Stillborn Birth (Stillbirth)

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Maternal-Fetal Medicine

2-7-2019

Objectives

- Define stillbirth and the impact of stillbirth in obstetrics
- Describe etiologies and conditions associated with stillbirth
- Describe the “workup” for stillbirth
- Describe management of subsequent pregnancy

Case #1

2/17/14

HPI:

23 yo G3P1011 @ 32w1d by LMP 7/8/13 EDD 4/14/14 c/w 19w sono presented with decreased fetal movement and lower abdominal cramps from 3 PM yesterday. No LOF/VB. No h/o trauma to abdomen. No HA/visual changes/epigastic pain. Denied tobacco or cocaine use. Admitted to marijuana use during current pregnancy. Pt was given betamethasone on 2/13 and 2/14 for IUGR. NST was reactive and BP was 127/60.

PNI:

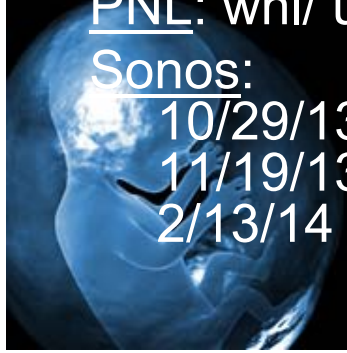
Intake BP 102/50 (102-132/ 50-90). Weight gain 158→ 189 (31 lbs).

1. IUGR dxed on 2/13/14 sono @ 31w. Fetus <3%tile. TORCH and thrombosis w/u negative. Amnio normal XY.

PNL: wnl/ unremarkable

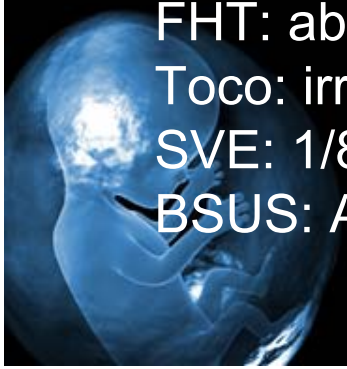
Sonos:

10/29/13 @ 15w3d. AFI nl.
11/19/13 @ 19w1d no anatomical anomalies. Fetus 20%tile.
2/13/14 @ 31w1d: Fetus <3%tile. SD ratio 4.8. AFI 11.



Case #1 cont.

POB:
2010 ectopic → R lap salpingotomy.
2011 FT NSVD of 6lb female. No complications.
PGyn: no cysts/ fibroids/ STIs/ abnl paps. 12/reg/5.
PMH: spina bifida occulta, chronic lower back pain
PSH: R lap salpingotomy
Meds: PNV, Reglan, Zofran
All: NKDA
PE:
BP 132/40 →→ max **170/102** (Hydralazine 5mg IVP given) HR 74 T36.6
Abd: +fundal tenderness
FHT: absent
Toco: irritability
SVE: 1/80/-2
BSUS: Absent fetal heart activity. Breech presentation. Minimal fluid.



A/P:

Labs:

INR 2.5	Cr 1.2	SGOT 46-57	Hct 28	Fibr <120
PT 22.8	Uric acid 6.0	SGPT 17-21	WBC 30.2	UA >300prot
PTT 30	LDH *hem		Plt 52-40-17-14	

23 yo G3P1011 @ 32w1d with IUGR fetus, now with IUFD and elevated BPs.

