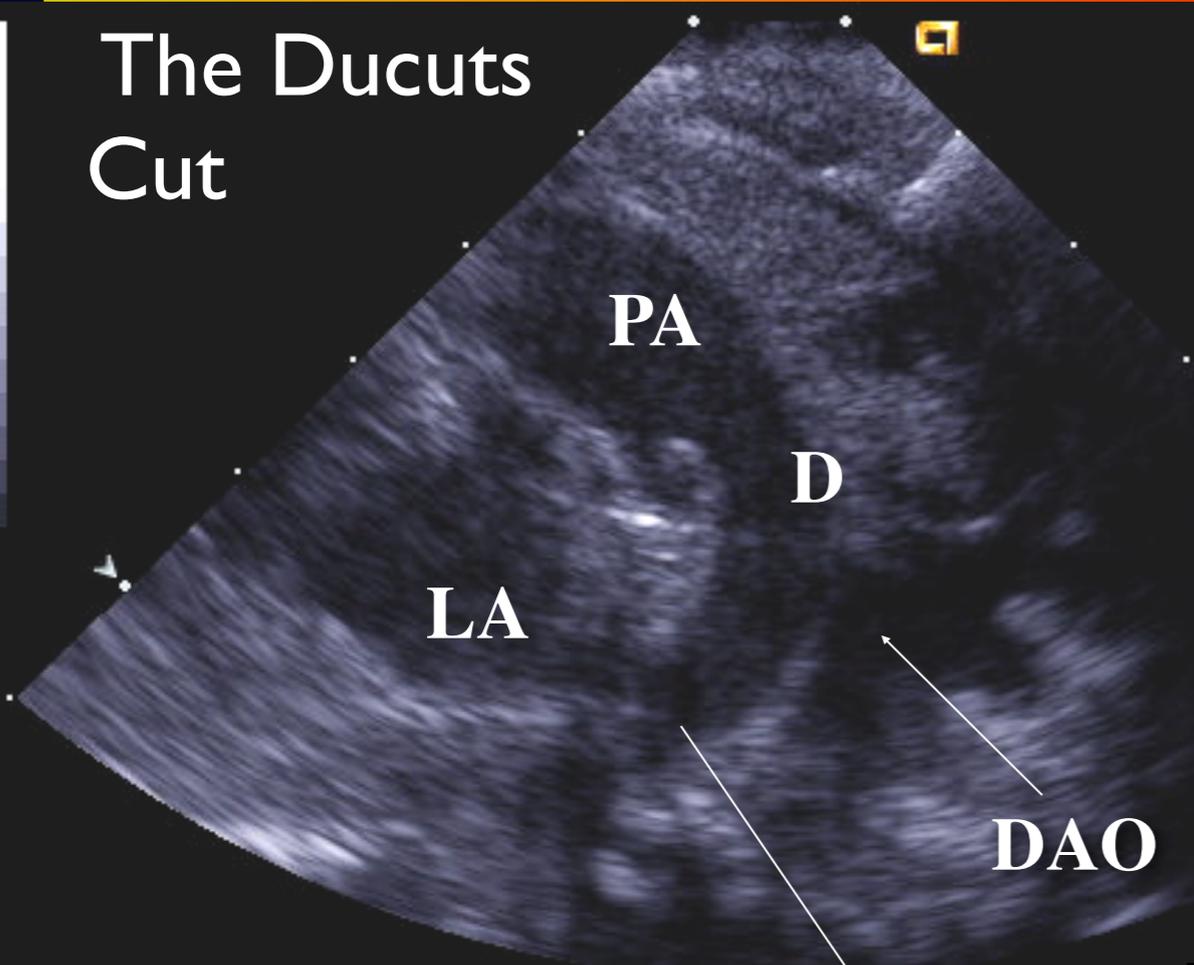


**Strength:** This is a measurement that is linear and easy to make. It certainly parallels whether the ductus is large, moderate or small

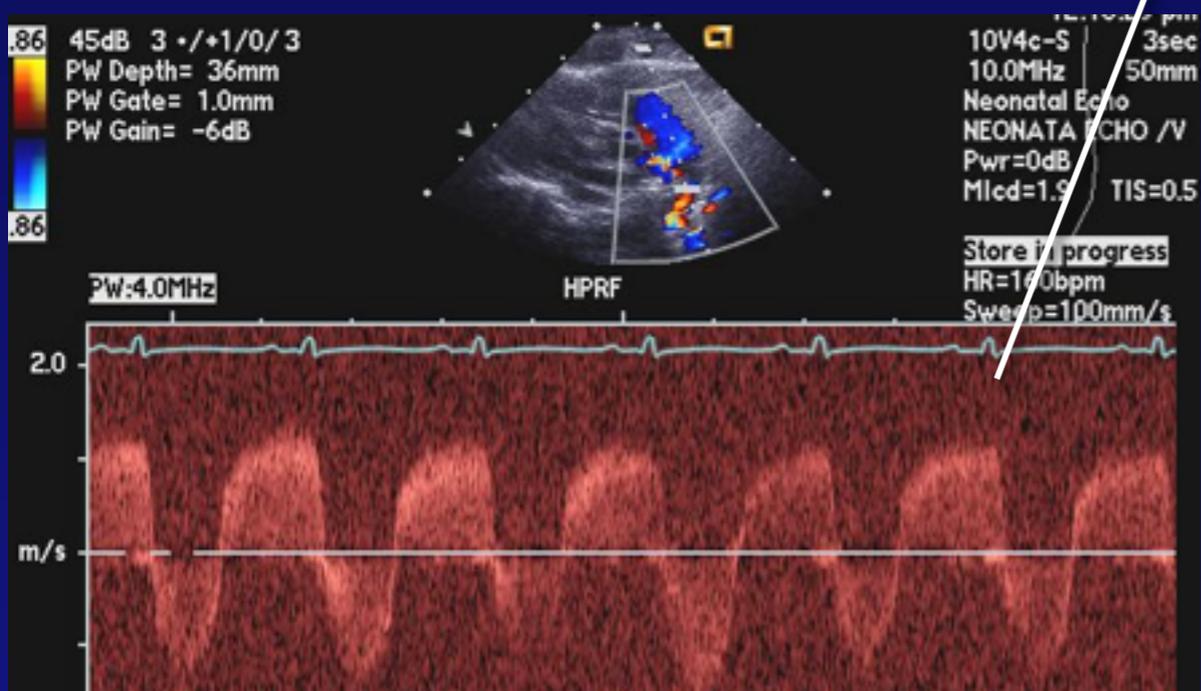
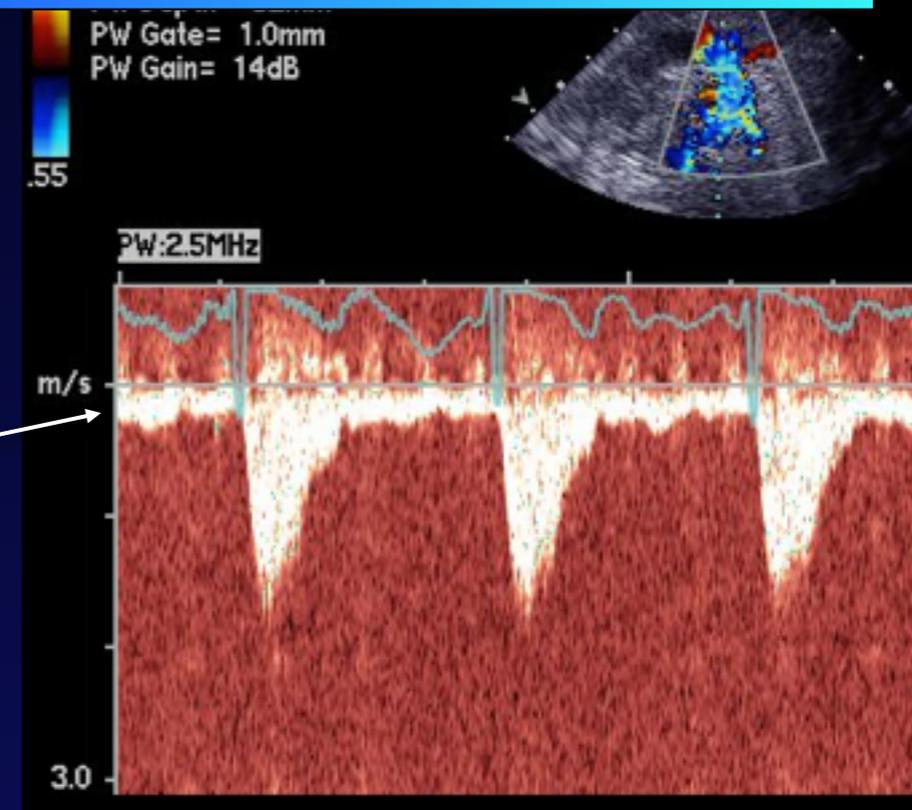
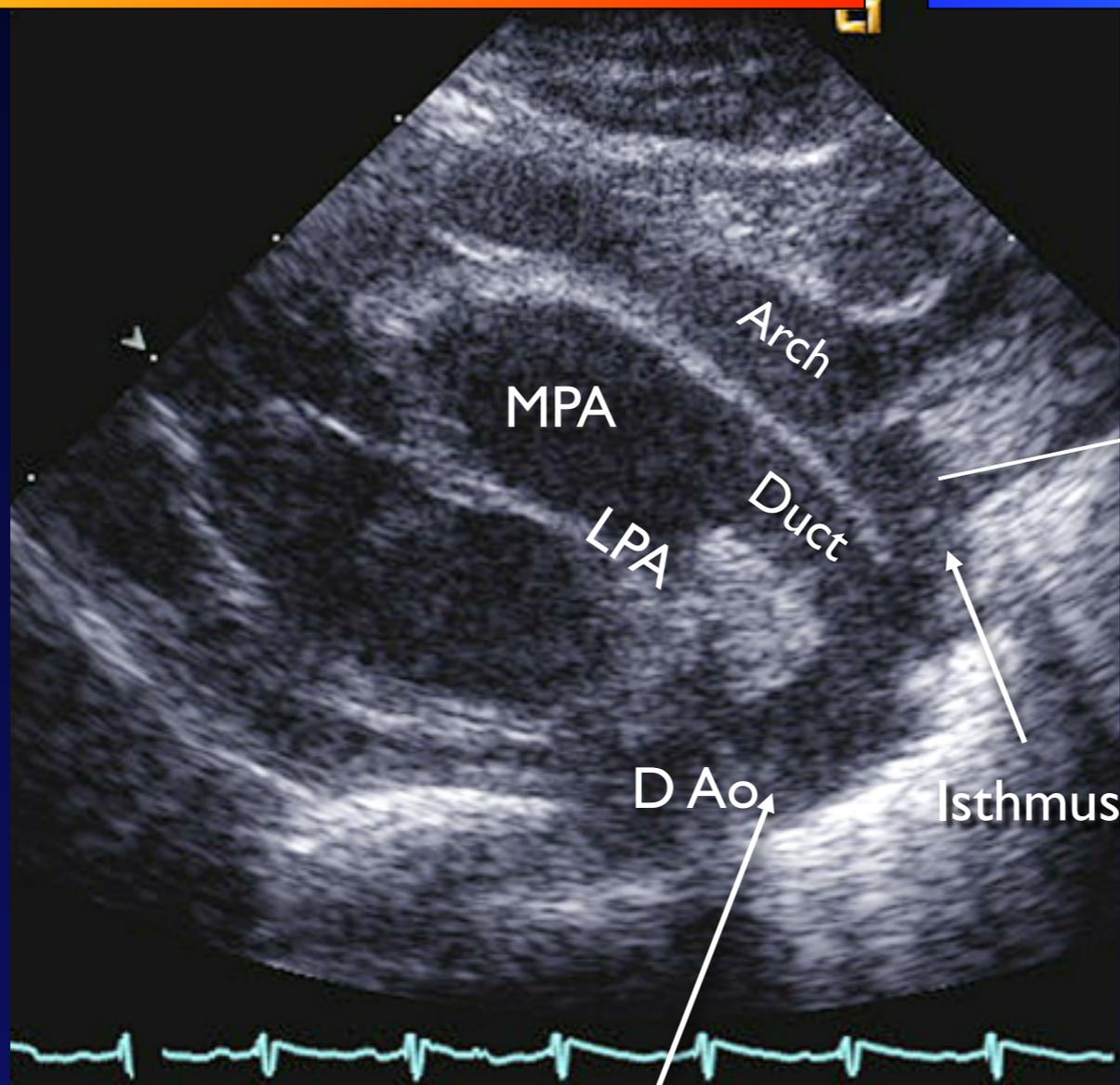
**Weakness:** Minor differences of the type that relate to pixels differences can make large differences in the amount of flow. The question of where the narrowest portion of the ductus might be makes it be difficult sometimes to see the exact point of narrowing

