INTRAUTERINE GROWTH RESTRICTION (IUGR): Diagnosis and Management

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OBJECTIVES:

- Define IUGR vs. SGA fetuses
- Recognize etiology
- Describe the role of ultrasound
- Discuss antenatal natural history
- Present antepartum and intrapartum management
- Discuss short and long term sequelae

IUGR

- **Nomenclature**: low birth weight, small for gestational age, retarded fetal growth, small for dates, intrauterine growth restriction
- **Definition:**
  - IUGR is defined as a birth weight less than the 10th percentile (? 5th percentile or ?>2SD below the mean) at given gestational age.
  - The fetus has not reached its growth potential at given gestational age due to one or more causative factors.
- Infant weight is the single most important factor affecting neonatal mortality!

IUGR: So what!

- 2nd leading contributor to perinatal mortality!!!
- Perinatal mortality: x6-10
- Intrapartum asphyxia: up to 50%
- As many as 40% stillborns are IUGR
- A portion of perinatal complications is preventable (morbidity and mortality)
- Association with multiple sequelae (short and long term morbidity)

INCIDENCE

- 10% of general obstetric population
- 4-7% of all infants born in developed countries
- 6-30% of all infants born in developing countries

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IUGR

- The fetus genetically programmed to be in the 90th percentile who is born in the 20th percentile may be in more trouble than a baby born to a jockey and a gymnast who is in the 8th percentile!

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Fetal factors

- Chromosomal abnormalities (2-5%)
  - Trisomy 13, 18, 21
  - Genetic syndromes (Turner Sy)
  - Chromosomal deletions
  - Uniparental disomy
  - Confined placental mosaicism

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Fetal factors

- Structural malformations
  - Anencephaly
  - Omphalocele / gastroschisis
  - Diaphragmatic hernia
  - Renal agenesis / dysplasia
  - Cardiac malformations
  - Multiple malformations
  - Osteogenesis imperfecta

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Fetal factors

- Multiple gestation
  - Monochorionic placentation
  - Single anomalous fetus
  - Twin-to-Twin Transfusion syndrome (TTTS)

Fetal factors

- Fetal infections
  - Rubella
  - CMV
  - Varicella-zoster
  - Listeria
  - Syphilis
  - Malaria
  - Toxoplasmosis

Placental factors

- Abnormal trophoblast invasion
- Placental infarction
- Abruption
- Vascular malformation
- Velamentous cord insertion
- Placenta previa
- Circumvallate placenta
- Chrioangioma

Maternal factors

- Constitutional factors
  - Race
  - Height / weight
- Nutritional factors
  - Poor pregnancy weight gain
  - Low pregnancy weight
  - Inflammatory bowel disease
  - Chronic pancreatitis
  - Gastrointestinal surgeries

Maternal factors

- Hypoxic conditions
  - Severe lung disease
  - Cyanotic heart disease
  - Sickle cell anemia
- Vascular problems
  - Chronic hypertension
  - Pre-eclampsia
  - Collagen vascular disease
  - Type I diabetes mellitus
  - Antiphospholipid syndrome
- Renal disease
  - Glomerulonephritis
  - Renal transplant
  - Chronic renal failure

Maternal factors

- Environmental factors:
  - High altitude
  - Cigarette smoking
  - Alcohol
  - Illicit drugs: narcotics
  - Medications: anti-epileptics, beta blockers
- Past obstetric history
  - Previous stillbirth
  - Previous IUGR
  - Previous preterm delivery

SONOGRAPHIC FINDINGS

- AC measurements most sensitive (liver size) - >2.5th percentile – sensitivity >95%)

- Error of measurements: up to 20%
- Recommend: serial measurements

SONOGRAPHIC FINDINGS

- 3D measurements
  - Fetal thigh (Chang et al. 1997)
  - EFW Error: 0.7%
- Detailed anatomical survey
- Oligohydramnios
- Fetal aneuploidy (amnio, PUBS)