1. IUGR, DIC- Unclear etiology, history and PE c/w abruption. Admit to L&D for IOL.
2. Preeclampsia/ HELLP syndrome

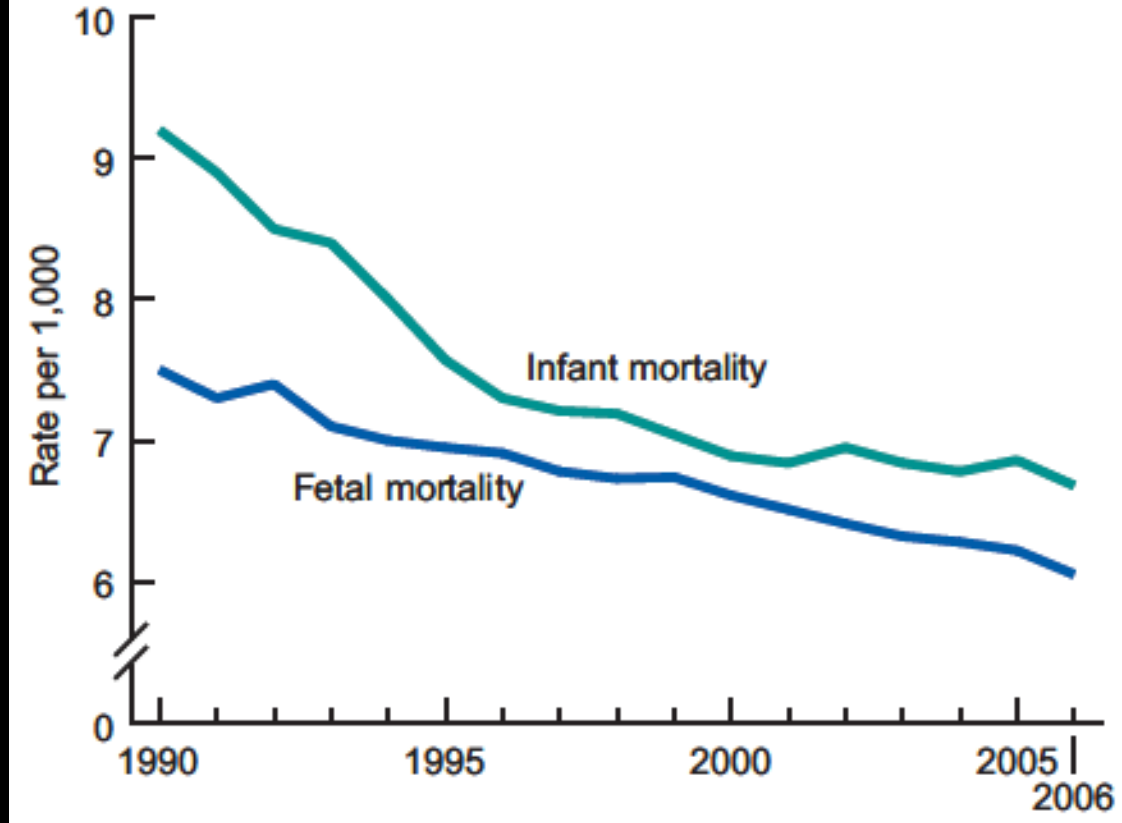
Delivery

2/17/14 6:15am

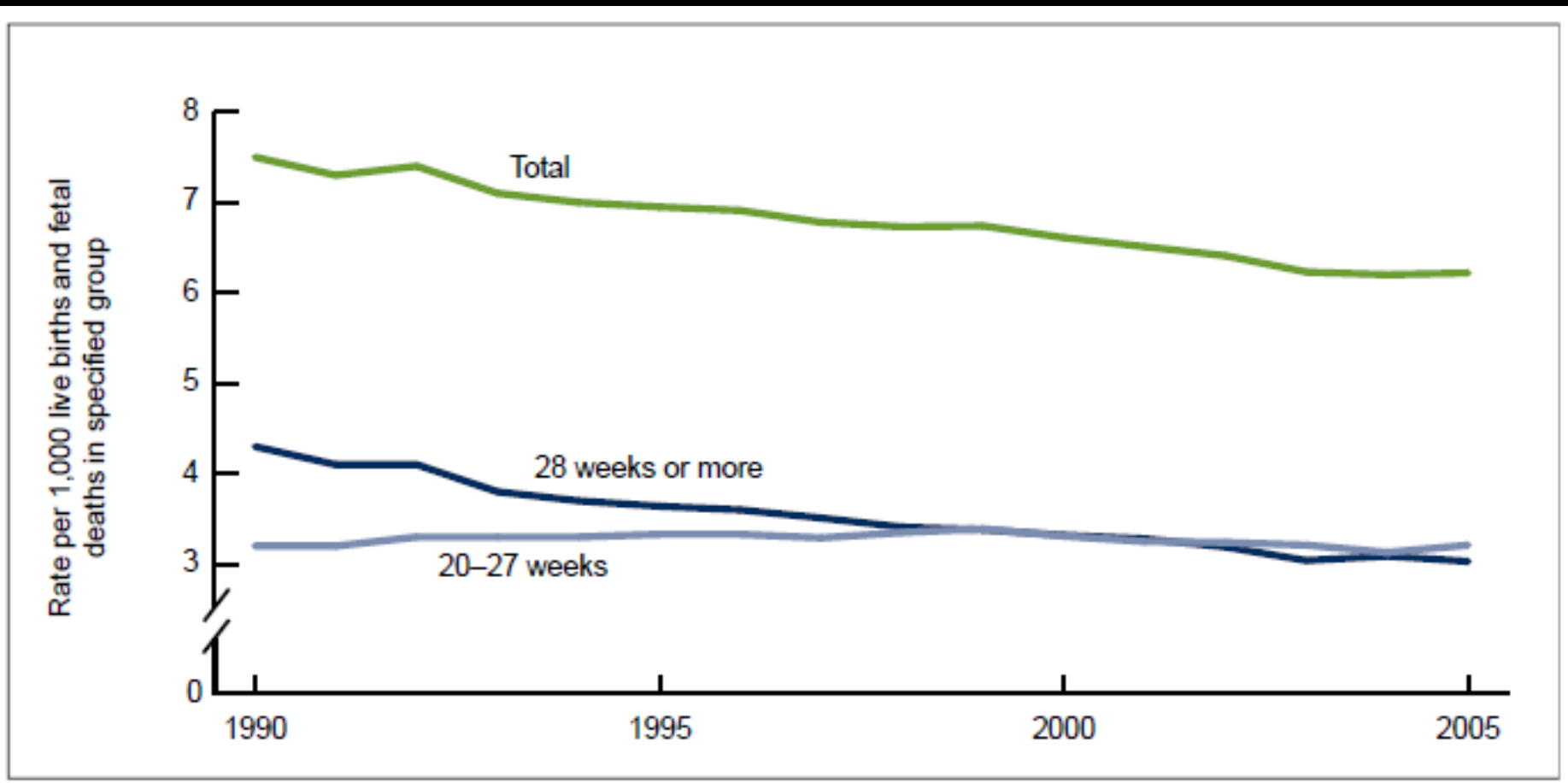
- Pt c/o pain. Female infant found to be delivered with approx 1000cc blood clot on bed. **No fetal heart rate**. Cord clamped x 2 and cut. Placenta promptly delivered spontaneously- 3v, intact. Fundus firm. Pitocin 20U in D5LR bolused and 1000mg cytotec given. No lacerations. Pt declined seeing fetus. Upon examination of fetus, no gross abnormalities- appeared SGA with small placenta.
- BP 151/100→ 151/83. MgSO4 bolus given.

Stillbirth

- Fetal death ≥ 20 weeks gestation
- ~26,000 per year in US
- US Stillbirth rate: 6.05 / 1,000 births* (2006)
- Similar in magnitude to the number of infant deaths



NOTES: Infant mortality rates are the number of infant deaths per 1,000 live births. Fetal mortality rates are the number of fetal deaths at 20 weeks of gestation or more per 1,000 live births and fetal deaths.
SOURCE: CDC/NCHS, National Vital Statistics System.



SOURCE: CDC/NCHS, National Vital Statistics System, fetal mortality data, 1990–2005.