# Large Patent Ductus Arteriosus

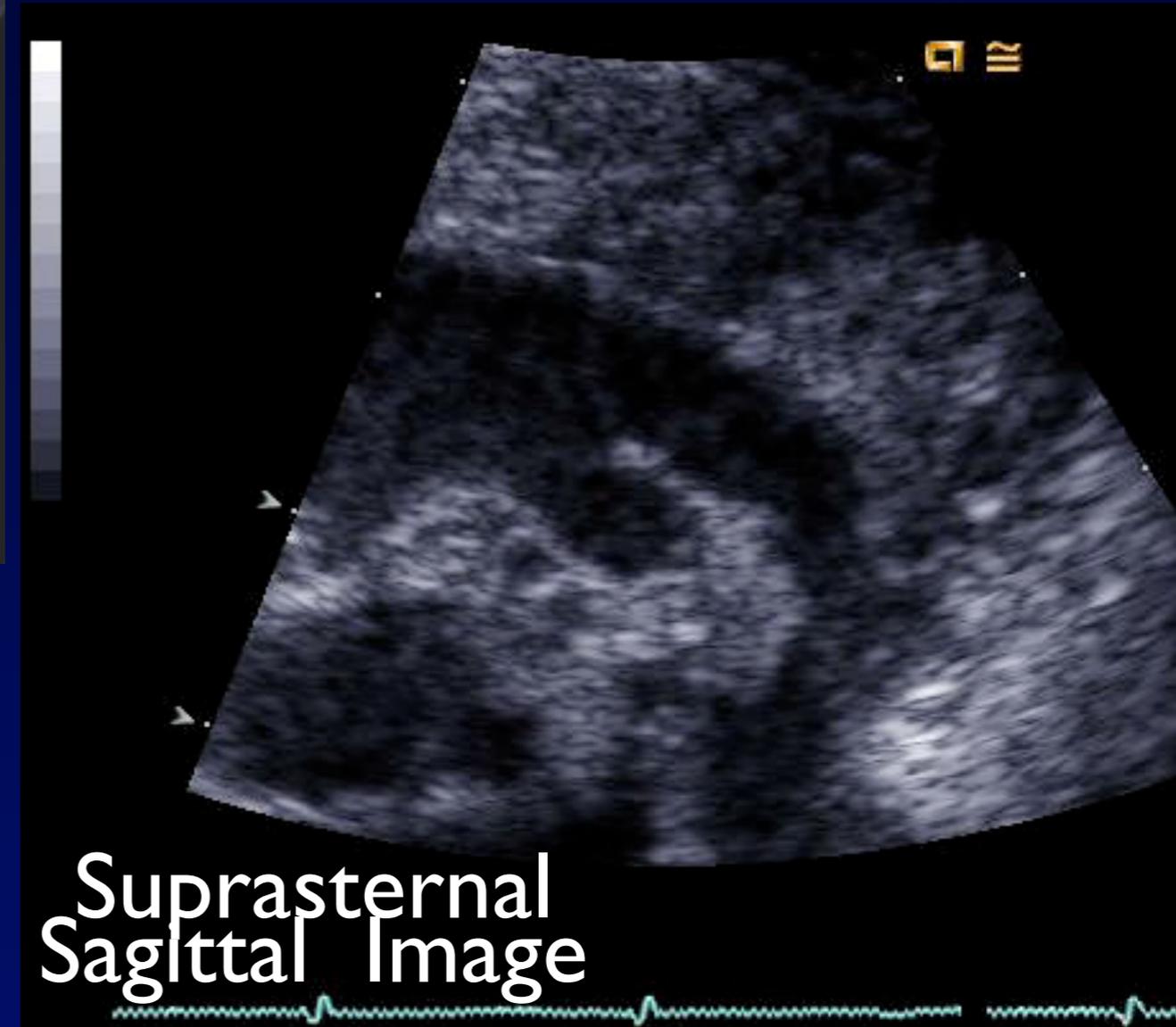
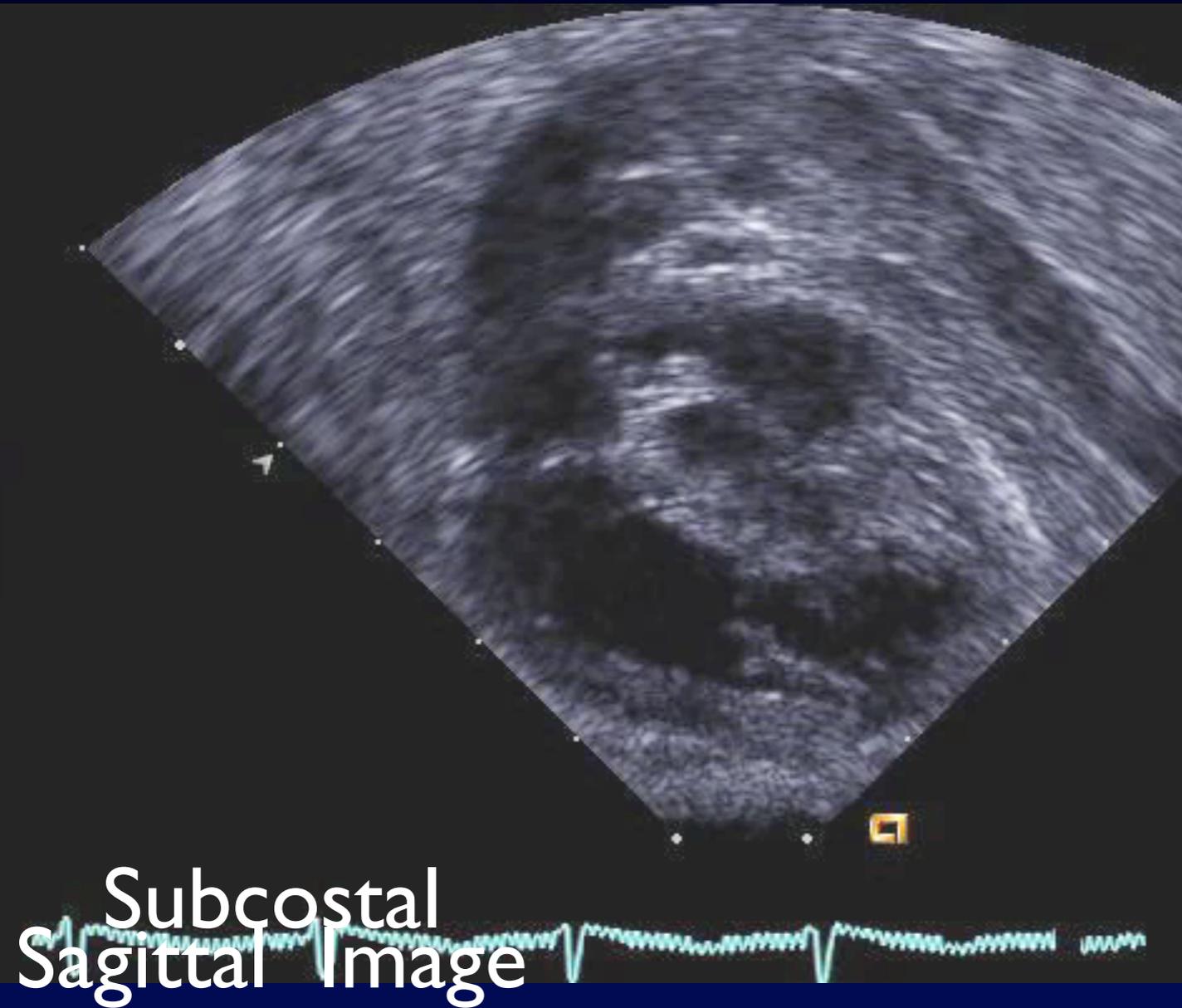
The Ducuts  
Cut



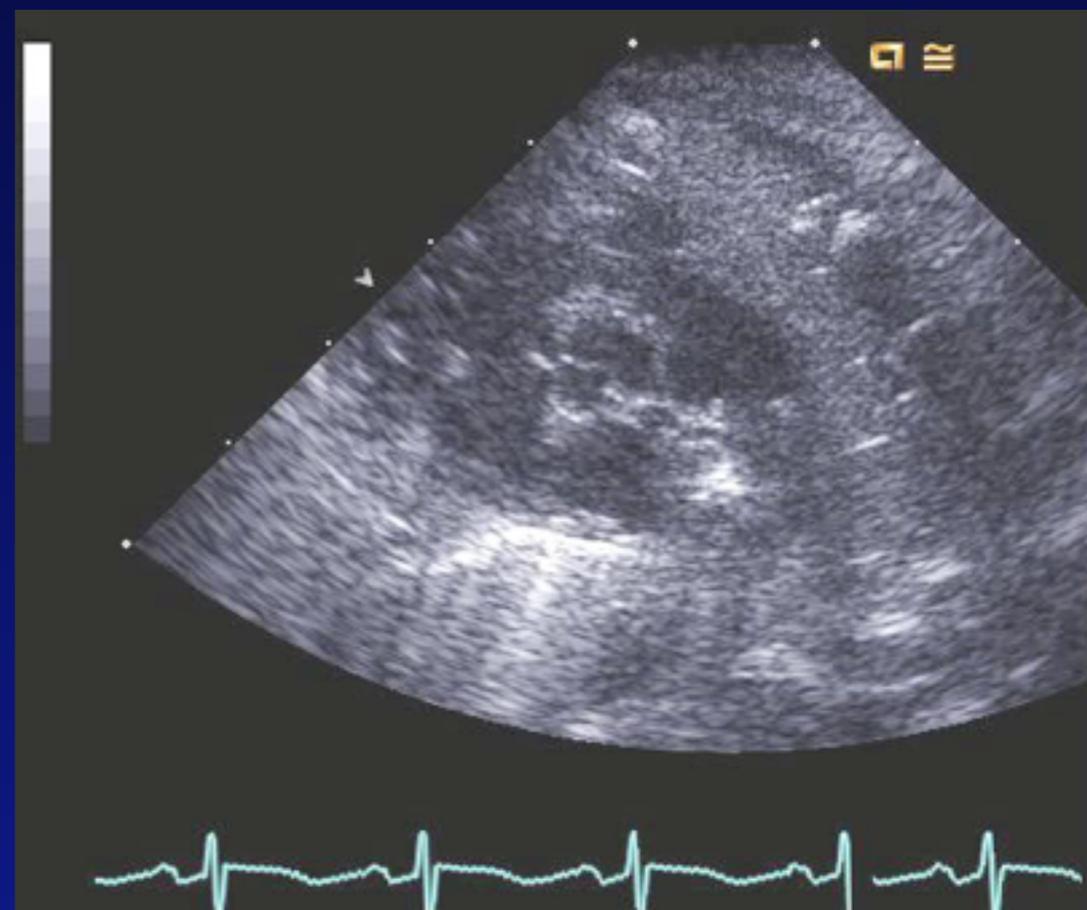
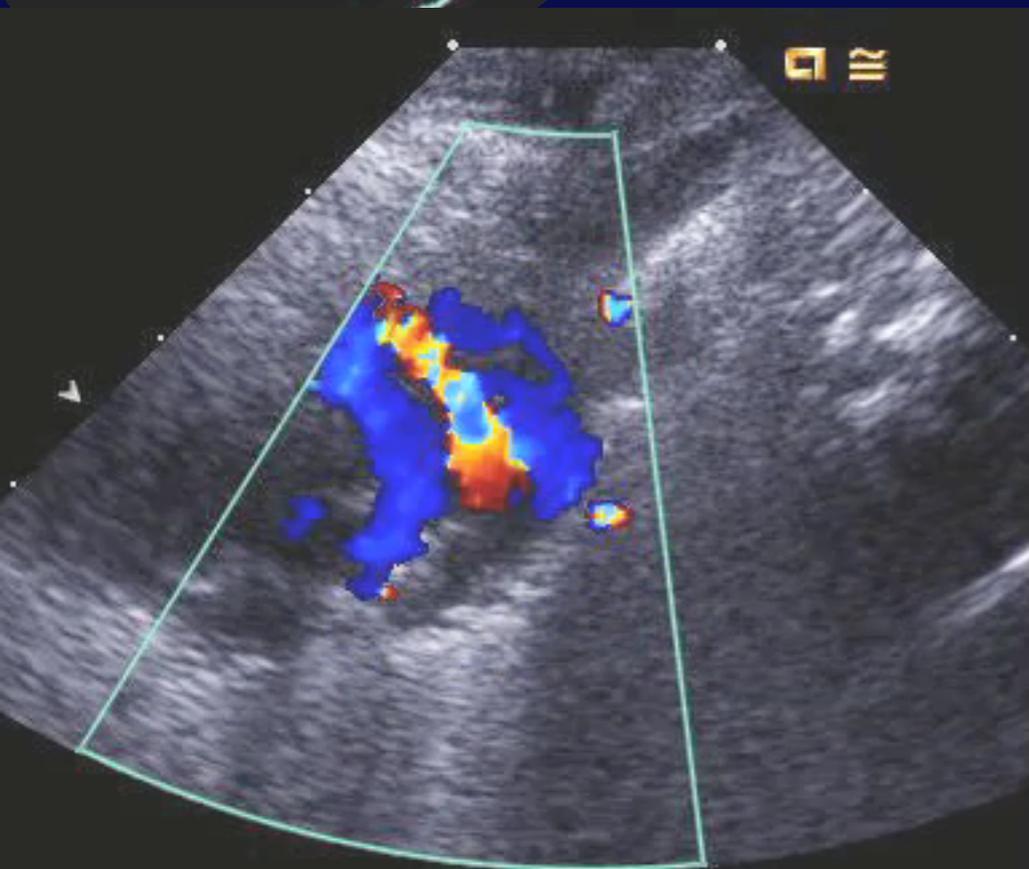
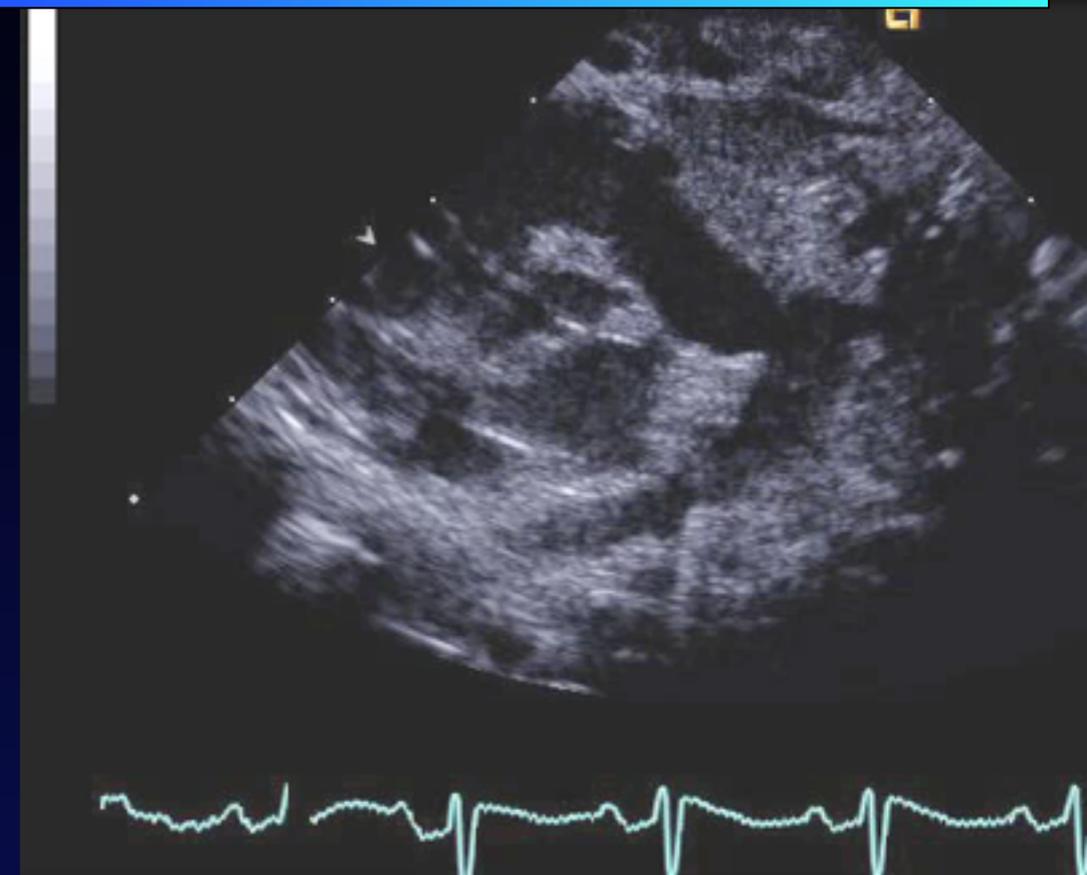
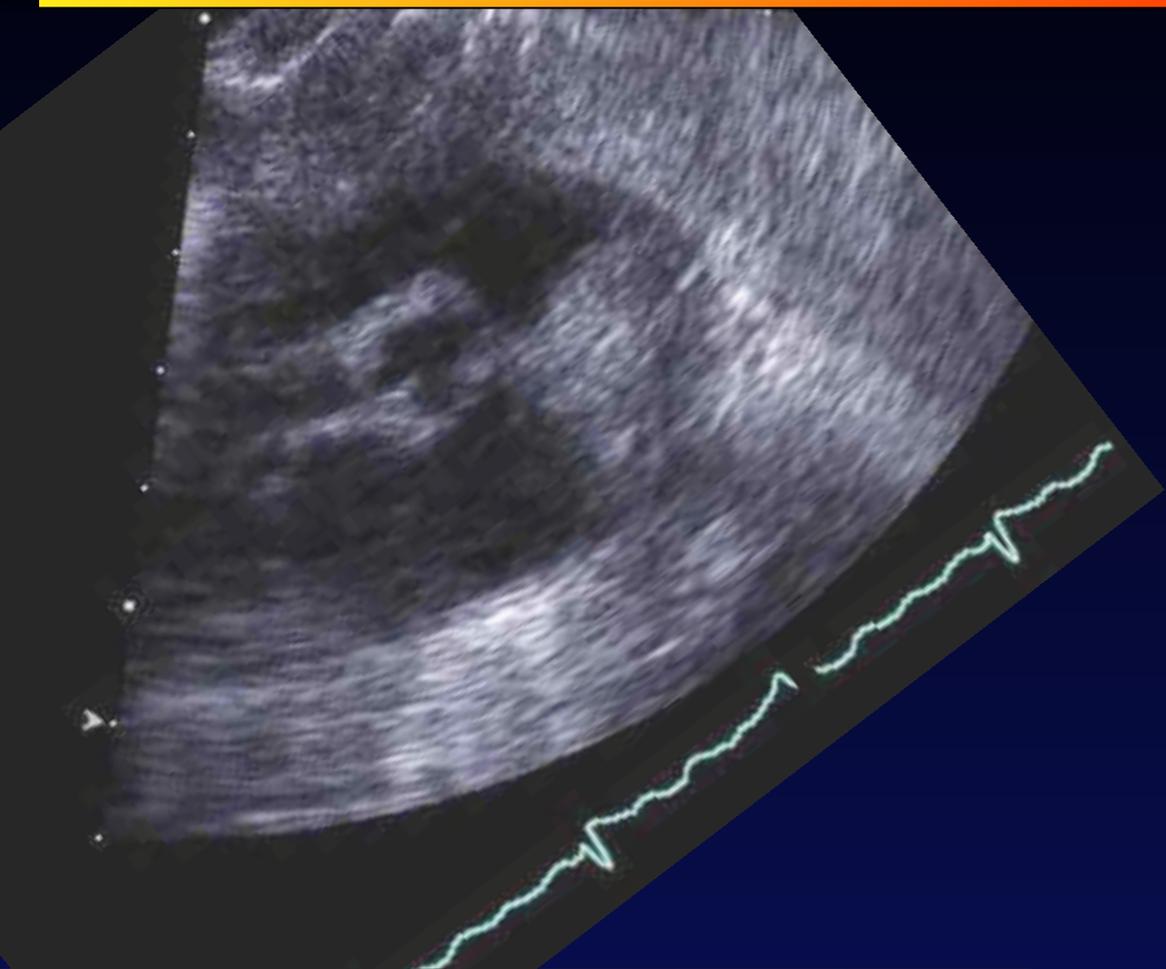
# Ductus Cut and Flow Dynamics



