PERINATAL WEBINAR: PATHOLOGY OF ABSENT END DIASTOLIC FLOW

July 1, 2016

12:00 Noon

Perinatal Education Series 2016

Michelle Flanagan, RNC, BSN
Obstetric Outreach Educator
Palmetto Health Richland - Perinatal Systems

Disclosure:

"Please note that this Power Point presentation is an educational tool that is general in nature. It is not intended to be an exhaustive review of the subject matter or the opinion of Palmetto Health. Materials presented in this presentation should not be considered a substitute for actual statutory or regulatory language. Always refer to your legal counsel and the current edition of a referenced statute, code and/or regulation for precise language."

Objectives

- State factors associated with fetal growth restriction
- Verbalize the pathology of absent and reverse end diastolic flow

FETAL GROWTH RESTRICTION

How do we classify fetal growth?

- From ACOG (American College of Obstetrics and Gynecologist)
  - "The terminology for classifying fetuses and newborns who have failed to achieve normal weight is inconsistent."
  - Fetal and newborn weight according to either the absolute weight or the weight percentile for a given gestational age.
    - Fetal growth restriction = used to describe fetuses with an estimated fetal weight that is less than the 10th percentile for gestational age.
    - Small for gestational age (SGA) will be used exclusively to describe newborns whose birth weight is less than the 10th percentile for gestational age.
- Intrauterine growth restriction is the 2nd leading cause of perinatal mortality according to Gabbe, et al in Obstetrics: Normal and Problem Pregnancies
  - "Compared to appropriately grown counterparts, perinatal mortality rates in growth-restricted neonates are 6 to 10 times greater; perinatal mortality rates as high as 120 per 1000 for all cases of IUGR and 80 per 1000 after exclusion of anomalous infants have been reported. As many as 53% of preterm stillbirths and 26% of term stillbirths are growth restricted."

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015.
Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition. Elsevier

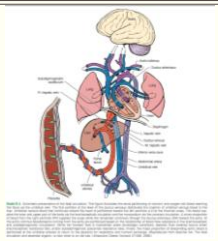
Normal Fetal Growth

- Fetal growth occurs at multiple levels and needs a successful interaction of maternal and fetal components
- Starting at the anchoring of the trophoblast at the uterine lining to all for development of maternal circulation and intervillous space. This will eventually support placental growth.
  - By term as much as 600 mL/min of maternal cardiac output reaches the placenta, the fetal blood flow volume of 200-300mL/kg/min throughout gestation.
- Normal growth involves hyperplasia and hypertrophy on the cellular level
- The growth potential of the placenta and the fetus are thought to be predetermined by maternal body mass index and ethnicity
- Several possible mechanisms may challenge compensatory capacity of the maternal-placental-fetal unit

Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition. Elsevier

Unique fetal circulation

- Main goal: autoregulatory mechanisms to enhance perfusion to the vital organs



Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition. Elsevier

Placental Circulation & Fetal Homeostasis

- depends on the efficiency of the maternal-fetal circulation
- maternal arterial pressure propels maternal blood flow through the placenta
- low-resistance uteroplacental vessels accommodate the increased perfusion need for the development of placental vasculature throughout the course of gestation.
  - uteroplacental and villous core vasoactivities are essential in maintaining the high-flow maternal blood perfusion into the low-resistance placental intervillous space.
  - Placental vascular reactivity is controlled by several vasodilator and vasoconstrictor systems including the renin-angiotensin system, arachidonic metabolites (thromboxane and prostacyclin), endothelin and its receptors, and NO.
- balance between vasodilators and vasoconstrictors from both the maternal and placental compartments is critical for the homeostatic balance of placental vascular function

Wang Y, Zhao S. (2010) Vascular Biology of the Placenta. Morgan & Claypool Life Sciences; http://www.ncbi.nlm.nih.gov/books/NBK53257/

Abnormal fetal growth

- Disturbance of growth dynamics can lead to reduced cell number, cell size or both
- This can lead to abnormal weight, body mass or body proportion at birth.
- First classifications of abnormal growth began in 1919 when neonates with birthweight less than 2500 grams were labeled "Premature" by Yippo.
- The terminology for classifying fetal growth has expanded and has led to much confusion. The general terms for classifying birthweight include (from the 1960's):
  - Low Birthweight <2500 grams
  - Very Low Birthweight <1500 grams
  - Extremely Low Birthweight <1000 grams
  - Macrosomia >4000 grams
- Studies in the 1970's led to classification by birthweight percentile
  - Very small for gestational age <3rd percentile
  - Small for gestational age <10th percentile
  - Appropriate for gestational age 10-90th percentile
  - Large for gestational age >90th percentile
- Small fetal/neonatal size should be a physical sign rather than a disease process, so that the underlying cause can be investigated further.

Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition. Elsevier

Symmetric versus Asymmetric Growth Restriction

Symmetric

- Early insult leading to a relative decrease in cell number and size
  - Ex: Chemical exposure, viral infection, or aneuploidy leading to cellular maldevelopment
- Causes proportionate reduction of both head and body size

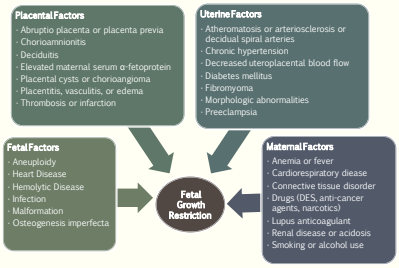
Asymmetric

- May follow late pregnancy insult (placental insufficiency)
  - Results in decreased glucose transfer and hepatic storage
  - Causes decrease in cell size not number
  - Abdominal circumference is reduced
- Brain-sparing
  - Preferential shunting of oxygen and nutrients to the brain
  - Preserves brain growth and function
  - Fetal brain is relatively large and the liver relatively small

Image from http://upload.wikimedia.org/wikipedia/commons/thumb/8/85/Human_development_WG750px-Human_development.PNG

Cunningham, FG, et al (2010) Williams Obstetrics 23rd Edition. McGraw-Hill

Defining Intrauterine Growth Restriction (IUGR)



- Fetal growth restrict is the failure of a fetus to achieve its genetic growth potential in utero.
  - Low birth weight (absolute)
  - Small for gestational age (relative)
    - Less than 1/3 or 10th percentile
    - More than 2 standard deviations below mean
- What causes alteration in growth
  - Malnutrition during the period of hyperplasia
    - Decreases the rate of cell division and results in organs or a fetus that is smaller in size with fewer cells.
  - Malnutrition during period of hypertrophy
    - Results in organs or a fetus smaller in size (reduction in cell size) but has normal number of cells

Blackburn, S. Maternal, Fetal & Neonatal Physiology - A Clinical Perspective 3rd Ed. Saunders Elsevier. 2007.

Fetal Growth Restriction – from ACOG

- Definition:
  - Fetuses with an estimated fetal weight that is less than the 10th percentile for gestational age
  - Small for gestational age (SGA) describes newborns whose birth weight is less than the 10th percentile for gestational age
- Etiology:
  - Broadly categorized into maternal, fetal and placental
    - Primary pathophysiologic mechanism are different but they often have same final pathway → sub-optimal uterine-placenta perfusion and fetal nutrition.

Box 1. Etiology of Fetal Growth Restriction

- Maternal medical conditions
  - Pregestational diabetes mellitus
  - Renal insufficiency
  - Autoimmune disease (eg, systemic lupus erythematosus)
  - Cyanotic cardiac disease
  - Pregnancy-related hypertensive diseases of pregnancy (eg, chronic hypertension, gestational hypertension, or preeclampsia)
  - Antiphospholipid antibody syndrome
- Substance use and abuse (eg, tobacco, alcohol, cocaine, or narcotics)
- Multiple gestation
- Teratogen exposure (eg, cyclophosphamide, valproic acid, or antithrombotic drugs)
- Infectious diseases (eg, malaria, cytomegalovirus, rubella, toxoplasmosis, or syphilis)
- Genetic and structural disorders (eg, trisomy 13, trisomy 18, congenital heart disease, or gastroschisis)
- Placental disorders and umbilical cord abnormalities

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015

Fetal Growth Restriction

- Fetal growth restriction is a syndrome that is marked by failure of the fetus to reach its growth potential with consequences that are related to the underlying disorder as well as the severity of fetal disease.
- Differential diagnoses: maternal disease, placental insufficiency, aneuploidy, nonaneuploid syndromes, viral infection
- Confirm small fetal size, then group for appropriate follow up management:
  - constitutionally small but otherwise normal fetus
  - fetuses with aneuploidy, nonaneuploid syndromes, or viral infection
  - fetuses with placental disease

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015

Growth Restriction and Morbidity/Mortality

- Most common pathology of fetal growth restriction is associated with abnormal placentation that leads to poor placental perfusion.
- Increased risk of Intrauterine demise, neonatal morbidity and neonatal death.
- Studies have also linked growth restricted fetuses with increase risk of developing:
  - Cognitive delay in childhood
  - Type 2 diabetes mellitus
  - Stroke
  - Obesity
  - Coronary artery disease
- Increased risk of stillbirth:
  - Fetal weight less than 10th percentile: risk of fetal death is 1.5%
  - Fetal weight less than 5th percentile: risk of fetal death is 2.5%

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015

Screening for Fetal Growth Restriction

- Who should be screened?
  - All pregnant patients should be screened for risk factors for growth restriction through a review of medical and obstetric history
  - Fundal height measurement at each prenatal visit after 24 weeks GA
  - Ultrasound screening in the presence of maternal factors that increase the risk of fetal growth restriction.
- SCREENING:

Physical Exam or History
- Fundal height measurements between 24 -38 weeks gestation
  - *If mother is obese or uterine leiomyomas limits the accuracy of fundal height, ultrasonography may be a better screening modality.*

→

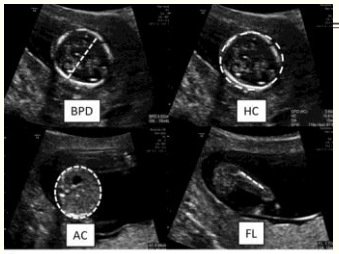
Ultrasound Diagnosis and Evaluation
- Estimated Fetal weight
  - Ultrasound measurements
    - 1) Biparietal diameter
    - 2) Head circumference
    - 3) Abdominal circumference
    - 4) Femur length

→

If less than 10th percentile for GA, further evaluation needed:
- Amniotic Fluid Assessment
- Doppler blood flow studies of the umbilical artery
- Ultrasound exam of fetal anatomy for structural and genetic abnormalities if not previously done

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015

Using Ultrasound to Estimate Fetal Weight



a.