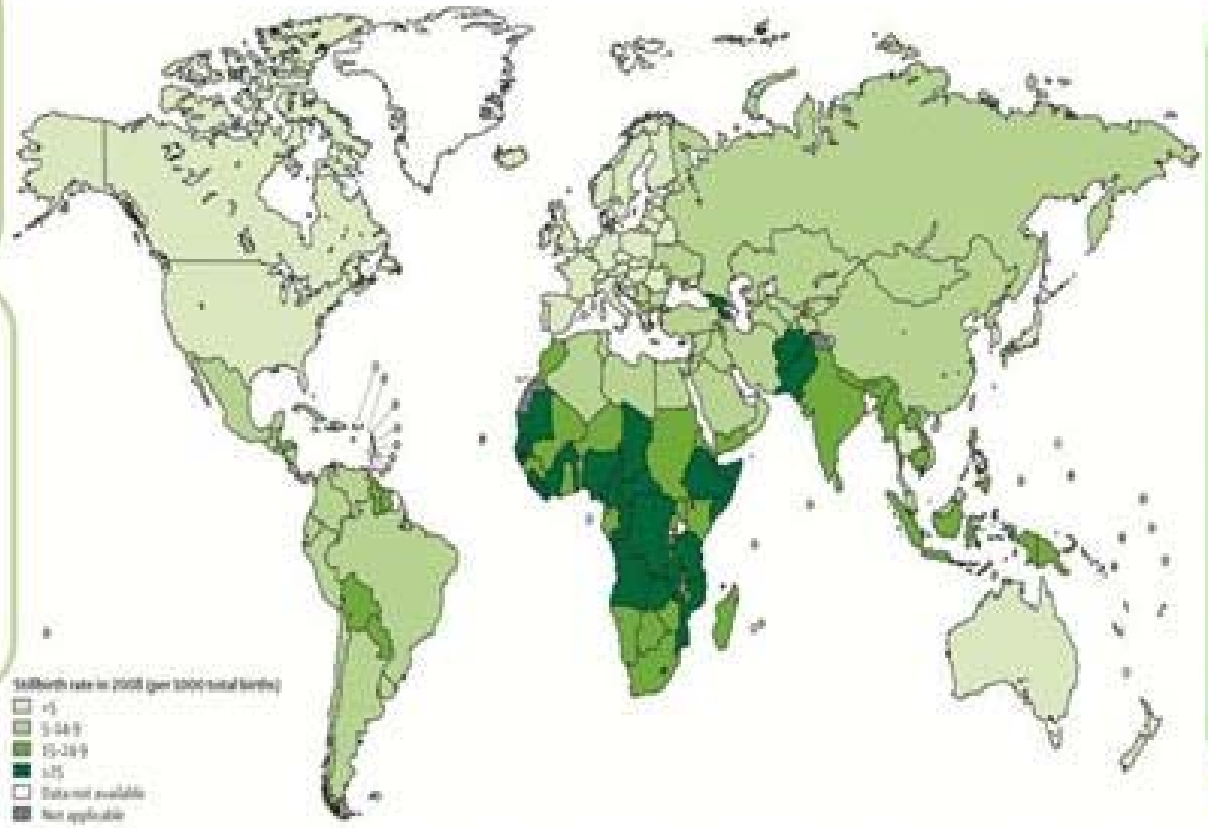
2.65 million third trimester stillbirths each year

Applying high-income country stillbirth definitions (including second trimester) this number may be 40% higher

Stillbirth rates
(deaths per 1000 livebirths)

Lowest 2 countries
1. Finland (2)
2. Singapore (2)

Highest 2 countries
192. Nigeria (42)
193. Pakistan (47)



10 countries account for 66% of the world's stillbirths – and also 66% of neonatal deaths and over 60% of maternal deaths

1. India
2. Pakistan
3. Nigeria
4. China
5. Bangladesh
6. Dem Rep Congo
7. Ethiopia
8. Indonesia
9. Tanzania
10. Afghanistan

Source: Lawn JE, Blencowe H, Pattinson R, et al, for The Lancet's Stillbirths Series steering committee. Stillbirths: Where? When? Why? How to make the data count? *Lancet* 2011; published online April 14. DOI:10.1016/S0140-6736(10)62187-3.