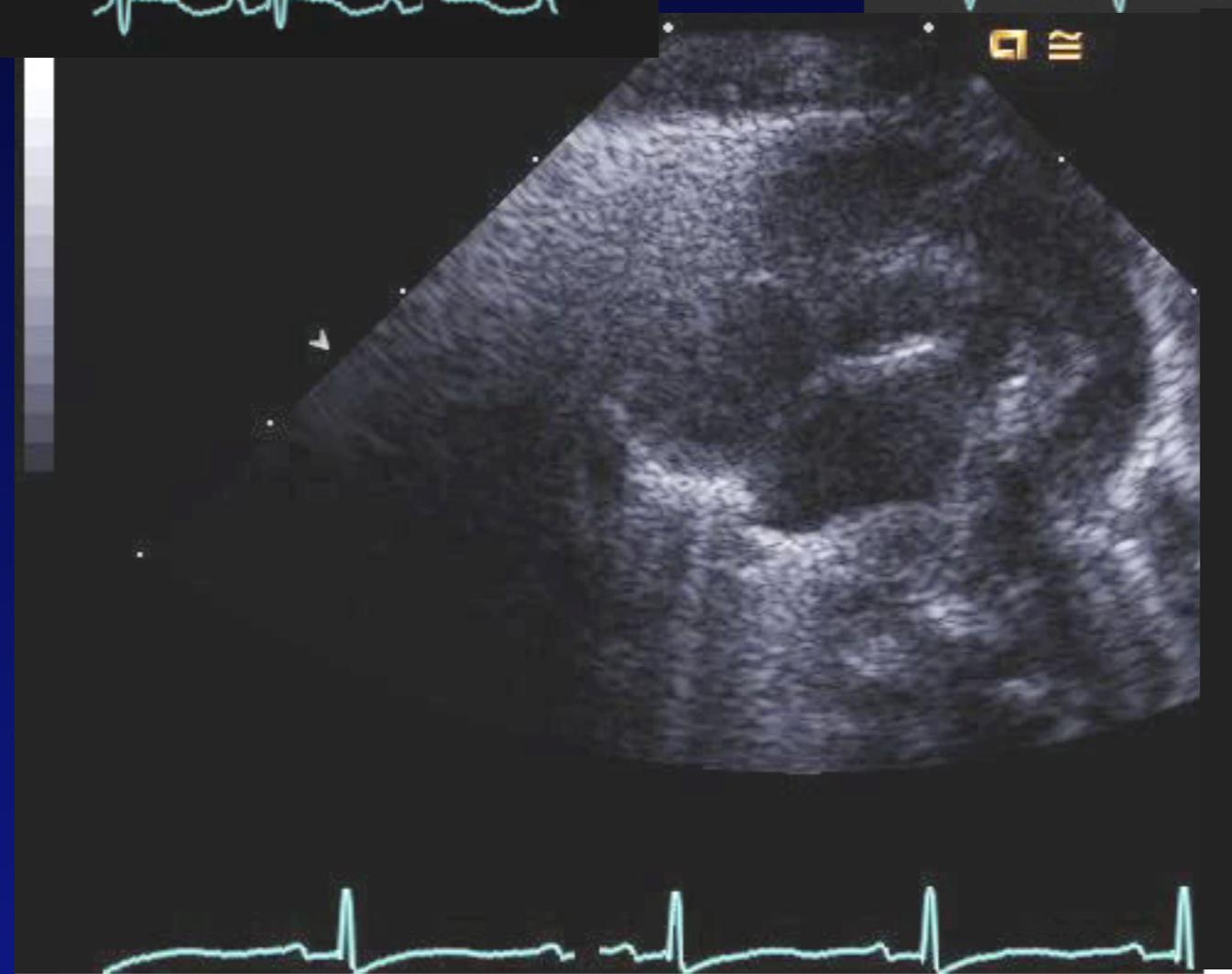
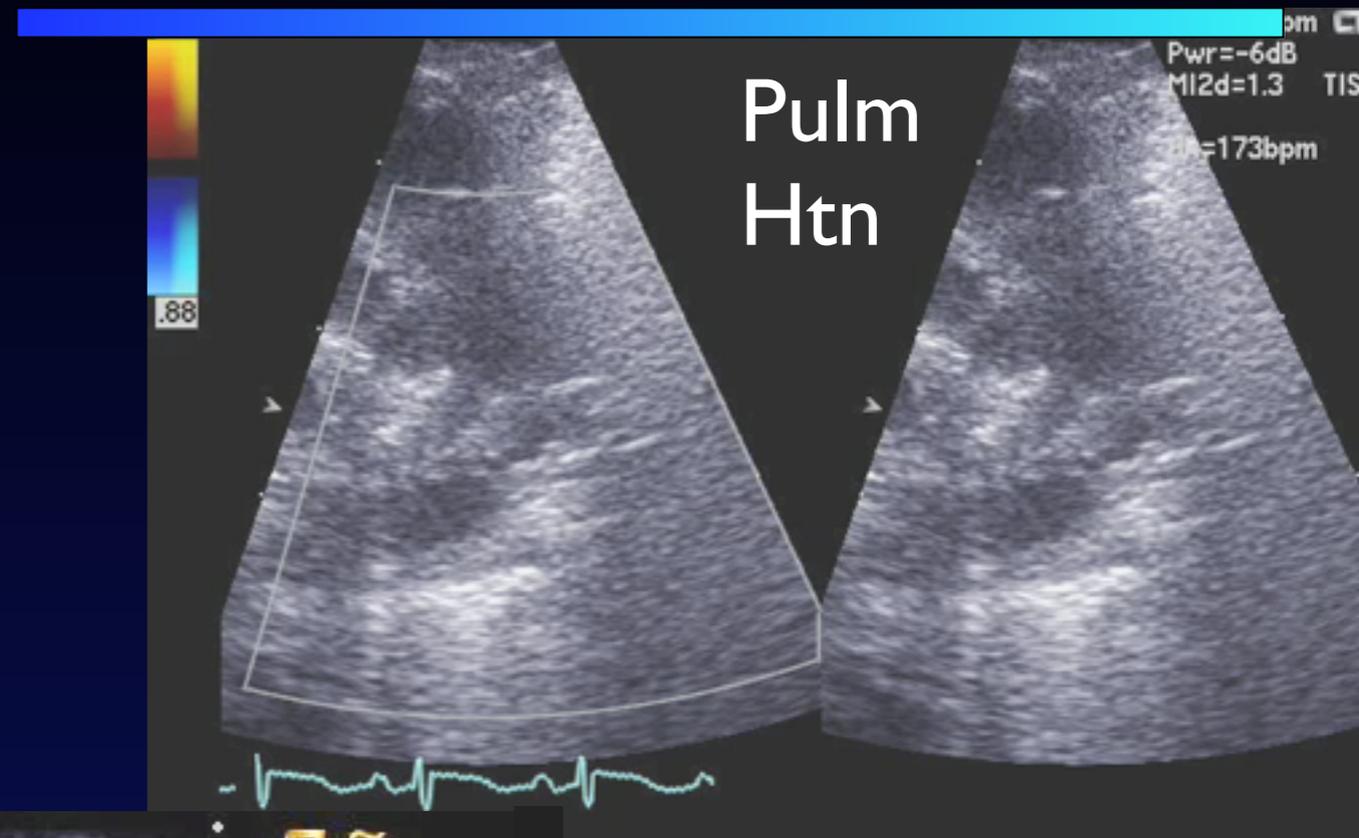
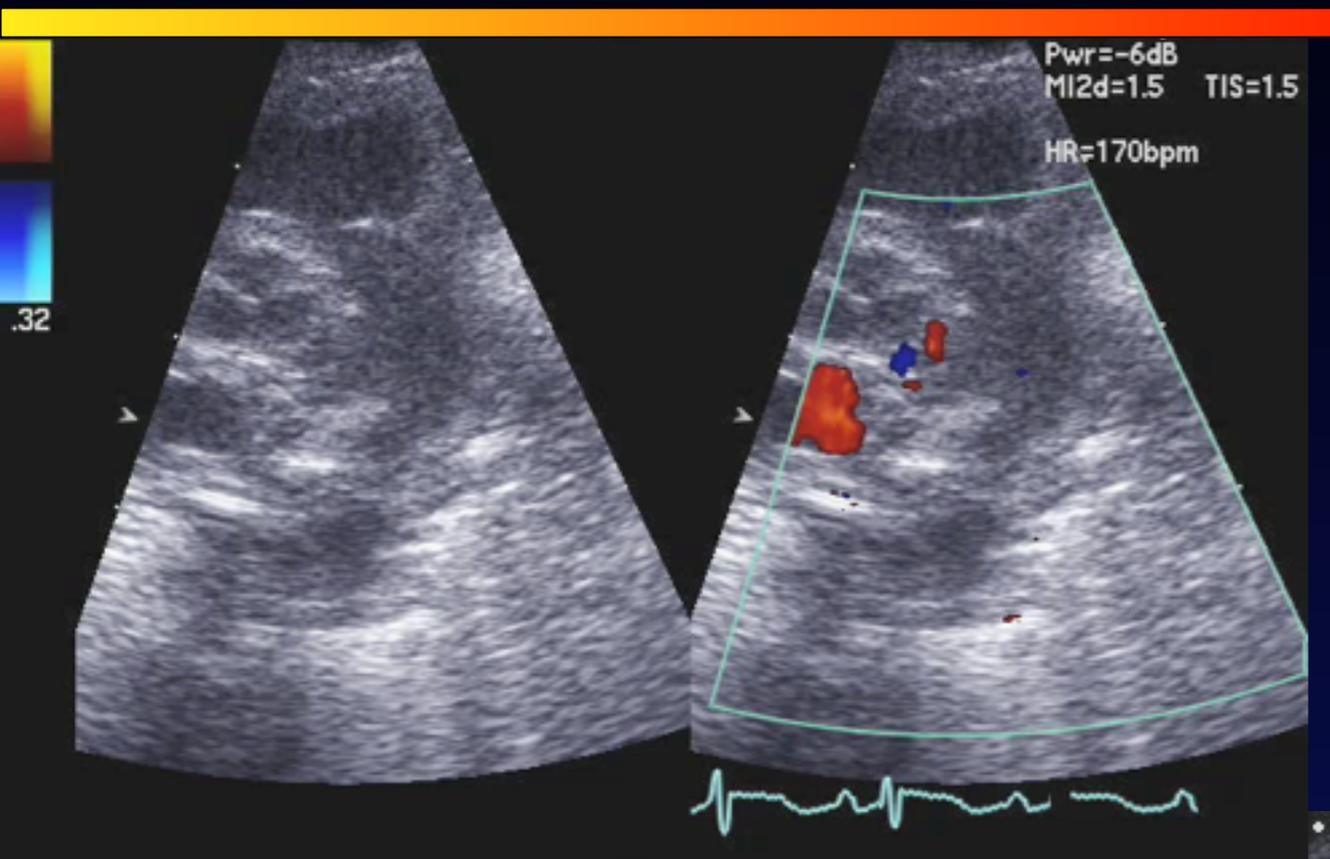
# Large PDA