BPD: Biparietal Diameter
HC: Head Circumference
AC: Abdominal Circumference
FL: Femur Length


b.

Rosenkrantz, Andrew, MD, MPA, et al. Clinical Utility of Quantitative Imaging. Academic Radiology, 2015-01-01, Volume 22, Issue 1, Pages 33-49.

ABSENT AND REVERSE END DIASTOLIC FLOW

Now we have a growth restricted fetus – What Now?

- Next Step – Assessment with Doppler Velocimetry
  - Used to determine the volume and rate of blood flow through maternal and fetal vessels
  - Column of red blood cells flowing through the circulation and the reflected sound waves are observed by the ultrasound transducer.
  - "Doppler ultrasound is a noninvasive technique to assess blood flow by characterizing downstream impedance." (Williams Obstetrics, 23rd edition)
    - Three vascular circuits that are used to determine fetal health and help time delivery for growth-restricted fetuses:
      1. Umbilical artery 2. Middle cerebral 3. Ductus venosus
  - "Normally, the end-diastolic velocity in the umbilical arteries increases with advancing gestation secondary to the decreased resistance in the placenta as more tertiary vessels develop." (Blackburn, s. Maternal, fetal & Neonatal Physiology – A Clinical Perspective.)

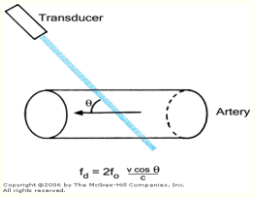
Why use Doppler flow studies?

- Ultrasound and Doppler flow measurements provide means to visualize the umbilical cord and to evaluate the fetal blood flow.
  - To gain an overall measure of fetal health - measuring the amount of forward blood flow through the umbilical artery during both fetal systole and diastole
    - the more forward blood flow from the fetus to the placenta through the umbilical artery, the healthier the fetus.
  - Assessment of fetal blood flow through the umbilical cord by ultrasound color Doppler sonography has proven to be a valuable noninvasive procedure for assessing fetal well-being during pregnancy.

Mari, G, MD & Hanif, F, MD. (2008) Fetal Doppler: Umbilical Artery, Middle Cerebral Artery, and Venous System Seminars in Perinatology, Volume 32, Issue 4, Pages 253-257

Doppler Basics

- The simplest is the systolic–diastolic ratio (S/D ratio), which compares maximum (peak) systolic flow with end-diastolic flow, thereby evaluating downstream impedance to flow.[1]
- Arterial Doppler waveforms provide information on downstream vascular resistance, which may be altered due to structural changes in the vasculature or regulatory changes in vascular tone.[2]
  - Three indices to analyze arterial blood flow:
    - systolic/diastolic ratio
    - resistance index
    - pulsatility index
  - An increase in blood flow resistance manifests itself with a relative decrease in end-diastolic velocity resulting in an increase in all three Doppler indices.



1. https://criticalcaremcqs.com/2011/01/20/
2. Gabbe. (2017) Obstetrics: Normal and problem pregnancies 7th ed.

Doppler Velocimetry

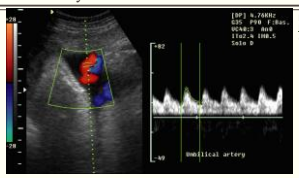


Image from: http://www.birthandbrain.org/velocimetry.html

- "Important to obstetrics, Doppler may be used to determine the volume and rate of blood flow through maternal and fetal vessels. In this situation, the sound source is the ultrasound transducer, the moving target is the column of red blood cells flowing through the circulation, and the reflected sound waves are observed by the ultrasound transducer."

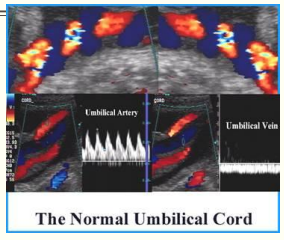
https://criticalcaremcqs.com/2011/01/20/

- Typically, flow velocity waveforms obtained by the analysis of Doppler signal derived from pulsating vessels display changes in flow velocity over the cardiac cycle.
- Flow velocity waveforms characteristics depend on the following variables:
  1. heart rate
  2. distance of the sampling site from the heart
  3. vessel elastic properties
  4. input pressure
  5. downstream impedance to flow that strongly affects diastolic velocity

Todros, T. et al. (2011) Review: Feto-placental vascularization: A multifaceted approach. Placenta 32, Supplement B, Trophoblast Research, Vol. 25. S165

Normal umbilical artery

- <20 weeks GA
  - Placental flow is in a high resistance bed and the value of umbilical artery velocimetry is limited.
  - End diastolic flow is often absent
- >20 weeks GA
  - Progressive increase in diastolic flow velocities resulting in a progressive decrease in measured indices.
  - A low resistance pattern with high forward flow velocities in both the systolic and diastolic component of the cardiac cycle.
  - The PI, RI and S/D ratio all decrease with advancing gestation, probably due to a decrease in placental vascular resistance.