Stillbirth:
Risk factors and etiologies

- Maternal Conditions
- Fetal Conditions
- Obstetric Conditions
- Other Conditions
- Unexplained

Stillbirth: Risk Factors

Condition	Prevalence	SB Rate / 1,000	SB: OR
Chronic HTN	6 – 10%	6 – 25	1.5 – 4.0
Mild PE	5.8 – 7.7%	9 - 51	1.2 – 4.0
Severe PE	1.3 – 3.3%	12 - 29	1.8 – 4.4
Diabetes (diet)	2.5 – 5.0%	6 - 10	1.2 – 2.4
Diabetes (insulin)	2.4%	6 - 35	1.7 – 7.0

SCRN, JAMA 2011; 306:2469-79

Fretts; Am J Obstet Gynecol 2005;193:1923-35

Reddy; Obstet Gynecol 2010;116:1119-26

Type 2 DM

- Auckland (1985-1997)
  - **434 Type 2, 160 Type 1, 932 GDM**
- Perinatal mortality
  - **Type 2 DM : 46/1000**
  - **Type 1 DM :12.5/1000**
  - **GDM: 9/1000**

$P < .0001$

- Excess in perinatal mortality greatest in SB risk ≥ 28 weeks, 7 fold increase
- Women: older, obese, present later for care than women with type 1 diabetes

Cundy, Diabet Med, 2000

Type 1 vs. Type 2 DM

- Meta-analysis of 33 studies
- Type 2 DM: perinatal mortality
  - **OR = 1.5 (95% CI 1.15 to 1.96)**
  - **Lower HbA1c throughout pregnancy**
- No difference: stillbirth, major congenital malformations and neonatal mortality

Balsells, J Clin Endocrinol Metab , 2009

Stillbirth: Risk Factors

Condition	Prevalence	SB Rate / 1,000	SB: OR
SLE	< 1%	40 - 150	6 - 20
Renal Disease	< 1%	15 - 200	2.2 - 30
Thyroid Disorders	0.2 – 2%	12 - 20	2.2 – 3.0
Thrombophilia	1 – 5%	18 - 40	1.2 – 5.0
Cholestasis	< 0.1%	12 - 30	1.8 – 4.4

Fretts; Am J Obstet Gynecol 2005;193:1923-35

Stillbirth: Risk Factors

Condition	Prevalence	SB Rate / 1,000	SB: OR
Smoking	10 – 20%	10 - 15	1.3 – 3.0
BMI 25 – 29.9	21%	12 - 15	1.1 – 2.7
BMI > 30	20%	13 - 18	1.3 – 2.8
< 12 years education	30%	10 - 13	1.3 – 2.0
Prior IUGR	6.7%	12 - 30	2.0 – 4.6

SCRN, JAMA 2011; 306:2469-79

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Stillbirth: Risk Factors

Condition	Prevalence	SB Rate / 1,000	SB: OR
Twins	2.7%	12	1.0 – 2.8
Triplets	0.14%	34	2.8 – 3.2
35 – 39 yrs	15 %	11 - 14	1.3 – 2.2
≥ 40 yrs	2%	11 - 21	1.6 – 2.2
Non-Hispanic Black	15%	12 - 14	1.4 – 2.2