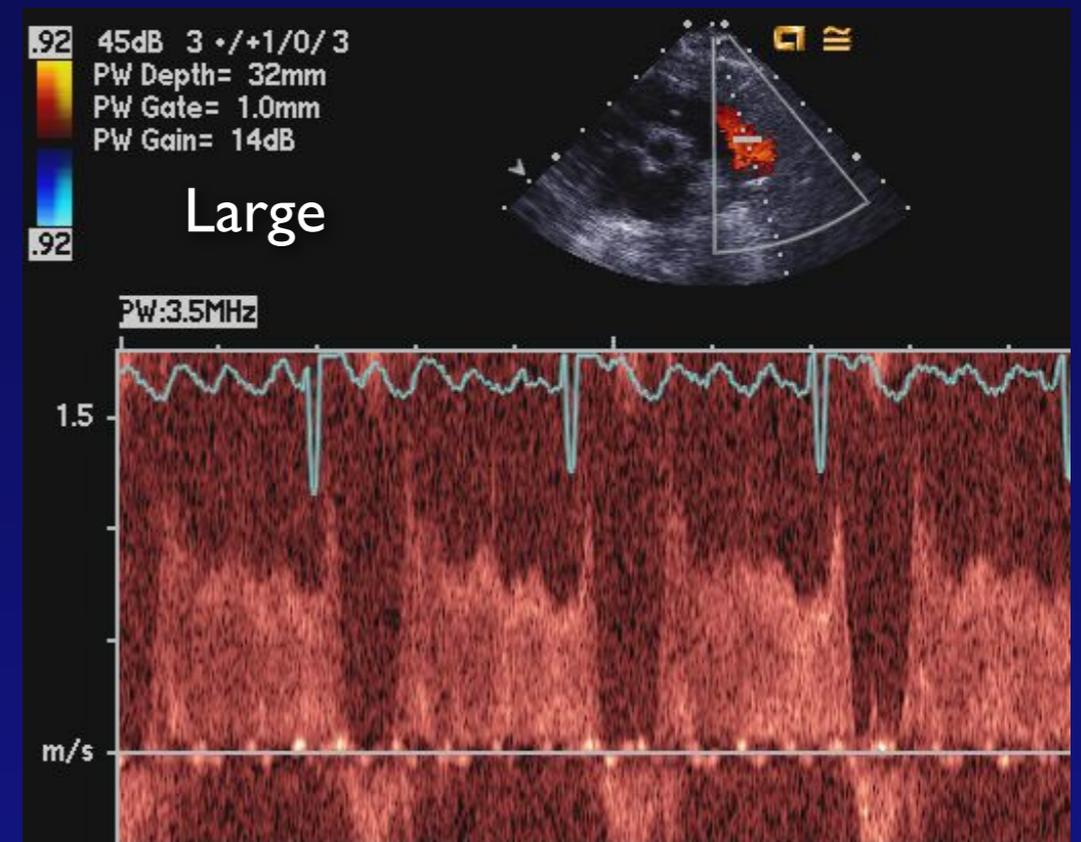
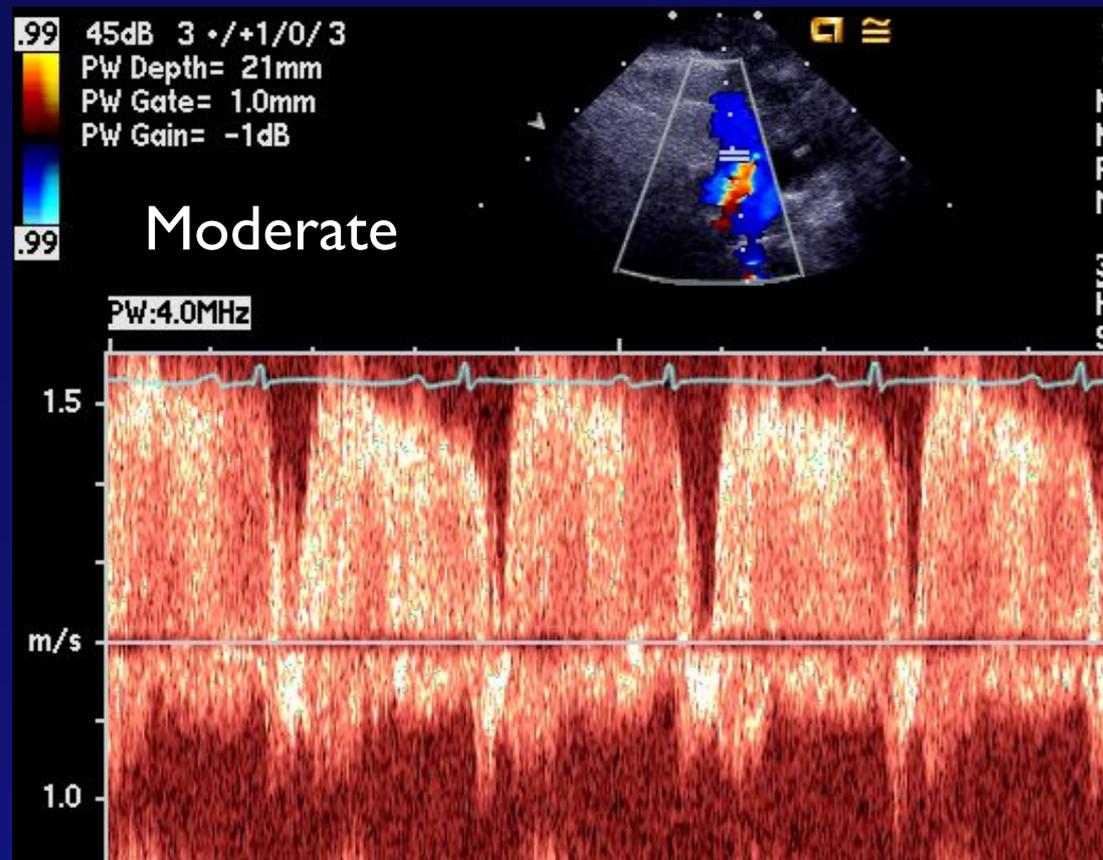
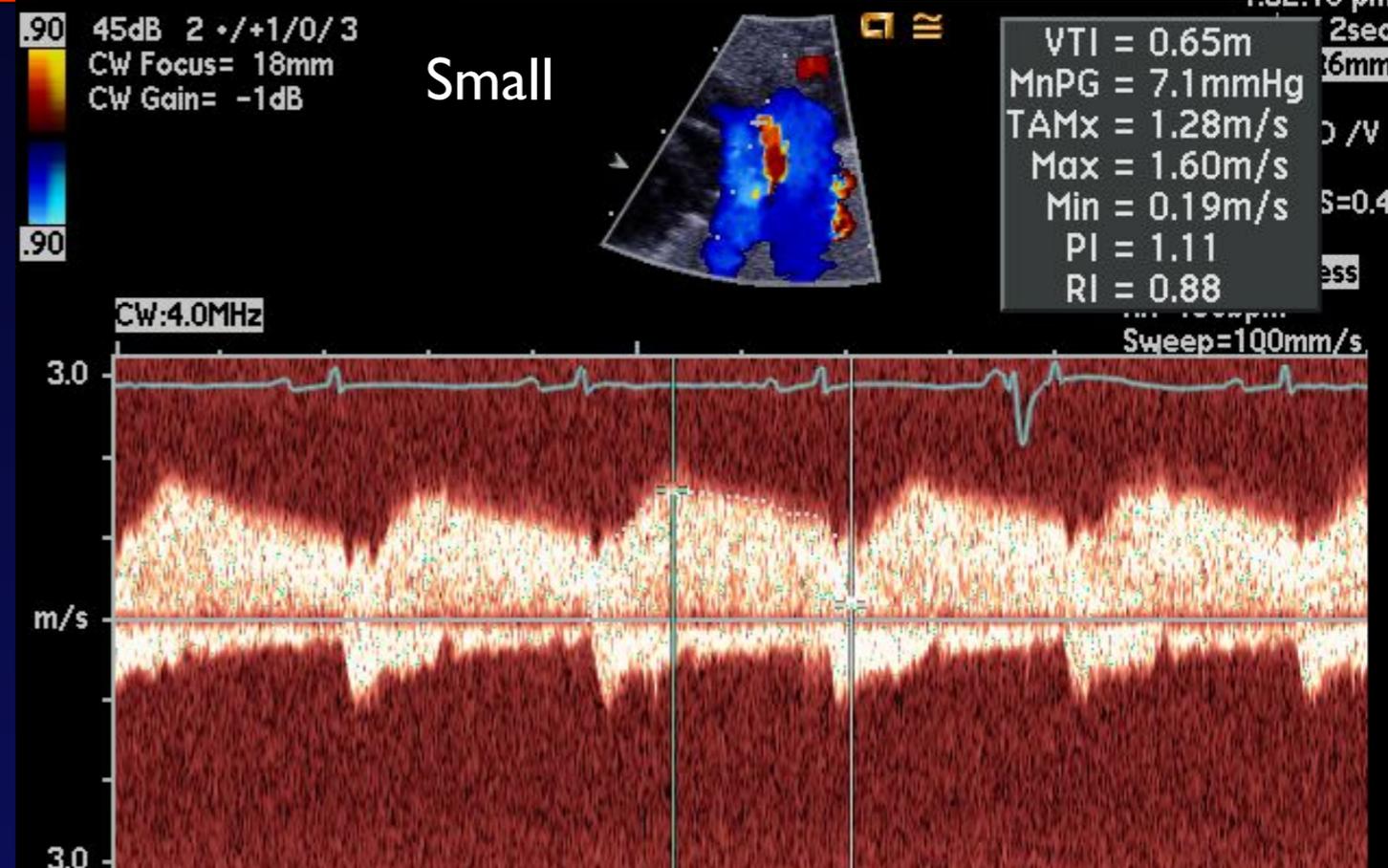
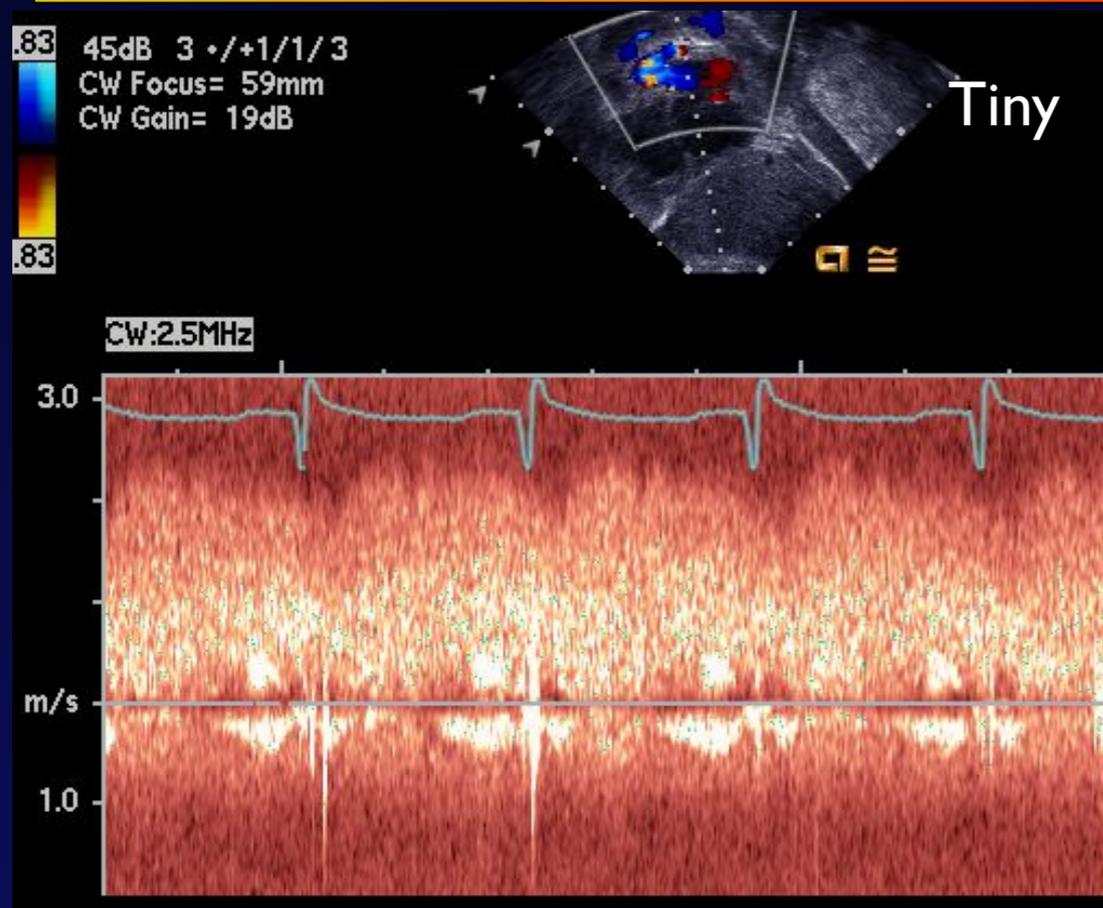
# Ductus Size



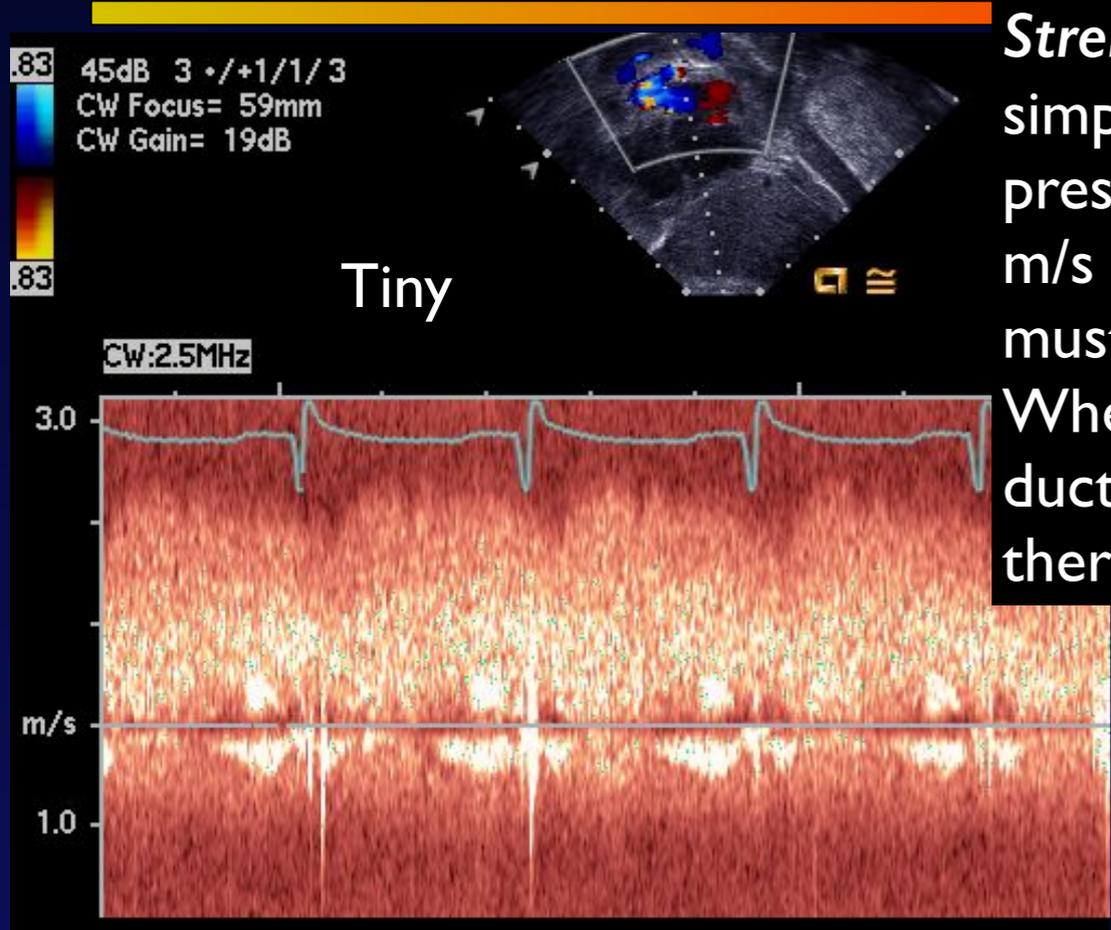
# Ductus Size



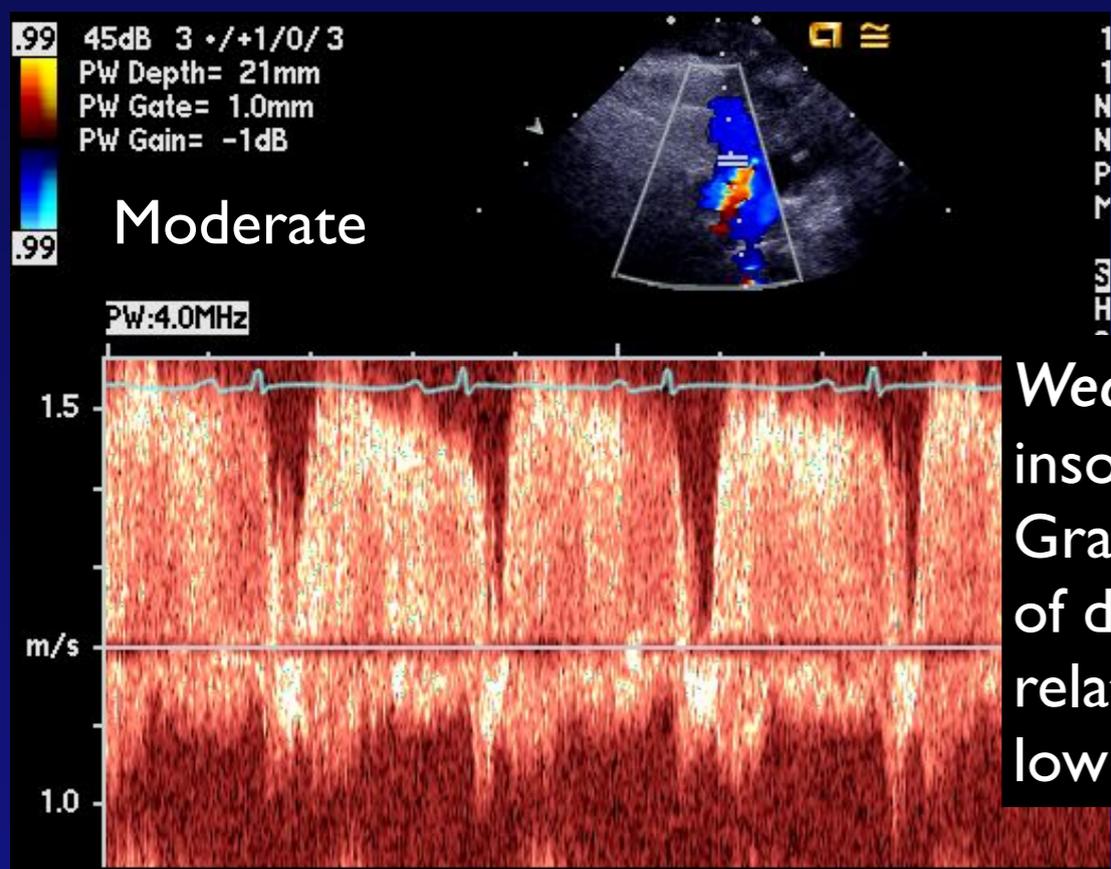
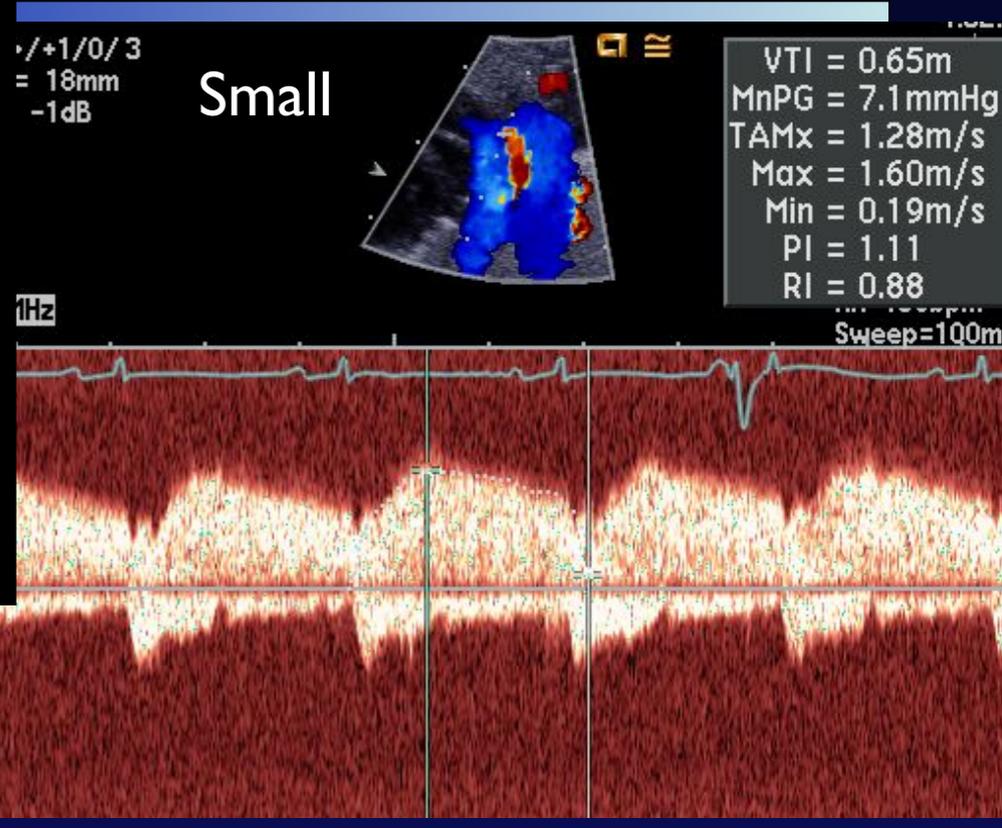
# Ductus Size: Doppler Velocities.