http://www.fetalultrasound.com/online/text/3-131.htm

Doppler Ultrasound in Pregnancy - NORMAL

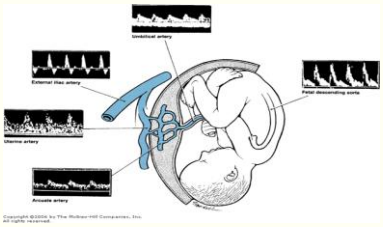


Image from: https://drkamaldeep.files.wordpress.com/2011/01/image12.png

https://criticalcaremcqs.com/2011/01/20/

Assessment of Doppler Velocimetry

- Umbilical Artery:
  - The umbilical artery normally has forward flow throughout the cardiac cycle and the amount of flow during diastole increases as gestational age advances.
  - Therefore the S/D ratio decreases from 4.0 at 20 weeks to 2.0 at term
  - If the S/D ratio is above the 95th percentile for gestational age, it is considered abnormal.
- Uterine Artery:
  - Characterized by high flow velocities similar to those in systole.
  - There is highly turbulent flow
  - Studies linked increased impedance of uterine artery velocimetry at 16-20 weeks was predictive of Superimposed Preeclampsia.
- Middle Cerebral Artery
  - Anatomically, the path of the artery allows for scan with ultrasound through the fontanel to make assessment easy.
  - 2 uses:
    - Fetal Anemia: Peak systolic velocity is increased with increased cardiac output and decreased blood viscosity
    - Growth restriction: progression of Doppler findings show increased impedance of flow detected in the umbilical artery first, followed by redistribution of blood flow to the brain with decreasing resistance (brain sparing), then noted abnormalities in flow.

Cunningham, FG, et al (2010) Williams Obstetrics 23rd Edition. McGraw-Hill

What is different in Growth Restricted Fetuses?

- In placenta-based IUGR the resistance does not fall, and may increase progressively.
- May lead to reduction of end-diastolic blood flow, which in severely affected fetuses may decline until there is absent end-diastolic velocity or even reversed end-diastolic velocity
  - For reversed end-diastolic velocity, elastic recoil in placental and cord vessels is so high that after the pulse wave passes, retrograde blood flow occurs.
  - When placental resistance reaches this point, ineffective placental circulation and hypoxemic stillbirth may ensue.

Harman, C, MD and Baschat, A, MD (2003) Arterial and Venous Dopplers in IUGR. Clinical Obstetrics and Gynecology. Volume 46, Number 4 (931-946)

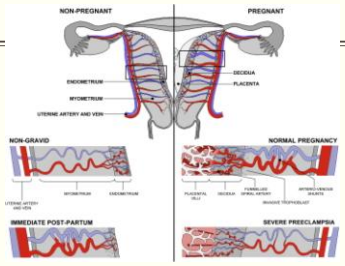
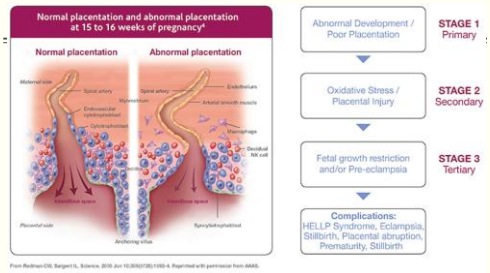


Image from:
https://www.clinicalkey.com/#!/search/placental%2520vasculature/%7B%22query%22:%22placental%20vasculature%22,%22facetquery%22:%5B%22+contenttype:IM%22%5D%7D?page=3



Christopher W. Redman, Ian L. Sargent. Latest Advances in Understanding Preeclampsia Science10 Jun 2005 : 1592-1594

Placental vessels (Normal & Absent End Diastolic Flow)

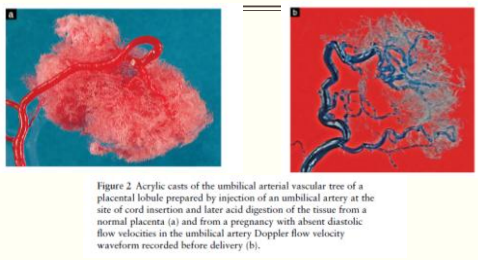


Figure 2 Acrylic casts of the umbilical arterial vascular tree of a placental lobule prepared by injection of an umbilical artery at the site of cord insertion and later acid digestion of the tissue from a normal placenta (a) and from a pregnancy with absent diastolic flow velocities in the umbilical artery Doppler flow velocity waveform recorded before delivery (b).

Editorial Doppler: more or less?* B. TRUDINGER *Ultrasound Obstet Gynecol 2007; 29: 243–246.*

Growth Restriction & Doppler Studies

- The utility of Doppler velocimetry evaluation, especially of the umbilical artery, has been studied and reviewed extensively in cases of fetal growth restriction.
- Absent or reversed end-diastolic flow in the umbilical artery is associated with an increased risk of perinatal mortality .
  - The rate of perinatal death is reduced by as much as 29% when umbilical artery Doppler velocimetry is added to standard antepartum testing in the setting of fetal growth restriction.
- Flow in the ductus venosus also has been measured in an attempt to assess fetal status, but its use has not been shown to improve outcomes.