SONOGRAPHIC FINDINGS

- Doppler studies
  - Arterial: UA, MCA
  - Venous: IVC, DV
  - Semi quantitative measurements:
    - Waveform analysis: RI, S/D, PI
    - Absent end-diastolic flow
    - Reversed end-diastolic flow

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Doppler in IUGR fetuses

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The Doppler effect

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Umbilical circulation

- Low impedance circulation
- S/D – Standard index
- Placental insertion has leas impedance
- Intervene for absent or reverse EDF

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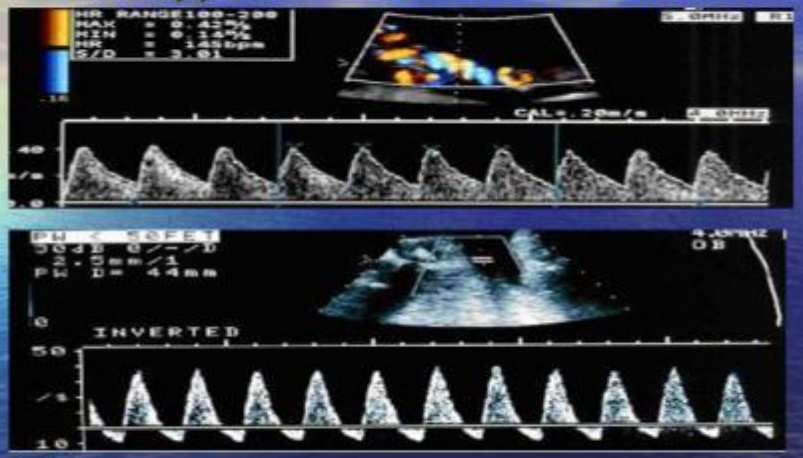
UA Doppler – reversed diastolic flow



This is an advanced stage of fetal compromise, associated with increased perinatal morbidity and mortality.

Umbilical Artery Doppler Meta-analyses

- Absent or reversed EDF – 80x increase in perinatal mortality (*Thornton 1993*)
- UA Doppler significantly reduces IUFD
  - *Divon 1995*: 8 studies, 6838 Pts
  - *Giles 1993*: 6 studies, 4335 Pts
  - *Alfirevic 1995*: 12 studies, 38% reductions in perinatal mortality

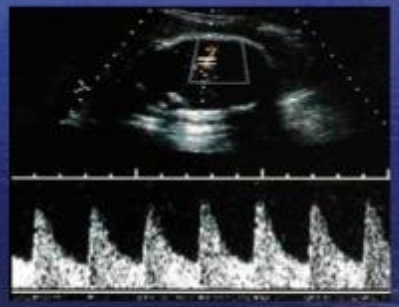
The Circle of Willis

Left and right MCA

Cerebral Circulation

- High impedance circulation
- PI – Standard measurement index
- Hypoxia results in increased flow to the brain
- Brain sparing effect (brain, heart, adrenals, spleen)