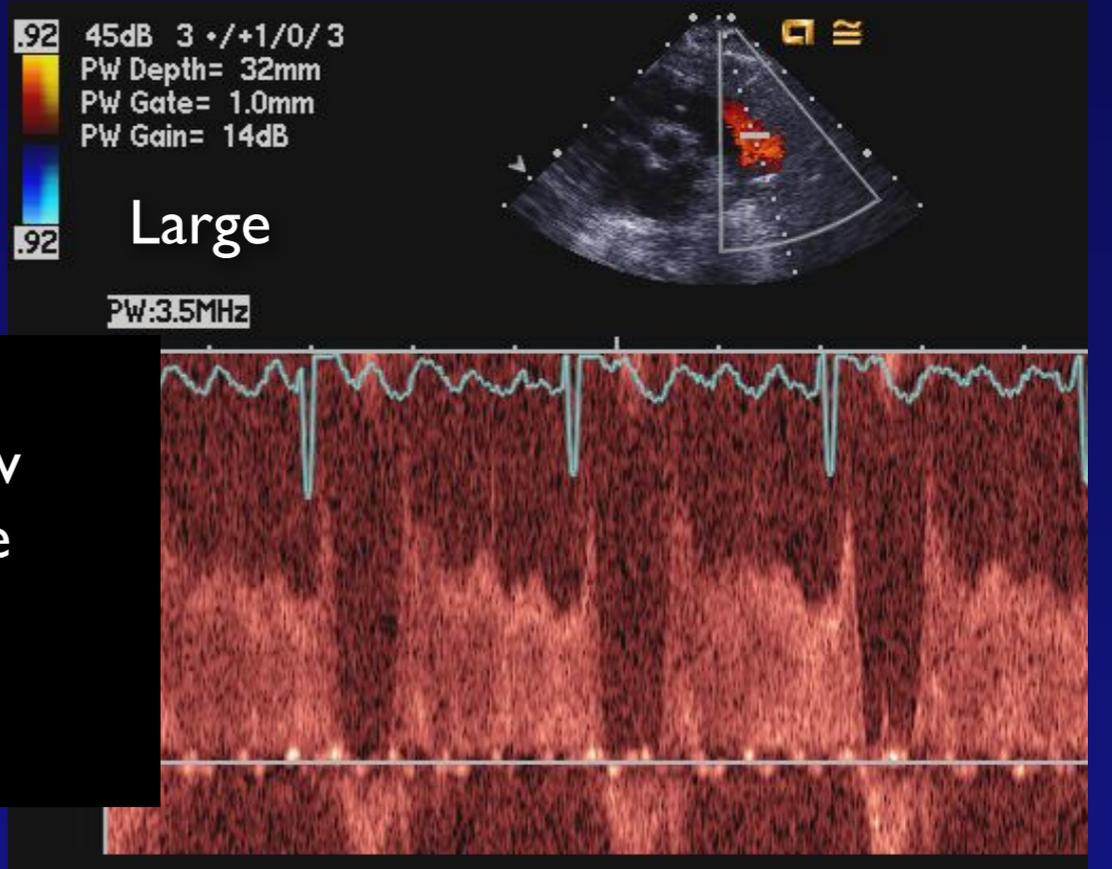
# Ductus Size: Doppler Velocities.



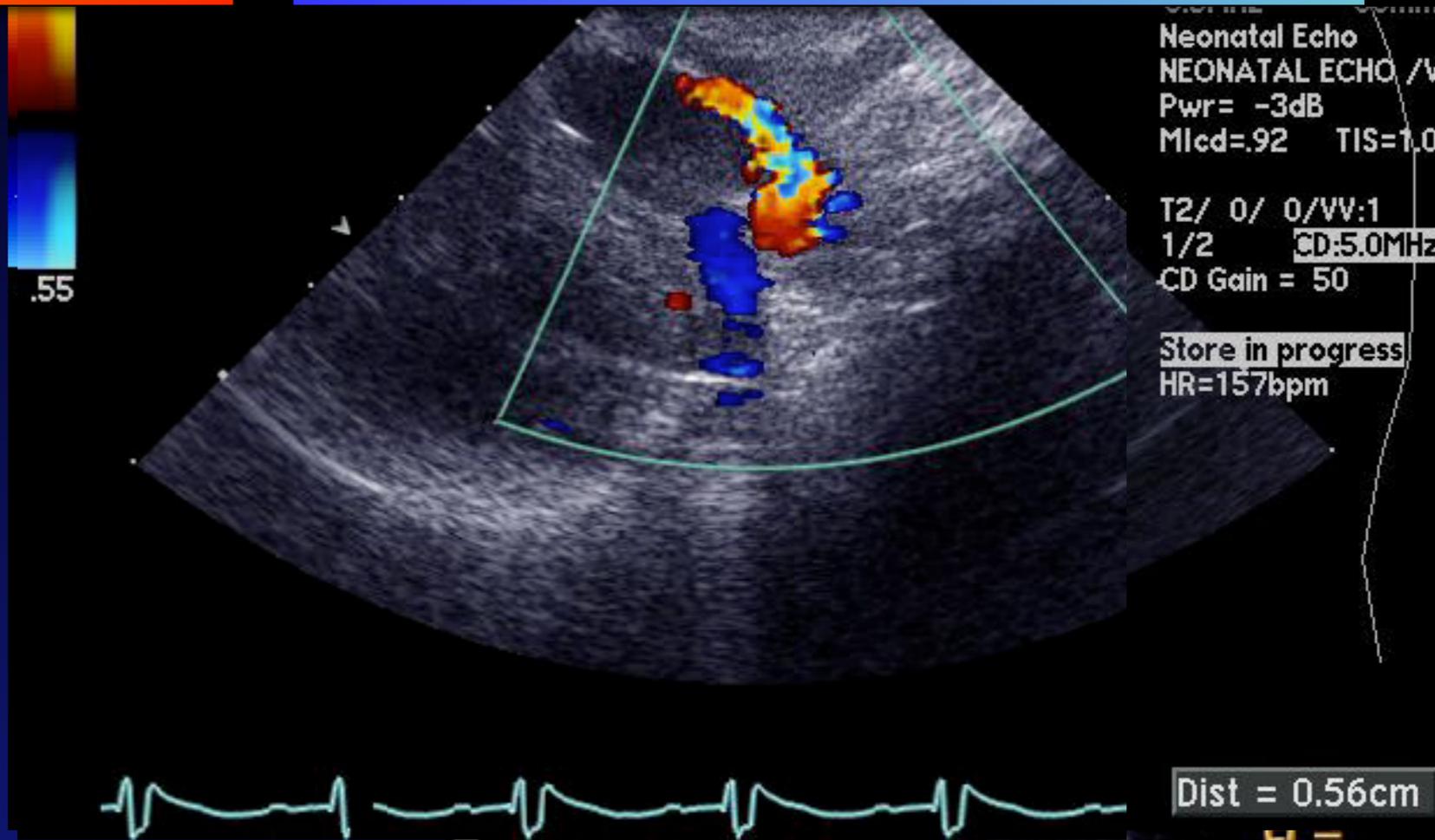
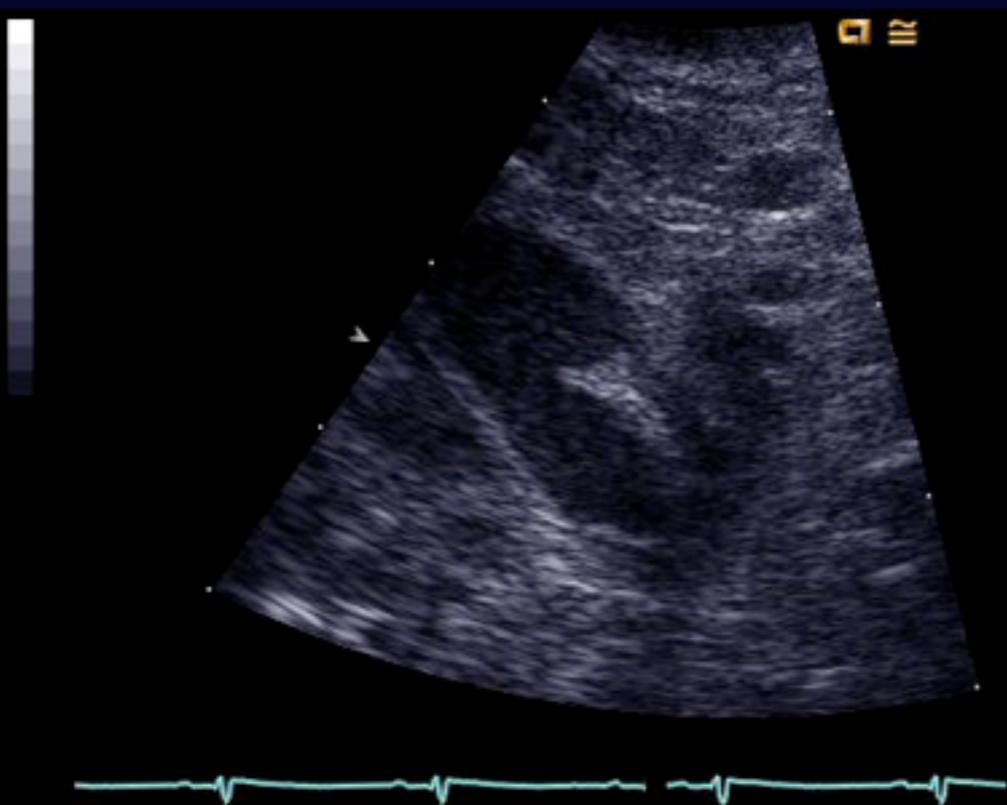
**Strength:** This is a simple measurement. A pressure difference  $> 1$  m/s means the duct must be constricted. When there is a large ducts and /or when there is PHT



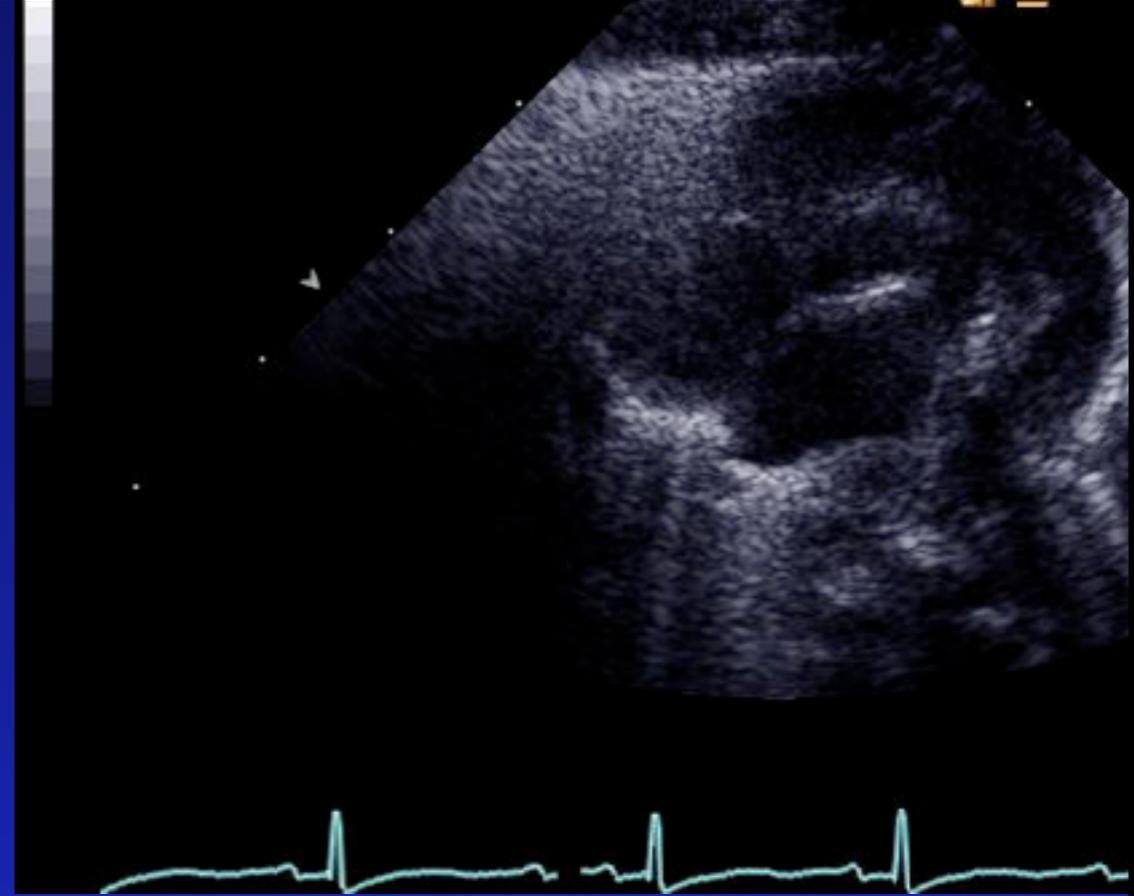
**Weakness** Angle of insonation has to be low  
Gradation of the degree of ductus constriction related to variations in low systemic pressures