ACOG Practice Bulletin #134 – Fetal Growth Restriction, May 2013, Reaffirmed 2015

Doppler Ultrasound Measurements

- Creasy and Resnik state that Gray-scale ultrasound is one of the most important tools in current obstetrics.
  - But, it is limited due to the decreased ability to see hemodynamics.
  - By using doppler ultrasound (with color added), blood flow can be seen through each vessel's unique blood flow velocity waveform.
  - Common ratios are:
    - Systolic to diastolic blood flow velocity (S/D)
    - Pulsatile index (PI)
    - Resistance index (RI)

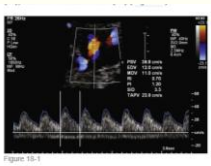


Figure 18-1

Measured and calculated Doppler ultrasound indices.

Where PSV = peak systolic velocity, EDV = end-diastolic velocity, MDV = mean diastolic velocity, RI = resistance index, PI = pulsatility index, S/D = ratio of systolic to diastolic blood pressure, and TAPV = time-averaged peak velocity, the following equations apply:

Doppler Velocimetry

- allows assessment of placental status
- helps to place other testing results in context as well as helping to determine the relative risk of sudden fetal deterioration.
- categories of risk can help to determine the frequency of BPP testing
- Extreme Doppler abnormalities may indicate intervention
- Umbilical artery Doppler - reflects placental vascular resistance.
  - strongly correlate with fetal growth restriction and multiple critical fetal and neonatal outcome characteristics, progressively worsening as reduction, loss, and reversal of diastolic flow in a deteriorating sequence.

TABLE 32-4 Doppler Abnormality Dictates Frequency of Biophysical Profile Scoring

Abnormality*	BPP Frequency*	Decision to Deliver (Fetal)†
Elevated indices only	Weekly	Abnormal BPP or term or >36 wk with no fetal growth
AEDV	Twice weekly	Abnormal BPP or >34 wk of proven maturity
REDV	Daily	Conversion to REDV Any BPP <10/10‡ or >32 wk of dexamethasone given
REDV-UVP	Three times daily	Any BPP <10/10‡ or >28 wk of dexamethasone given

*The biophysical profile (BPP) determines management. Must be viable to enter: ≥25 weeks' gestation, >500 g, normal anatomy, normal karyotype.
†Umbilical artery and complete venous-free Doppler; cerebralization of blood flow confirms umbilical artery abnormality as serious but does not directly alter management.
‡Minimum testing frequency, which is increased on basis of severity, based on maternal conditions, degree of IUGR, gestation.
§Neonatal consultation, maternal condition or instability, and direct fetal parameter by cordocentesis impact this decision.
¶Any BPP ≤6/10, or 8/10 oligo, or repeated 6/10.
#BPP of 8/10 with cyclic absence of FBM is the only exception, in which case, repeat BPP in less than 6 h.
AEDV, absent end-diastolic velocity; FBM, fetal breathing movement; IUGR, intrauterine growth restriction; oligo, oligohydramnios; REDV, reversed end-diastolic velocity; UVP, umbilical venous pulsations.

Absent End Diastolic Flow

- Abnormal wave forms correlate with hypovascularity of the umbilical placental villous structure.
  - 60-70% of the small placental arterial channels need to be lost before Doppler waveform becomes abnormal.
- As placental resistance increases, the flow of blood through the major vessels like the umbilical artery and middle cerebral artery will have a loss of forward flow.
  - Simualtaneous to the loss of flow, there is a loss in the normal elasticity of the vessel as well.
  - If the flow continues to be restricted the flow may eventually go in reverse (back to the fetus) – Reverse End Diastolic Flow.

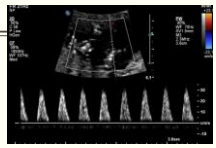
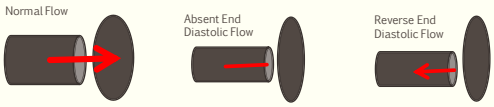
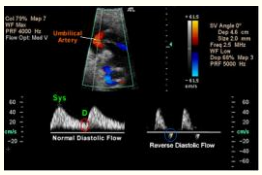


Image from:
https://iame.com/online/multi_vessel_doppler/content.php



Reverse End Diastolic Flow

- When the resistance in the placenta increases further, absent diastolic flow becomes reverse diastolic flow in which the Doppler waveform is observed to be below the baseline.
- When the fetus develops this type of abnormality, intense surveillance is required if the fetus is less than 32 to 34 weeks and delivery if it is greater than 32 to 34 weeks.
- Currently recommendation is evaluation of the ductus venosus and/or inferior vena cava, and antepartum testing.



http://www.fetal.com/IUGR/_umbilical2.html

DOPPLER VELOCIMETRY OF THE UMBILICAL ARTERY

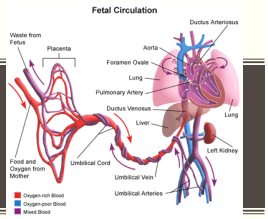


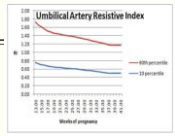
Image from:
http://www.aicdheart.com/patient_education/heart_HTML_scaleable/heart/feticirc.htm

Umbilical Artery

- Arises from the common iliac arteries and represent the dominant outflow of the distal aortic circulation
- Mirrors the downstream resistance of the placental circulation
- Normal umbilical artery - resistance falls progressively through pregnancy, reflecting the increased numbers of tertiary stem villous vessels
- In pathologic conditions increased resistance in the umbilical arteries represents pruning of the placental arterial tree
  - As umbilical artery resistance rises, diastolic velocities fall and ultimately become absent
  - As resistance rises even further, an elastic component is added, which induces reversed end-diastolic velocity as the insufficient, rigid placental circulation recoils after being distended by pulse pressure.