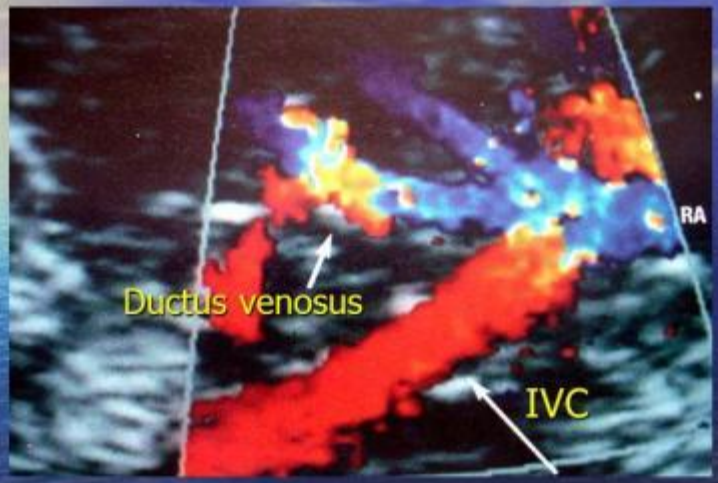
MCA Doppler



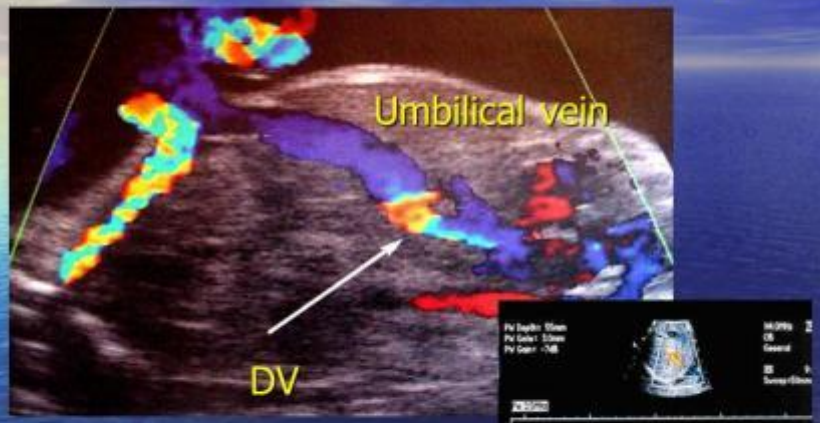
Normal

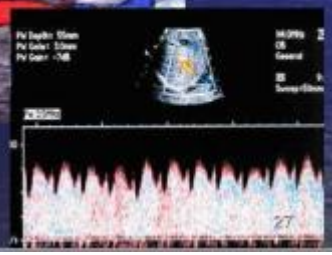
Abnormal – fetal hypoxia

Coronal view of fetal chest and abdomen

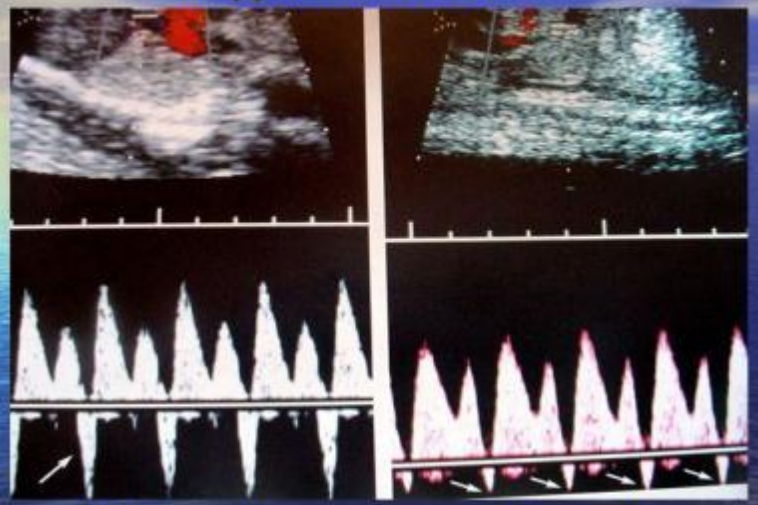


Ductus venosus turbulence (DV)





Hypoxic fetus



IVC Doppler

DV Doppler

Uterine circulation

- Low impedance circulation in pregnancy
- S/D, RI – Standard indices
- Low EDF & notching are abnormalities
- Abnormal waveforms: IUGR, pre-eclampsia, FHR abnormalities

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Does Doppler improve outcomes in IUGR fetuses?

- It can, when used in conjunction with other diagnostic tools.
- Early compensatory phase (fetal hypoxia):
  - Biometry & arterial Doppler
- Late phase (fetal acidosis and impending cardiovascular collapse):
  - Venous Doppler, FHR analysis & BPP

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IUGR Challenge

- Diagnose true IUGR
- Identify markers of morbidity
- Intervene in a timely fashion

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Fetal Surveillance

- Risk of NRFS is 86% when both umbilical & MCA Dopplers are abnormal
- Risk of NRFS is 4% when both umbilical & MCA Dopplers are normal