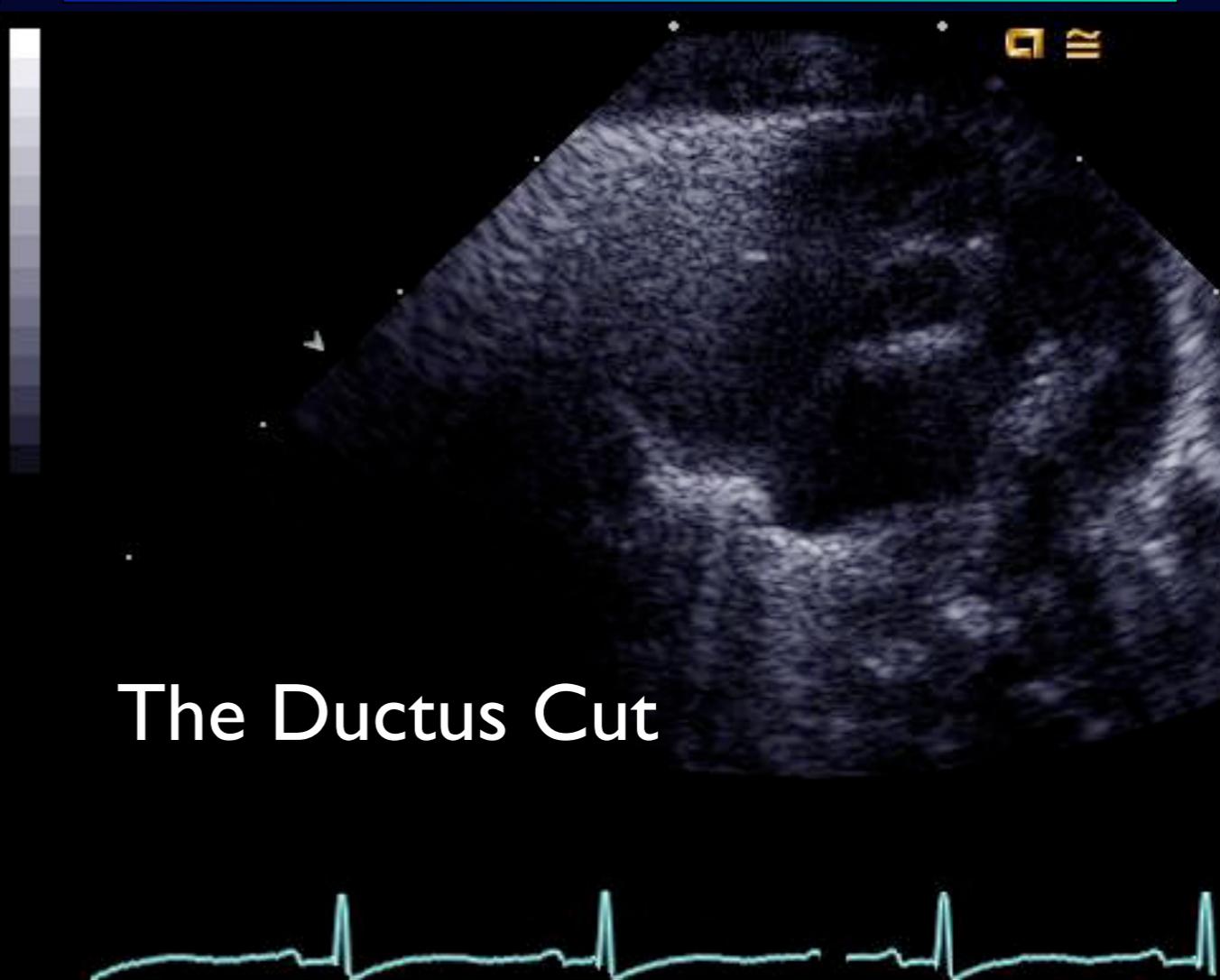
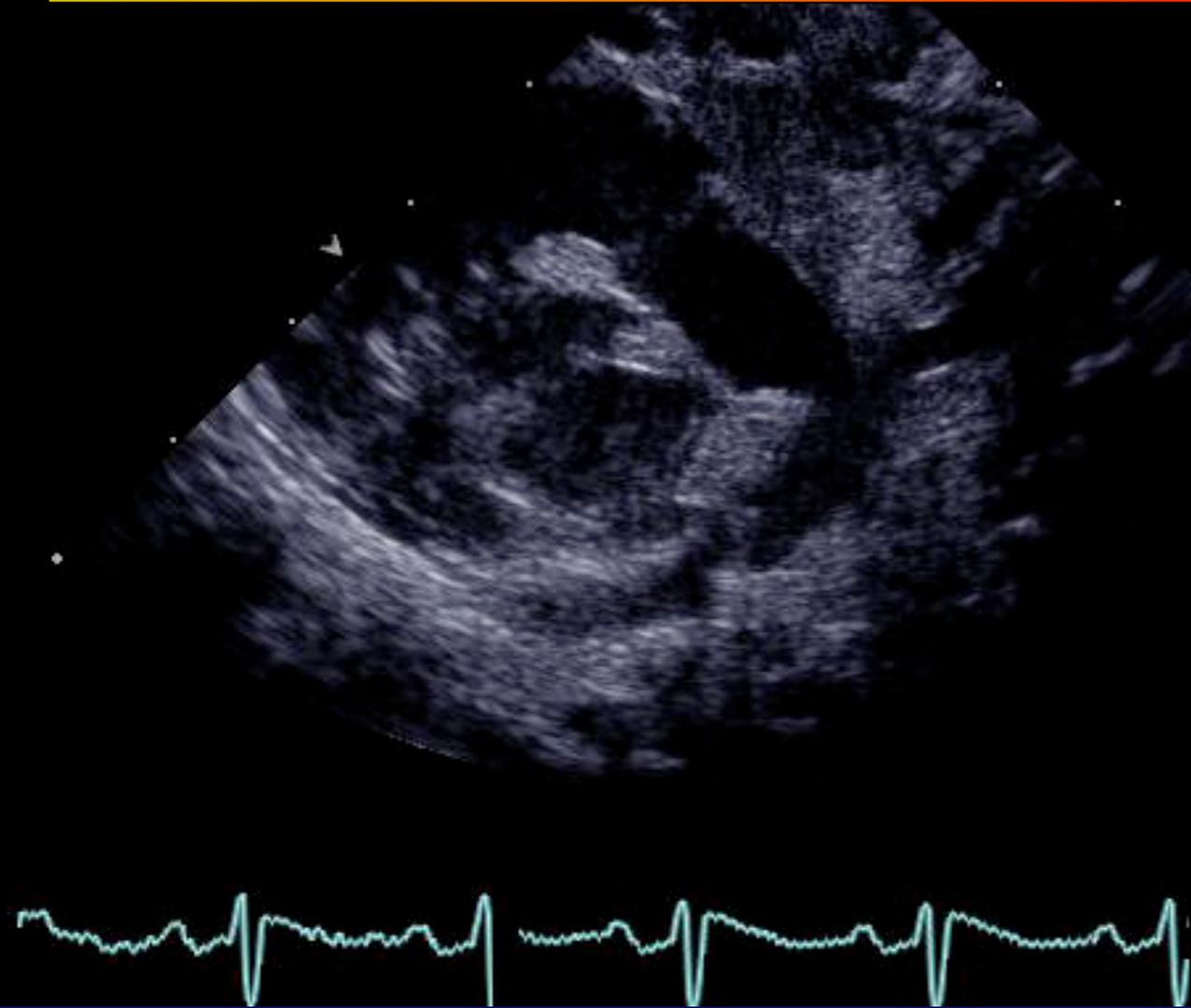
# Patent Ductus Size Assessment by Color



$$\begin{aligned}
 Q &= \frac{2\pi r^2 \cdot NL \cdot 60}{1000} \\
 &= 2.22/7 (0.04\text{cm})^2 \cdot 55 (= NL) \\
 &= 6.29 \times 0.0016 \times .55 \\
 &= 0.5532 \text{ ml/sec} \quad \dots \times 60 \text{ secs/min} \\
 &= 33.211 \text{ ml/min} \quad \dots \div \text{BSA } 0.18 \\
 &= 185 \text{ ml/min/m}^2 \text{ BSA} \quad \dots \div 1000 \\
 &= 0.185 \text{ l/min/m}^2 \text{ BSA}
 \end{aligned}$$