Understanding Diastolic Flow

- **Umbilical Artery**
  - Normally has forward flow throughout the cardiac cycle
  - Amount of flow during diastole increases as gestation advances
    - S/D ratio *decreases*, from about 4.0 at 20 weeks to 2.0 at term.
    - The S/D ratio is generally less than 3.0 after 30 weeks
  - Umbilical artery Doppler may be a useful adjunct in the management of pregnancies complicated by fetal growth restriction.
  - Umbilical artery Doppler is considered abnormal if the S/D ratio is above the 95th percentile for gestational age.



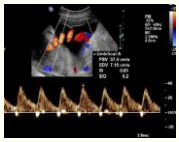


Image from:
http://www.ultrasoundpaedia.com/normal-3rdtrimester/

DOPPLER VELOCIMETRY OF THE MIDDLE CEREBRAL ARTERY

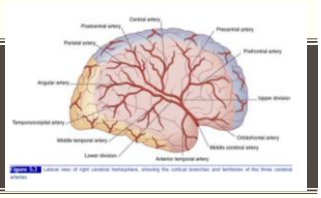
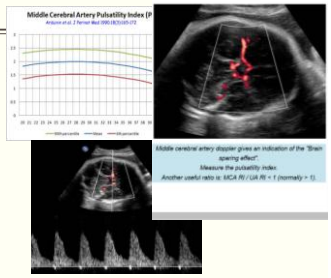


Image from http://clinicalgate.com/blood-supply-of-the-brain/

Middle Cerebral Artery

- The MCA is short, straight, and uniformly positioned relative to the fetal skull and other intracranial landmarks. Doppler measurements taken from this vessel are more reproducible than those taken from other vascular beds and have few collateral circulatory influences while representing a critical component of the fetal circulation.



Images from: http://www.ultrasoundpaedia.com/normal-3rdtrimester/

DOPPLER VELOCIMETRY OF THE DUCTUS VENOSUS

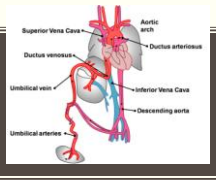
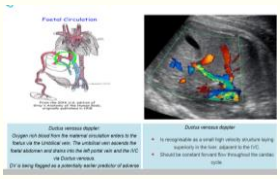


Image from:
https://classconnection.s3.amazonaws.com/801/flashcards/3736801/jpg/ductus_venosus-1451409493600.334E6C.jpg

Ductus Venosus

- The ductus venosus is a sharply tapered conduit that shunts blood from the proximal umbilical vein directly into the inferior vena cava at its connection to the right atrium.
  - Hourglass shape regulates inflow to the central circulation through a narrow aperture that is constricted in the healthy near-term fetus, allowing only 20% of umbilical venous return into the right atrium.
  - this narrow jet delivers highly oxygenated blood at high velocity directly to the foramen ovale, keeping it open and promoting right-to-left shunting of this nutrient-rich stream.
  - In healthy fetuses, the ductus venosus regulates the distribution of oxygen and placental nutrients by restricting the centralization of flow.
- The reflected wave seen in the ductus venosus waveform represents the impact of cardiac actions



Images from : http://www.ultrasoundpaedia.com/normal-3rdtrimester/

DOPPLER VELOCIMETRY OF UTERINE ARTERY

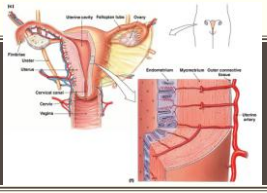


Image from:
http://www.austincc.edu/rfofi/NursingRvw/PhysText/Reproductive.html

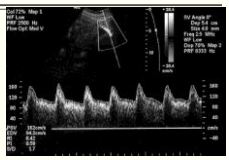
Uterine Artery

- Uterine blood flow increases from 50 mL/min early in gestation to 500 to 750 mL/min by term.
- The uterine artery doppler waveform is unique and characterized by high diastolic flow velocities similar to those in systole, and by highly turbulent flow, which displays a spectrum of many different velocities
- Increased resistance to flow and development of a diastolic notch have been associated with pregnancy-induced hypertension

Creasy, R; Resnik , R; et al. (2014) Creasy and Resnik's Maternal-Fetal Medicine – Principles and Practice 7th Ed. Elsevier

Uterine Artery

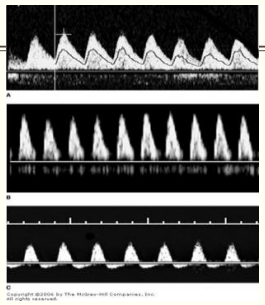
- Abnormal uterine artery flow velocimetry waveforms are a manifestation of delayed trophoblast invasion
  - Associated with GHTN, IUGR, FDIU.
- Changes in the uterine artery flow patters precede those observed in the umbilical artery and preceeds fetal growth restriction.
- Uterine artery doppler is better at predicting severe rather than mild disease



Monitoring of Fetal Well-Being: Role of Uterine Artery Doppler
Seminars in Perinatology
Ghidini, Alessandro, MD; Locatelli, Anna, MD. Published August 1, 2008. Volume 32, Issue 4. Pages 258-262. © 2008.
Figure 2 Normal uterine artery Doppler waveform at 28 weeks.

Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition. Elsevier

SIGNIFICANCE OF RESULTS / BENEFITS OF TESTING/ OUTCOMES



Umbilical artery Doppler waveforms

A. Normal diastolic flow.

B. Absence of end-diastolic flow.

C. Reversed end-diastolic flow

Cunningham, FG, et al (2010) Williams Obstetrics 23rd Edition. McGraw-Hill

Gabbe, G, Et al. (2017) OBSTETRICS: NORMAL AND PROBLEM PREGNANCIES, SEVENTH EDITION Elsevier

Patterns of Deterioration

- Placental abnormalities may persist for months before other Doppler parameters deteriorate.
- As placental resistance increases, the cerebroplacental ratio eventually shifts, reflecting a change in balance between placental and systemic perfusion and resulting in cerebral redistribution.
  - Brain sparing is seen as progressive abnormalities in umbilical artery circulation, which are associated with increasingly higher diastolic velocities in the MCA.
  - By this time, subjective elements of behavior, such as increasing intervals of quiet sleep, decreased velocity of fetal movements, and elements of subjectively decreased amniotic fluid may begin to appear.
- With onset of AEDV:
  - progressive redistribution yields overt centralization,
  - oligohydramnios becomes more common.
  - The NST parameters often become flatter,
  - reversal of end-diastolic velocities in the umbilical artery may occur , along with progressive loss of fetal breathing movements, loss of fetal tone, and abolition of all movements as the BPP becomes overtly abnormal

Creasy, R; Resnik , R; et al. (2014) Creasy and Resnik's Maternal-Fetal Medicine – Principles and Practice 7th Ed. Elsevier

Clinical Significance

BOX 32-1 ABNORMAL UMBILICAL ARTERY DOPPLER PREDICTS ADVERSE OUTCOMES

Cesarean section for fetal distress
Acidosis
Hypoxemia
Low Apgar score
Ventilator required
Long-term oxygen
Bronchopulmonary dysplasia
Anemia
Increased number of nucleated red blood cells (NRBCs)
Thrombocytopenia
Prolonged NRBC release
Neutropenia
Transfusions required
Intraventricular hemorrhage
Necrotizing enterocolitis
Perinatal mortality

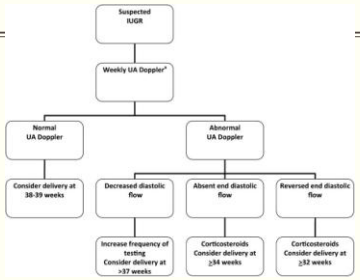
*The frequency of all of these outcomes rises exponentially from abnormal indices to absent end-diastolic velocities to reversed end-diastolic velocities.

- Absent flow and reversed flow represent progressively ominous findings necessitating close monitoring or consideration of delivery based on the gestational age.
- AEDV may exist in equilibrium over a long period, particularly in the very preterm fetus, but in many fetuses, AEDV is not stable and will progress to REDV over time.
- REDV is frequently an unstable clinical state that may precede fetal death by only hours to days.
- REDV is often associated with very significant abnormality of cerebral and venous circulations

Is There Benefit to Using Doppler Ultrasound?

- A recent opinion paper from the Society for Maternal-Fetal Medicine addressed the issue of the utility of Doppler ultrasonography for the assessment of the fetus with IUGR.
  - It summarized all published studies with the highest level of evidence and concluded that umbilical arterial Doppler studies significantly decreased the likelihood of perinatal death, cesarean delivery, and labor induction.
  - The opinion further stated that, because of the lack of randomized trials to prove benefit, the use of middle cerebral artery and ductus venosus Doppler studies should be considered experimental
- The temporal sequence of Doppler-measured flow abnormalities in the arterial and venous circulations of the IUGR fetus has been delineated.
- It is readily apparent that abnormal venous Doppler waveforms in the preterm IUGR fetus are indicative of poor acid-base status and outcome.
  - Issue then becomes when to optimize delivery timing in the very preterm fetus, before significant abnormalities in the venous circulation occur.

Management



Impacts of Monitoring on Perinatal Mortality and Long-Term Outcomes

- Use of the BPP and Doppler velocimetry for fetal assessment has been implemented in clinical practice, but it remains difficult to obtain robust data on the impact of this testing in a variety of populations.
- Lower BPP scores have been associated with higher perinatal mortality rates, and early studies comparing the perinatal mortality rate for an untested population to that for a tested, high-risk population demonstrated a lower rate of perinatal mortality in the tested population
- Although the strength of this evidence is not ideal, it does suggest that monitoring can identify fetuses at risk and allow for timely delivery to reduce the risk of perinatal mortality.

Doppler Ultrasound for Fetal Surveillance

- REDV at any gestational age beyond 28 weeks should prompt immediate delivery.
  - Some experts would consider continuously monitoring these fetuses and giving a course of betamethasone prior to delivery, and continuing expectant management until 32 weeks as long as fetal surveillance remains reassuring.
  - Use of venous Doppler appears to improve the prediction of stillbirth and acidemia when arterial Doppler has identified a fetus at risk. This is the next step in the evaluation of these fetuses and may help to identify fetuses who require immediate delivery versus those in whom delivery can be delayed.
- In general, cesarean delivery is a reasonable choice in most cases of AEDV, as fetal tolerance to labor is poor in this situation. Cesarean delivery is clearly indicated in the presence of REDV or ominous fetal monitoring findings.