Ultrasound Obstet Gyencol 2002;19:225

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DIFFERENTIAL DIAGNOSIS

- Incorrect pregnancy dating
- SGA fetus
- Error of measurements

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TIMELINE FOR FETAL HYPOXIA

- Abnormal fetal growth
- Abnormal arterial Doppler (UA, MCA)
  - ~ 2 weeks
- Abnormal venous Doppler (IVC & ductus venosus)
  - ~ 1-2 days??
- Abnormal NST / BPP score

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PREGNANCY MANAGEMENT

- The crux of management: hazards of prematurity vs. threat of IUFD
- Referral to maternal fetal medicine subspecialist – targeted ultrasound and counseling
- Search for etiology: fetal, placental, maternal
- Fetal karyotype (2-5% abnormal – *Creasy & Resnik 1999)*
- NST, BPP, CST, UA Doppler
- Serial biometry (q 3-4 weeks) – watch head growth

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PREGNANCY MANAGEMENT

- **37 or more:** prompt delivery
- **<34 weeks:**
  - Expectant management if reassuring fetal status – course of corticosteroids for fetal benefits
  - Modified bed rest, smoking cessation, Rx hypertension (*Lin & Santolaya-Forgas 1999*)
  - Antepartum testing: NST/AFI & BPP twice weekly, daily kick counts, UA Doppler
  - Abnormal UA Doppler: daily NST and at least twice weekly BPP for up to 2 weeks
  - Non-reassuring status: prompt delivery

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PREGNANCY MANAGEMENT

- **34-37 weeks**
  - Management individualized
  - Fetal lung maturity study – delivery if mature
  - Expectant management till 37 weeks than delivery (*Craigo et al. 1996*)
  - Antepartum testing: NST/AFI twice weekly, UA Doppler
  - Non-reassuring status: prompt delivery
  - Oligohydramnios and abnormal UA Doppler: more frequent antepartum testing but not delivery (unless non-reassuring status)

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PREGNANCY MANAGEMENT

- Mode of delivery
  - Based entirely on standard obstetric practice
  - No evidence to support routine C/S
  - Consideration for C/S if non-reassuring antepartum testing with an unfavorable cervix (*Creasy & Resnik 1999*)
  - Labor induction with or without cx ripening
    - Continuous electronic fetal monitoring
    - FHR monitor: Increased risk for decreased variability and late decelerations
    - Meconium
  - Optimum: Tertiary care centers with MFM and NICU available

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LONG-TERM OUTCOME

- Depend on underlying cause
- Poor cognitive function
- Adverse neurological outcome in childhood
- Impaired gross motor development, hyperactivity, poor concentration, lower IQ, speech and reading disabilities (*Gembruch & Gortner 1998*)
- Cerebral palsy

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LONG-TERM OUTCOME

- **David Barker**, epidemiologist from England
  - Fetal origin of adult diseases: The risk of coronary artery disease, stroke and hypertension
  - Intrauterine conditions could program development of the cardiovascular system later in life
  - Infants with birth weight less than 5.5 lb had a 3x increase in death due to coronary artery disease later in life.
- Other risks:
  - Abdominal obesity, type 2 diabetes mellitus, hyperlipidemia

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KEY POINTS:

- Of the all U/S derived biometric parameters, AC is the most sensitive indicator of IUGR and should be closely monitored in at-risk fetuses.
- Arterial Doppler abnormalities in UA and MCA confirm the presence of hypoxia in IUGR fetuses and are early warning signs.

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KEY POINTS:

- The most important abnormal findings to look for on UA Doppler are absent and reversed end-diastolic flow.

Note: The clinical use of venous Doppler in IUGR management should await the results of randomized trials.

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KEY POINTS:

- In managing IUGR pregnancies, timing of delivery is the most critical step.
- The challenge is to balance the risk of prematurity with the risk of IUFD, neonatal morbidity and mortality and long term neurodevelopmental delay.

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FUTURE

Randomized studies will shed more light on the pathophysiology of IUGR and on the various interactions of diagnostic tools in fetal surveillance.