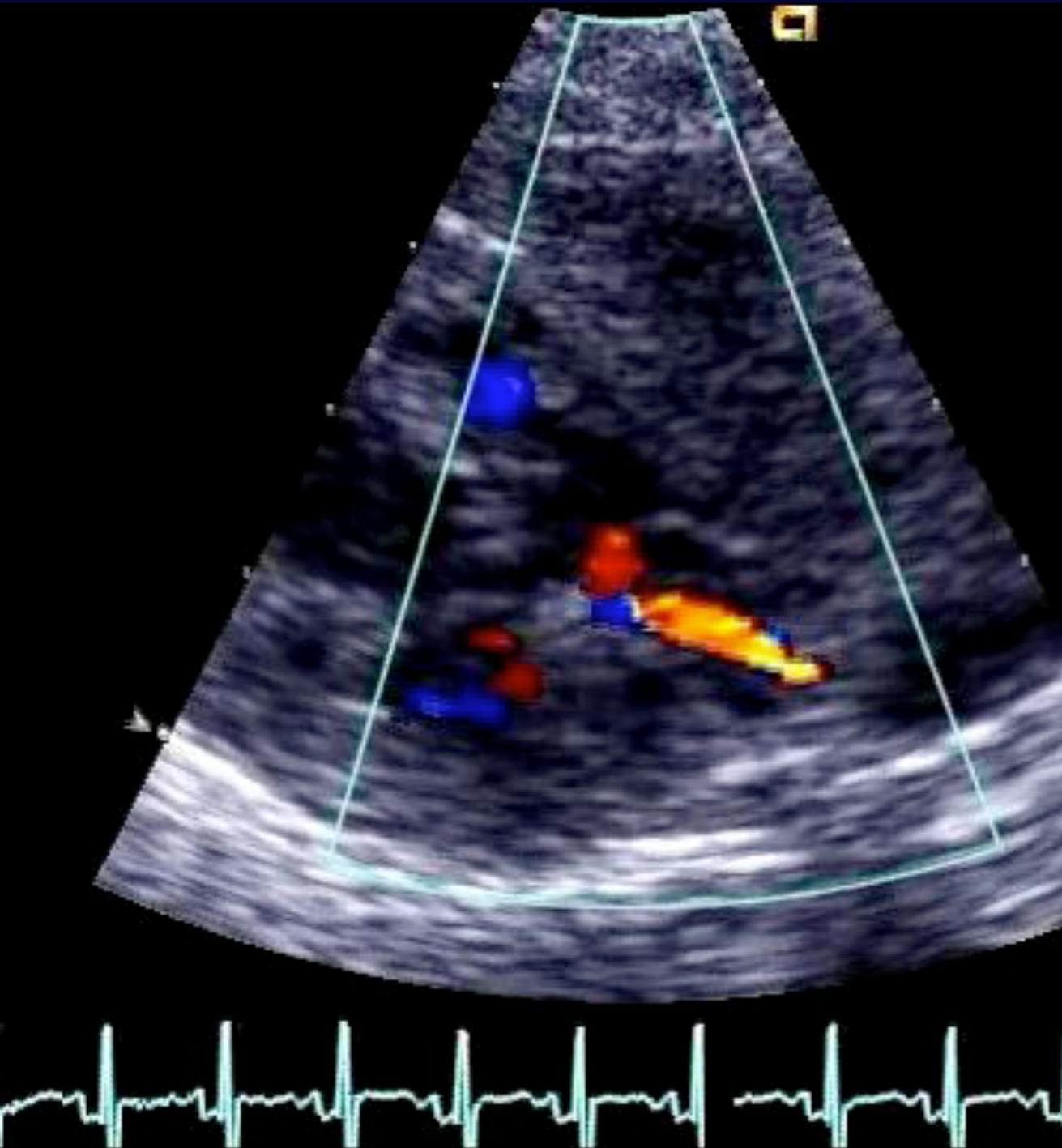
# Large PDA: PISA



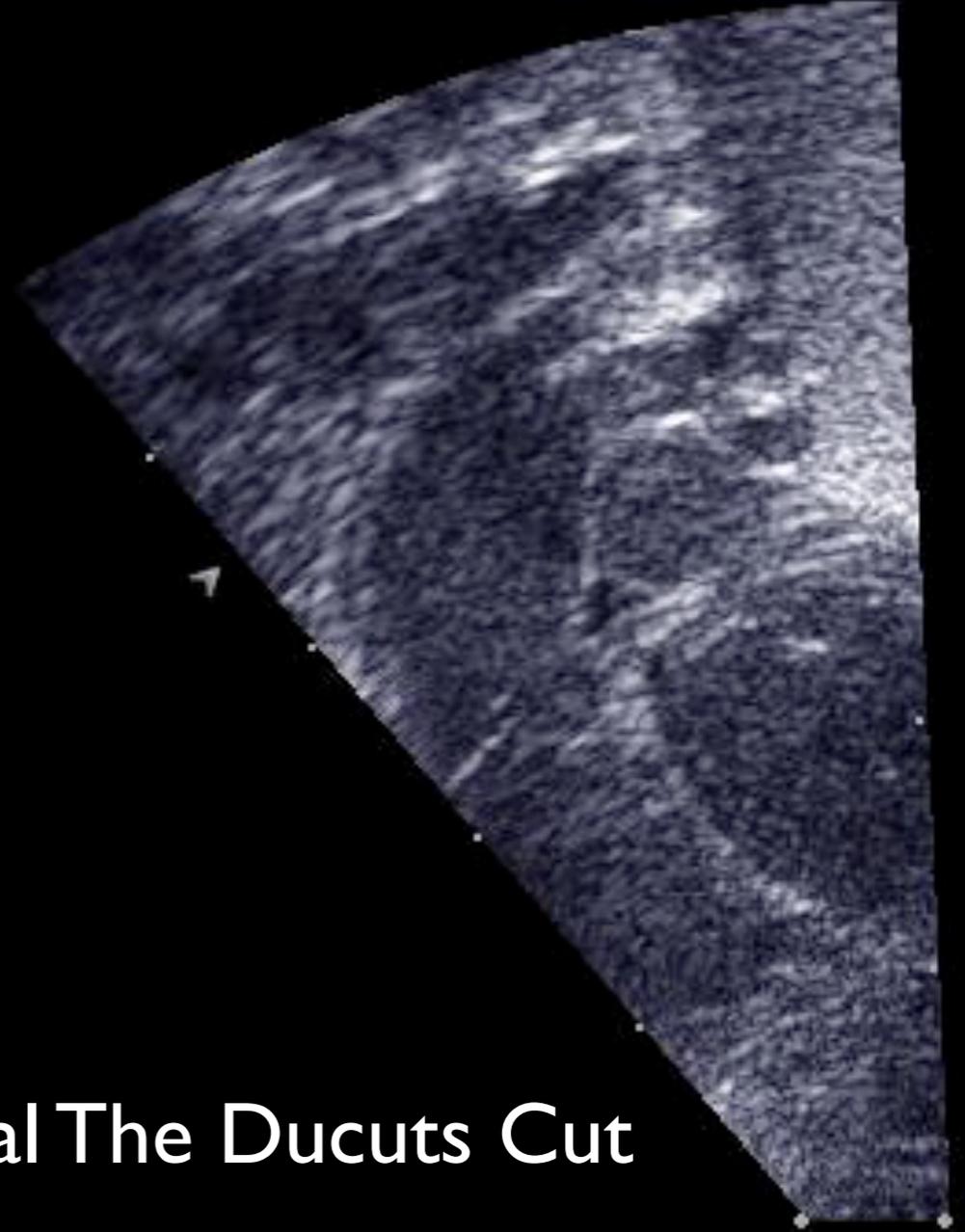
The Ductus Cut



# Small Ducts : Pisa & Vena Contracta

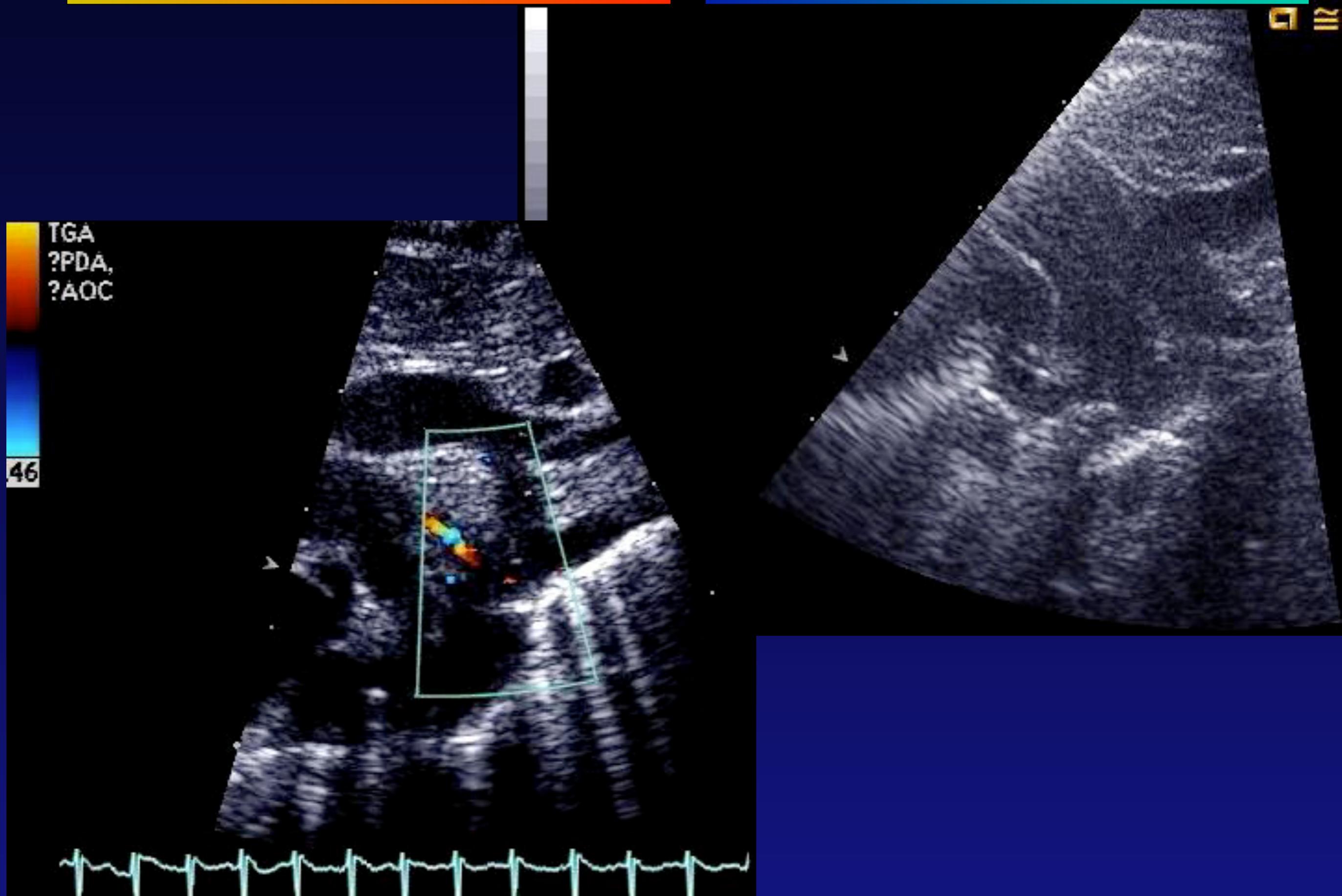


Parasternal Ducts Cut

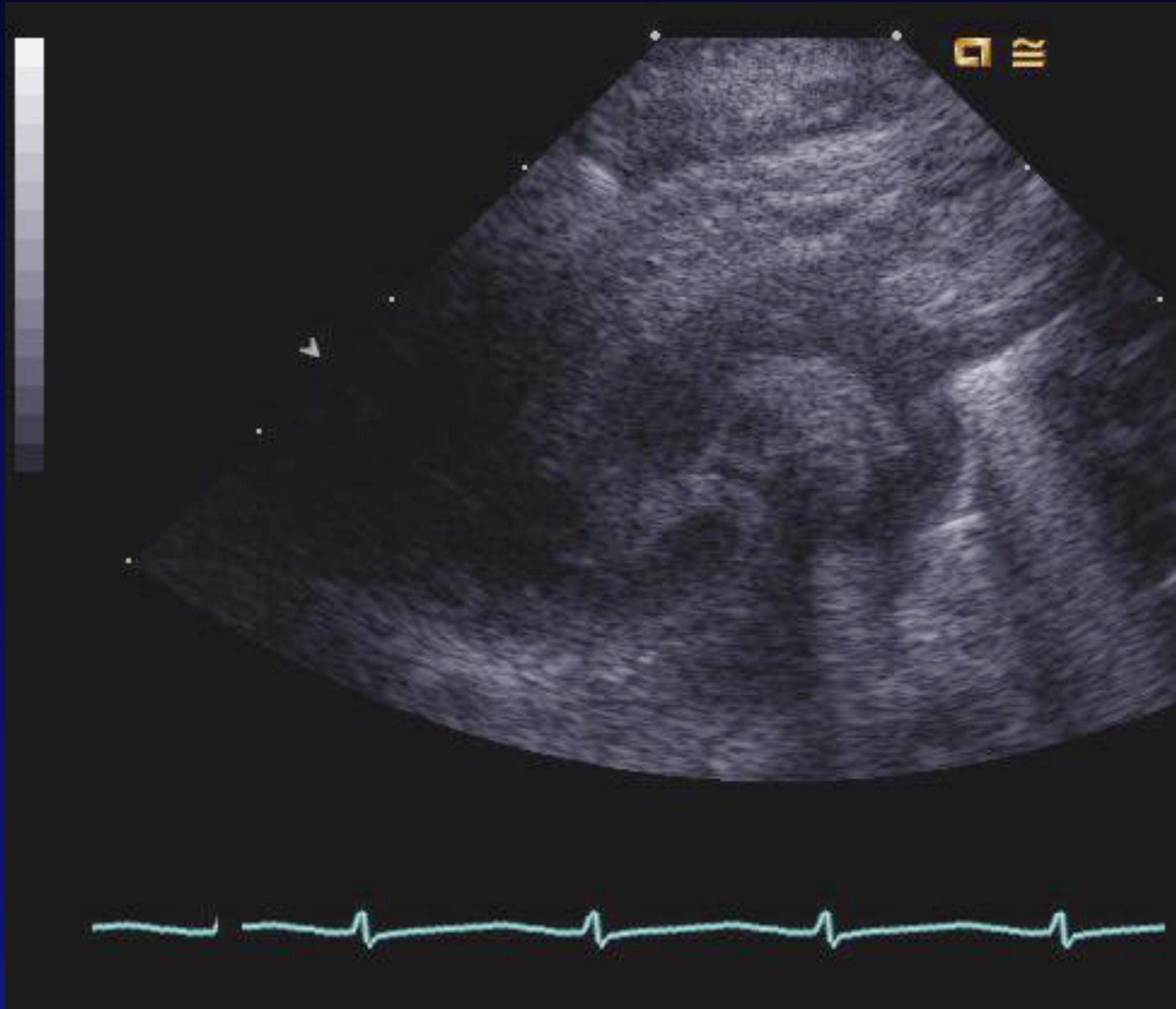


Subcostal The Ducts Cut

# Smaller PISA



# Closing Ductus



# Color Techniques

**Strength:** Doppler color flow is often more sensitive than imaging in defining flow, defining blood flow better than imaging, particularly with smaller ducts also more 3- dimensional in its character as the slice thickness is as limited in the regular image.

**Weakness:** With all Color Doppler modalities the techniques is sensitive to machine type, gain, filtering, and changes in the Nyquist limit. So we can have a variety of possibilities, which make assessments somewhat artifactual.

## (i) The PISA Method.

**Strength:** This technique has been validated in laboratory situations permitting fairly accurate assessment for flow on the proximal side of a jet. This is the only Doppler technique which allows for the assessment of flow within a jet system

**Weakness:** Unfortunately, it requires two circumstances to be accurate. The first is the orifice through which the flow occurs has to be round and the second is that the jet should not be interfered with by the lateral confines of the duct.

Not being a free jet and some of it may be confined and altered by the shape of the duct. There are many confounding problems in assessing flow across the duct by this means because there is no free jet in this situation. What we have observed is that when there is a large ductus with large amount of flow, there is no PISA because there is no constriction, when there is a moderate sized ductus with a moderate amount of flow, there is a large PISA and when there is when there is a small ductus with small amount of flow, there is a small PISA.

# Color Techniques

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**(ii) Vena Contracta and Color Doppler Jet Width Measurement.**

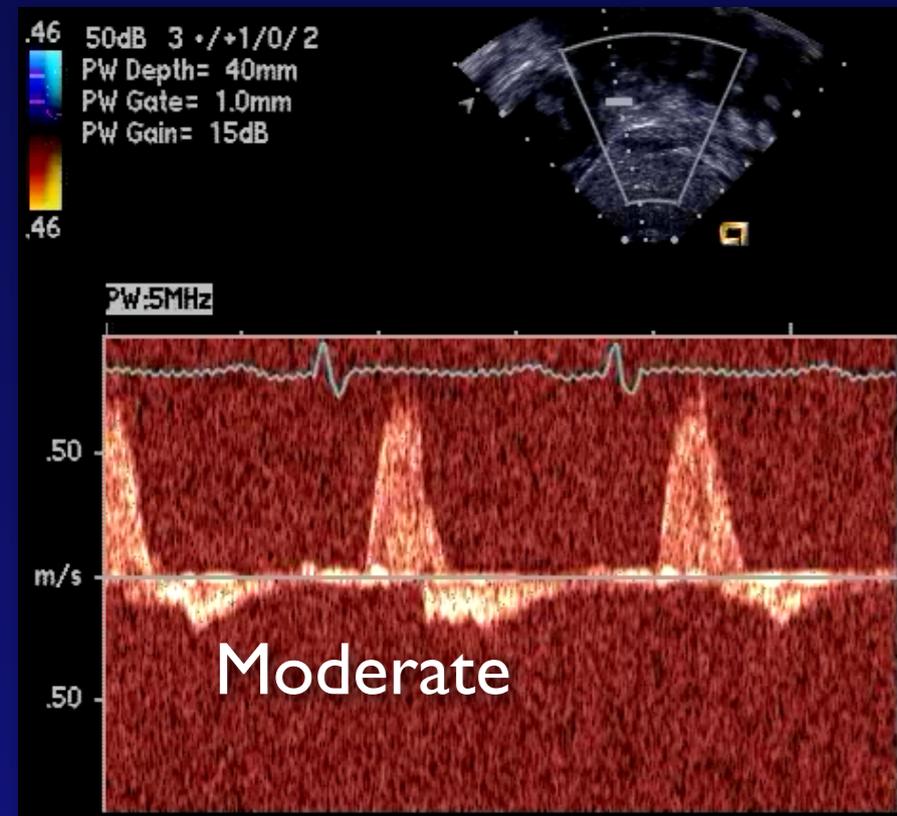
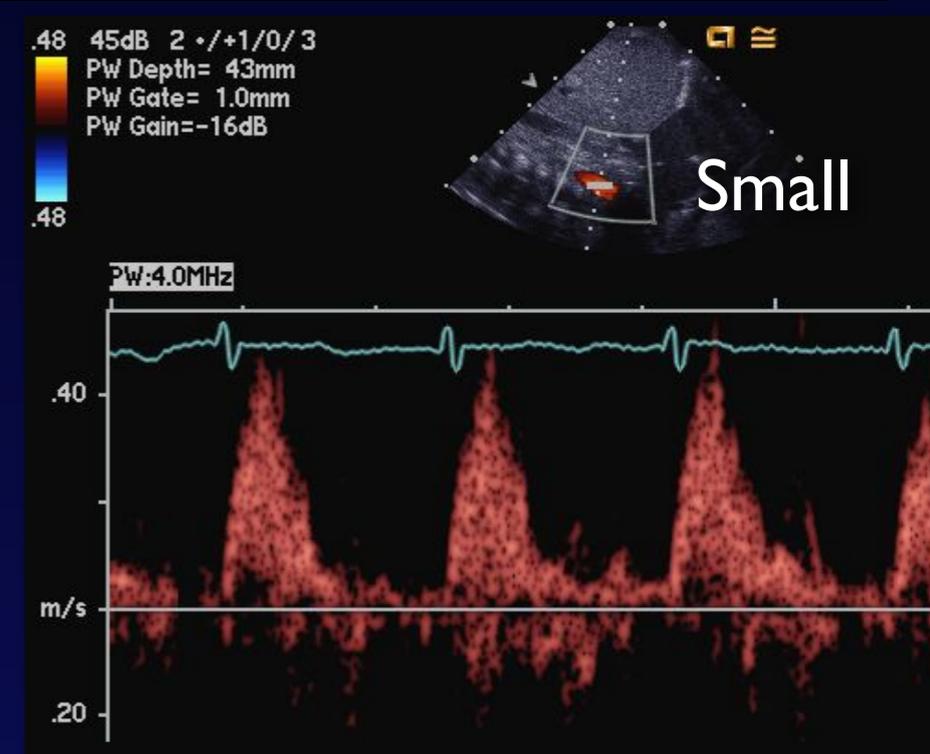
***Strength:*** The same as for the previous sections on Doppler color flow.

***Weakness:*** The same as for the previous sections on Doppler color flow

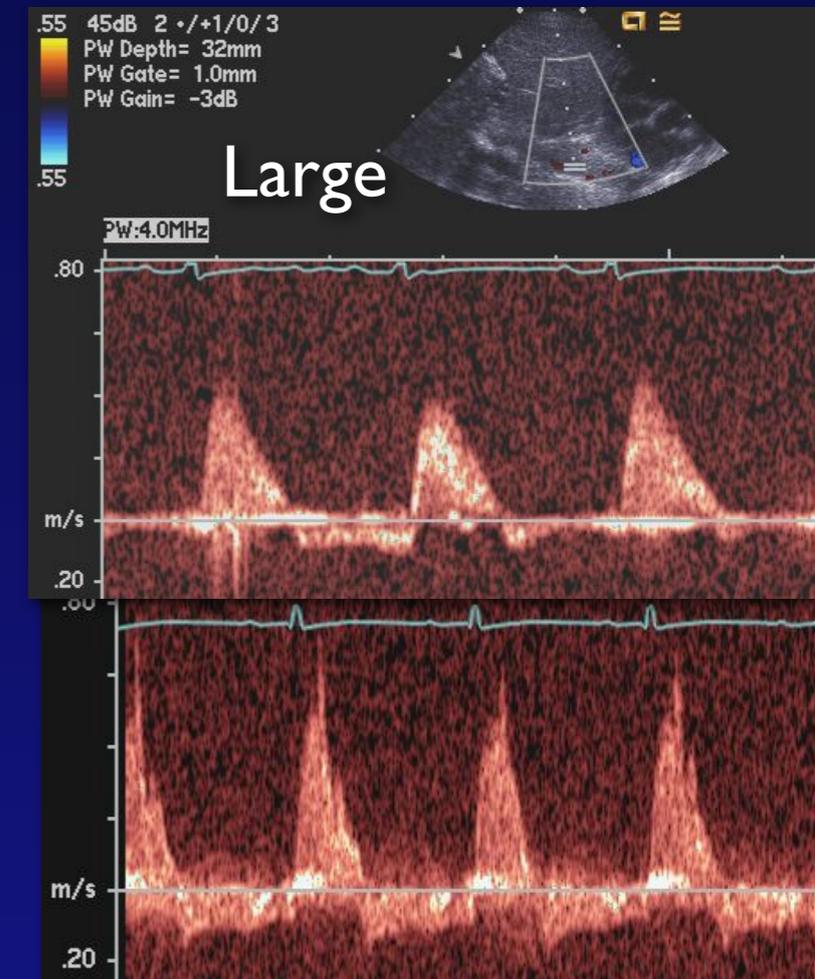
# Ductus Size: Doppler Velocities in the Abdominal Aorta.