Neonatal Impact of Growth Restriction

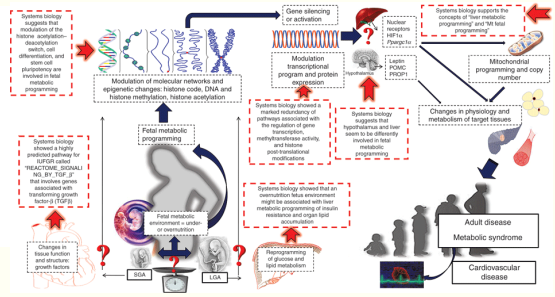
- Complications in the neonatal period related to the etiology of the growth insult as well as antepartum and intrapartum factors:
  - Neonatal asphyxia
  - Meconium aspiration
  - Hypoglycemia
  - Metabolic abnormalities
  - Polycythemia
- Beyond the neonatal period
  - Negative effect on cognitive function
  - strong association between IUGR and spastic cerebral palsy in newborns born after 33 weeks' gestation.
- Maternal and fetal malnutrition seem to have both short- and long-term effects
  - Multifactorial
    - Includes genotype of both mother and fetus, maternal size and obstetric history, postnatal and lifestyle factors.

Image from: http://www.womens-health-advice.com/assets/images/low-birth-weight.jpg

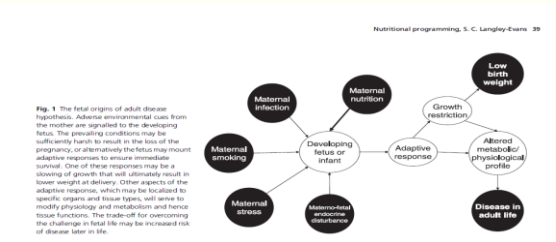
Long Term Outcomes

- Growth potential for growth-restricted infants
  - The degree of catch-up growth observed in several longitudinal studies suggests that these infants can be expected to have normal growth curves and a normal, albeit slightly reduced size as adults.
  - In general, those infants who suffered growth restriction near the time of delivery do tend to catch up. However, those neonates with earlier onset and more longstanding growth restriction in utero continue to lag behind.
- Long-term neurologic sequelae – still not fully understood – multiple studies with varying outcomes
  - One thought is that the studies while all have varied outcomes, it is thought that the neurologic outcome depends on the degree of growth restriction, especially the impact on head growth, its time of onset, the gestational age of the infant at birth, and the postnatal environment.
- GRIT study:
  - The Growth Restriction Intervention Trial (GRIT) compared two management strategies: immediate versus delayed delivery in high-risk pregnancies when clinical uncertainty prevailed.
    - The results demonstrated that differences in perinatal morbidity and mortality, neurological outcome 2 years after birth, and long-term outcome were not statistically significant between the two groups.
    - Antenatal testing via BPP and Doppler (with the exception of the umbilical artery) were not used for fetal surveillance in all cases.
    - In addition, the growth-restricted fetuses included in the study represented a heterogeneous population because, in this study, one-fourth of the fetuses had normal umbilical artery flow velocity waveforms, indicating they may have simply been SGA.
- Gestational programming of growth-restricted fetuses has received considerable attention over the past 10 to 15 years.
  - Infants born growth restricted have an increased risk of metabolic syndrome, obesity, hypertension, diabetes, and stroke from coronary artery disease.
  - Fetal Programming – Epigenetic effects that could be multi-generational are a concern.

Gabbe, G. (2017) Obstetrics: Normal and Problem Pregnancies, 7th Edition, Elsevier
Mari, G, MD & Tate, M, MD. (2013) Detection and surveillance of IUGR. Contemporary OB/GYN October 1, 2013, obtained from: http://contemporaryobgyn.modernmedicine.com/contemporary-obgyn/content/tags/intrauterine-growth-restriction/detection-and-surveillance-iugr?page=full



Sookoian, S. et al. (2013) Fetal metabolic programming and epigenetic modifications: a systems biology approach. Pediatric Research (2013) Volume: 73, Pages:531-542. http://www.nature.com/pr/journal/v73/n5/images/pr2013329f1.gif



Langley-Evans (2009) Nutritional programming of disease: unravelling the mechanism. Journal of Anatomy 215: 36-51.

Questions?

- Post your questions in the box...
- Lines now open
  - please make sure your phone is not muted so we can hear your questions!

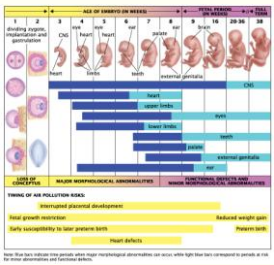


Image from:
http://www.environment.ucla.edu/media/images/Fetal_dev5-large.jpg

Thank you!

- Upon completion of this archived webinar, please complete the Evaluation you were provided on the website or via email.
- Return the evaluation to the Perinatal Systems office and you will receive your Nursing CE electronically via email. Please be sure to include your email address on the evaluation form.
- Any further questions, please contact our Michelle at the following:
  - 803.434.7243
  - Michelle.flanagan@palmettohealth.org