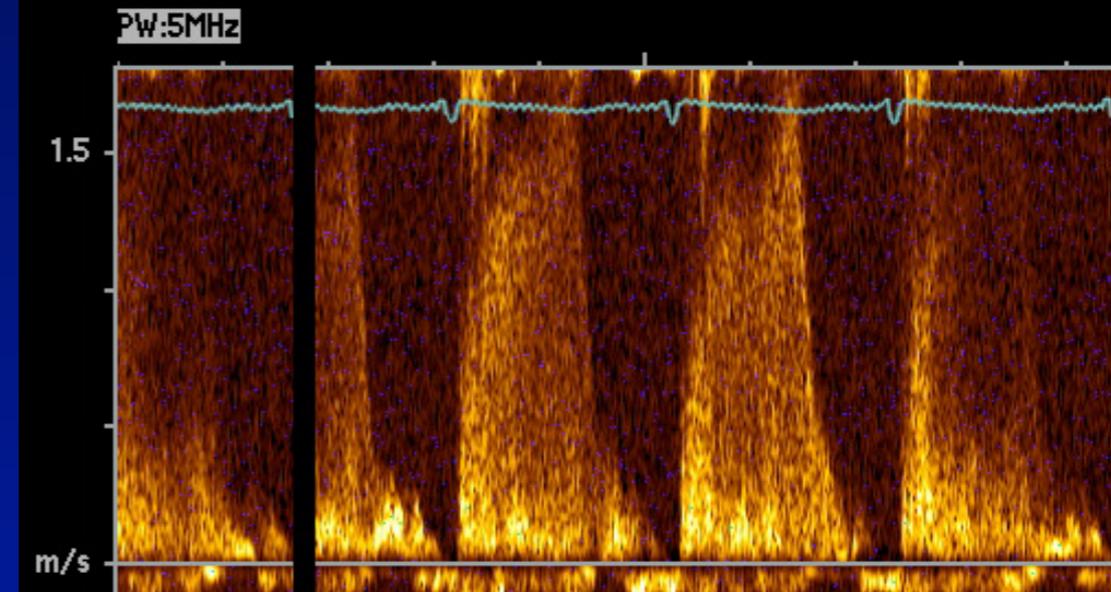
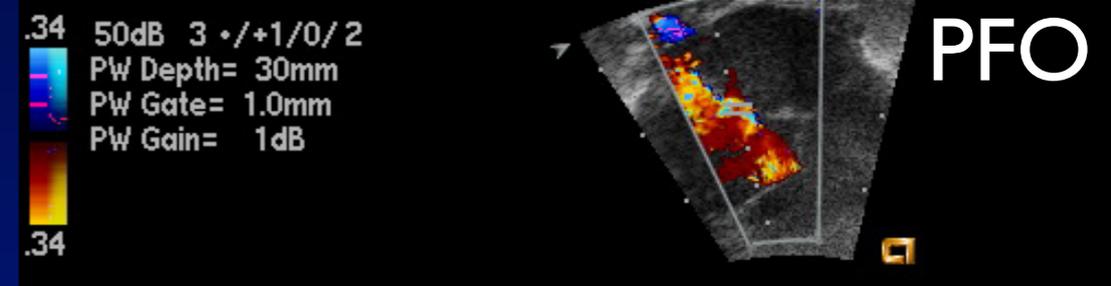
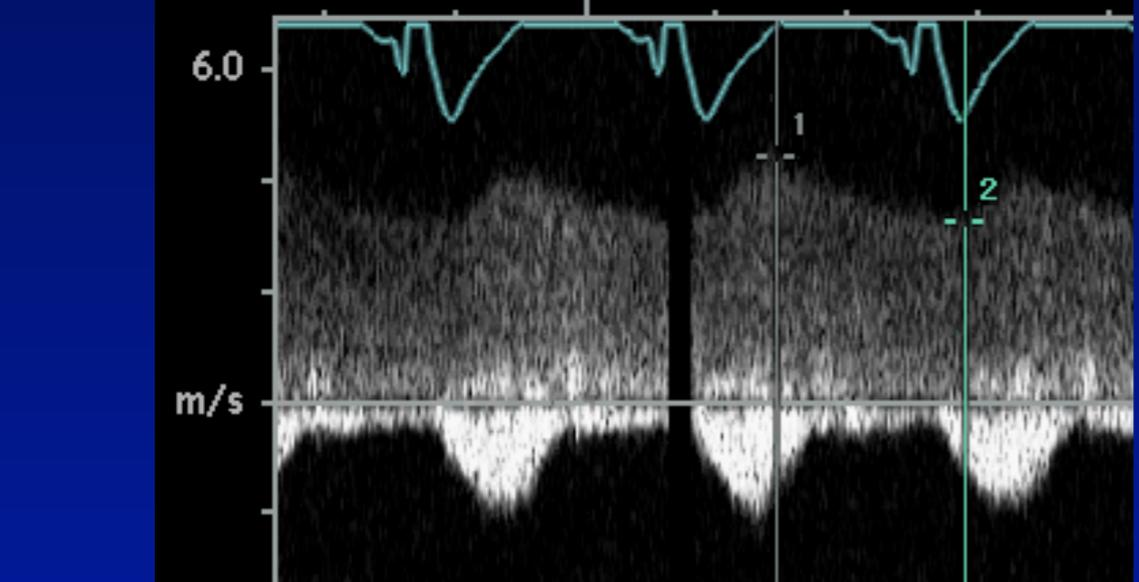
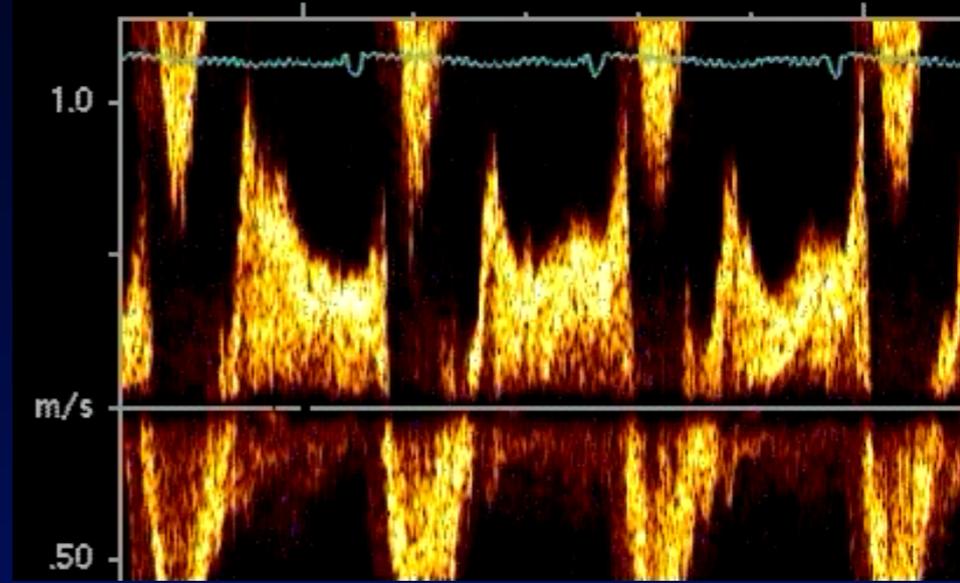
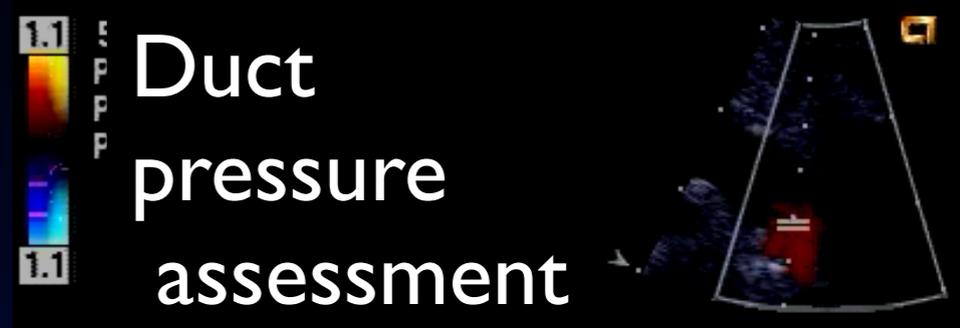
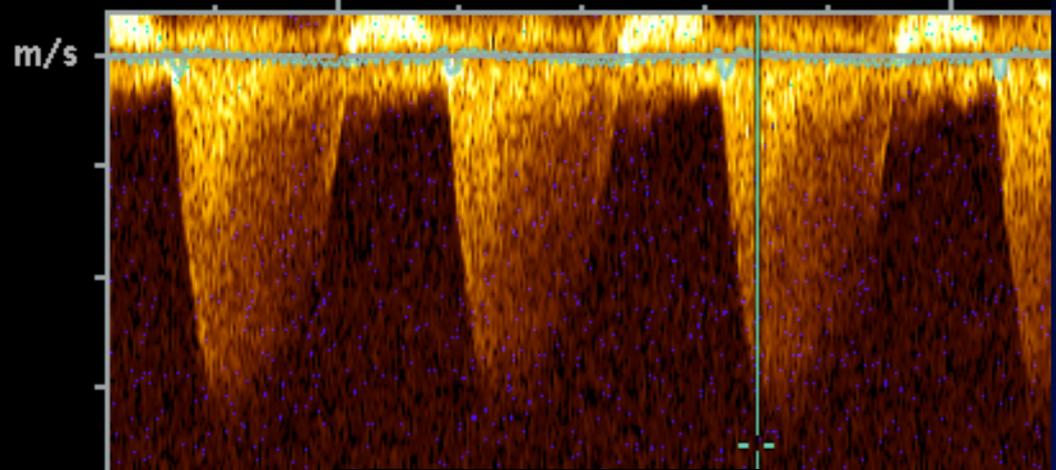
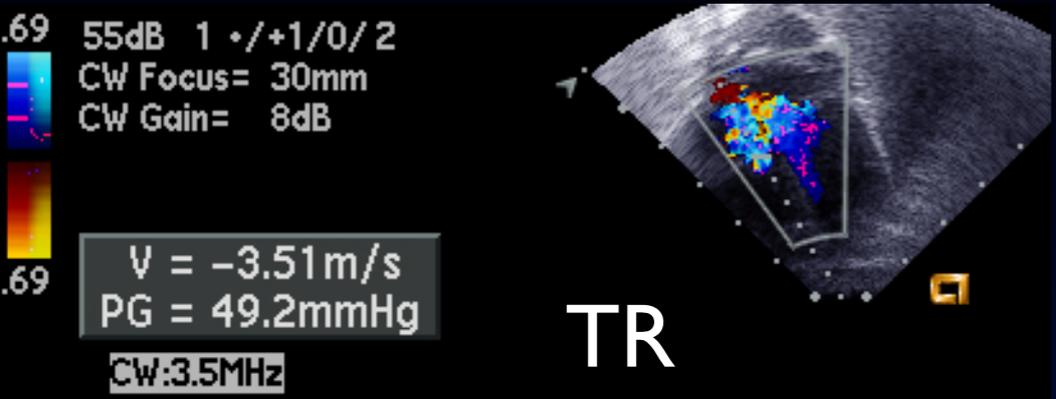
**Strength:** Surrogate for blood pressure measurement, It really looks for runoff of a large shunt and for retrograde flow. Lesser degrees of flow are found to occur with lesser shunts.



**Weakness:** Technologists often don't get axial enough to evaluate flow adequately and in that circumstance the low velocity of the retrograde flow can be lost. Wall Filter issues: If the wall filter- if too high, obfuscates the low flow



# The Ductus and Pressure Assessment



# Ductus Assessment.

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- ♥ There are many critical issues in measurement of ductus size. We need to get better at measurements
- ♥ What we need to concentrate on is which ductus is critical in terms of defining outcomes
- ♥ Perhaps we need to concentrate only on the large PDA in terms of outcomes
- ♥ Clearly prospective trials are necessary
- ♥ We have been examining too many ductuses by Echo in preemies!



# What about Cox inhibitors?

- ♥ Based on current evidence, prophylactic indomethacin is not recommended for the treatment of PDA in preterm infants.
- ♥ There are well-established side effects of indomethacin, such as significant reduction in cerebral, mesenteric, and renal blood flow velocities as measured by Doppler ultrasonography, as well as possible adverse effects on platelet function, have raised serious questions on the prophylactic use of this drug
- ♥ With growing concerns over the side effects of indomethacin, a safer alternative was requested. Ibuprofen has been shown to be less nephrotoxic than indomethacin.
- ♥ It has been found that 85.2% of PDAs closed if the first dose of indomethacin was administered within 24 hours of birth. However, this rate decreased to 48.1% when treatment was started 72 hours or later after birth. It has been shown that although early indomethacin treatment improved PDA closure rates, it was associated with increased renal side effects and offered no respiratory advantage over late indomethacin administration in ventilated surfactant-treated infants



# What about Surgical Ligation?

- ♥ They found that even though infants were exposed to larger PDA shunts for longer durations in the conservative treatment period, the rates of BPD, sepsis, retinopathy of prematurity (ROP) neurological injury, and death did not change. However, their overall rate of was significantly lower.
- ♥ It has also been shown in experimental models that early surgical ligation of the duct impedes lung growth in preterm baboons.
- ♥ The lack of any respiratory or neurological benefit shown by these studies, recent research also indicates that surgical ligation of the duct may in fact cause more harm than good. It has been shown that secondary surgical closure was associated with increased odds for neurodevelopmental impairment and increased adjusted odds for BPD but decreased adjusted odds for death



# What About Interventional Catheterization?

## Trans-catheter Closure of Patent Ductus Arteriosus (PDA) in Extremely Low Birth Weight (ELBW) Premature Infants: A New Treatment Option for an At-Risk Population

June 2014; Volume 12; Issue 6

By Evan M. Zahn, MD; Ruchira Garg, MD;  
Alistair Phillips, MD

**C O N G E N I T A L**  
C A R D I O L O G Y T O D A Y

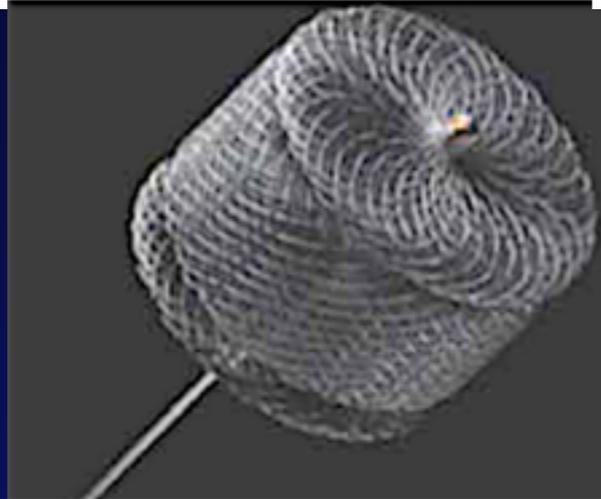


Table 1. Demographic Data

Patient	Birth Weight (gm)	Gestational age (weeks+days)	Sex	Procedure Weight (gm)	Procedure Age (days)	Ventilator Dependence	Inotrope Dependence
1	2480	31+6	Female	2240	18	yes	yes
2	440	26+4	Male	1610	80	yes	no
3	1050	26+3	Male	1140	16	yes	no
4	1077	26+3	Male	1220	20	yes	no
5	856	26+3	Female	960	21	no	no
6	675	29+0	Female	870	30	yes	no
7	900	28+3	Male	1155	22	no	no
8	610	27+0	Female	1655	78	yes	no
9	1000	26+2	Female	1400	30	no	no

# Conclusion From Mitra

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♥ There is no generally accepted understanding of the echocardiographic markers of hemodynamic significance and their importance for treatment or prognosis. Echocardiography could be looked upon as the best representation of the circulatory state, but a fundamental problem is the lack of gold standard for the physiologic effects of a ductal shunt related to the echocardiographic findings. The relative importance of pulmonary over circulation, vascular resistances, and systemic hypoperfusion also remain to be clarified.

# ACP High Value Care

Misuse and overuse of medical interventions that do not directly improve a patient's health contribute significantly to the unsustainable growth of healthcare spending. ACP's goal is to determine whether diagnostic tests and treatments for various diseases provide good value, i.e. medical benefits that are commensurate with their costs and outweigh any harm. We do this by analyzing their benefits, harms, and costs based on the best available evidence.

Approximately 30% of healthcare costs (more than \$750 billion annually) are spent on wasted care.

ACP has developed clinical recommendations, physician resources, curriculum and public policy recommendations around this initiative.



# Comparison of Data Points on Stanford Study

- ♥ Left atrial size by M-mode normalized to the aorta as LA:Ao ratio
- ♥ Also Left atrial by 2 D area as a reflection of LA Size
- ♥ Ventricular Function. Fractional Shortening index as a surrogate for ejection fraction
- ♥ Mitral regurgitation and atrial left to right shunt which might compromise estimate of LA size
- ♥ Retrograde diastolic flow by Doppler ultrasound in the abd. aorta as a surrogate for systolic: diastolic and pulse pressure.
- ♥ Ductus size measurement by 2 D or and by Doppler color flow at the vena contracta, measured by Doppler or Doppler color flow
- ♥ Pulmonary artery size as a reflection of the size of the Ductus. A ratio between the Duct: LPA  $> 1$  suggests a large duct.
- ♥ Proximal Isovelocity Surface acceleration as a reflection ductus left to right shunt.
- ♥ Aortopulmonary pressure differences across the arterial duct measured by Doppler or Doppler color flow.

# Impressions

- ♥ The data on the original study used patient data unrelated to the temporal time of the decision making process.
- ♥ It seemed that the neonatologists neither read the reports or consulted with cardiology about ductus closure. I reread the reports to see if I disagreed with anyone in the Echo lab who read a report and found near 100% concordance.
- ♥ Looking at the data it seemed that once the ductus was constricted there was very little chance that patient was going to reopen the duct. I have encountered only one patient in the series
- ♥ Following on this point it seems that there was a large number of patients who got unnecessary Echoes @ \$4,600.<sup>00</sup>
- ♥ 8/10 patients sampled for the surgically closed ductus cohort of 70 patients had no hemodynamic reason for having their ductus ligated!
- ♥ Compliance between the two observers was much better than in the original study.



# Lessons

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- ♥ Check and re-check your data.
- ♥ Remember garbage in + garbage out!
- ♥ If you want to do good research you have to do it your self!  
or at least have a close supervision of the plan, measurements  
and results.



# Plan



- ♥ Will we be able to make inferences from our retrospective study?
- ♥ What can we do going forward?
- ♥ We must do a better job talking to each other and pay as a team for the benefit of our patients
- ♥ We need a prospective study.
- ♥ This is a neonatology study, involving cardiology.



Thank You!