SCRN, JAMA 2011; 306:2469-79

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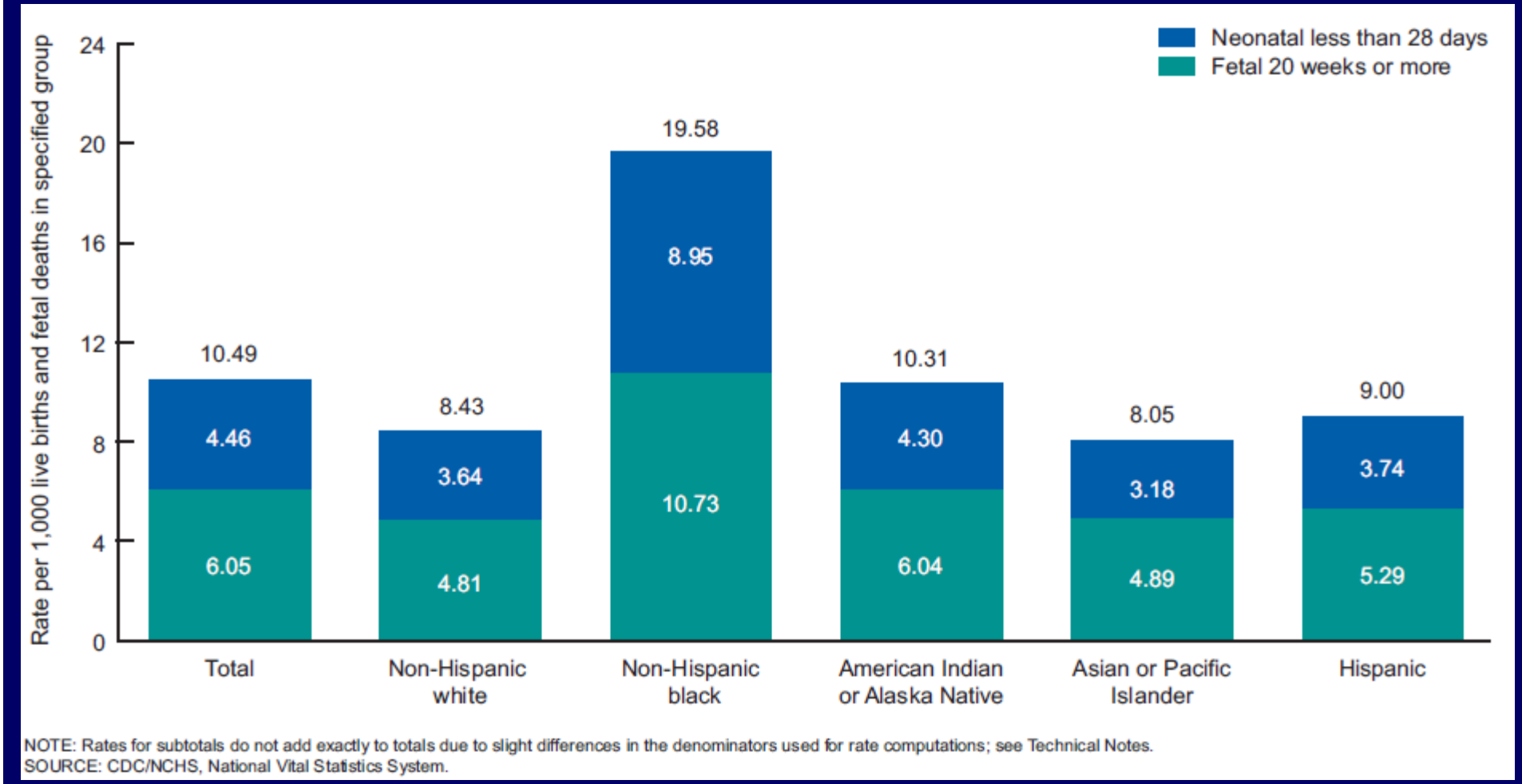
U.S. Perinatal Mortality Rates in 2006 by Maternal Race / Ethnicity



NOTE: Rates for subtotals do not add exactly to totals due to slight differences in the denominators used for rate computations; see Technical Notes.
SOURCE: CDC/NCHS, National Vital Statistics System.

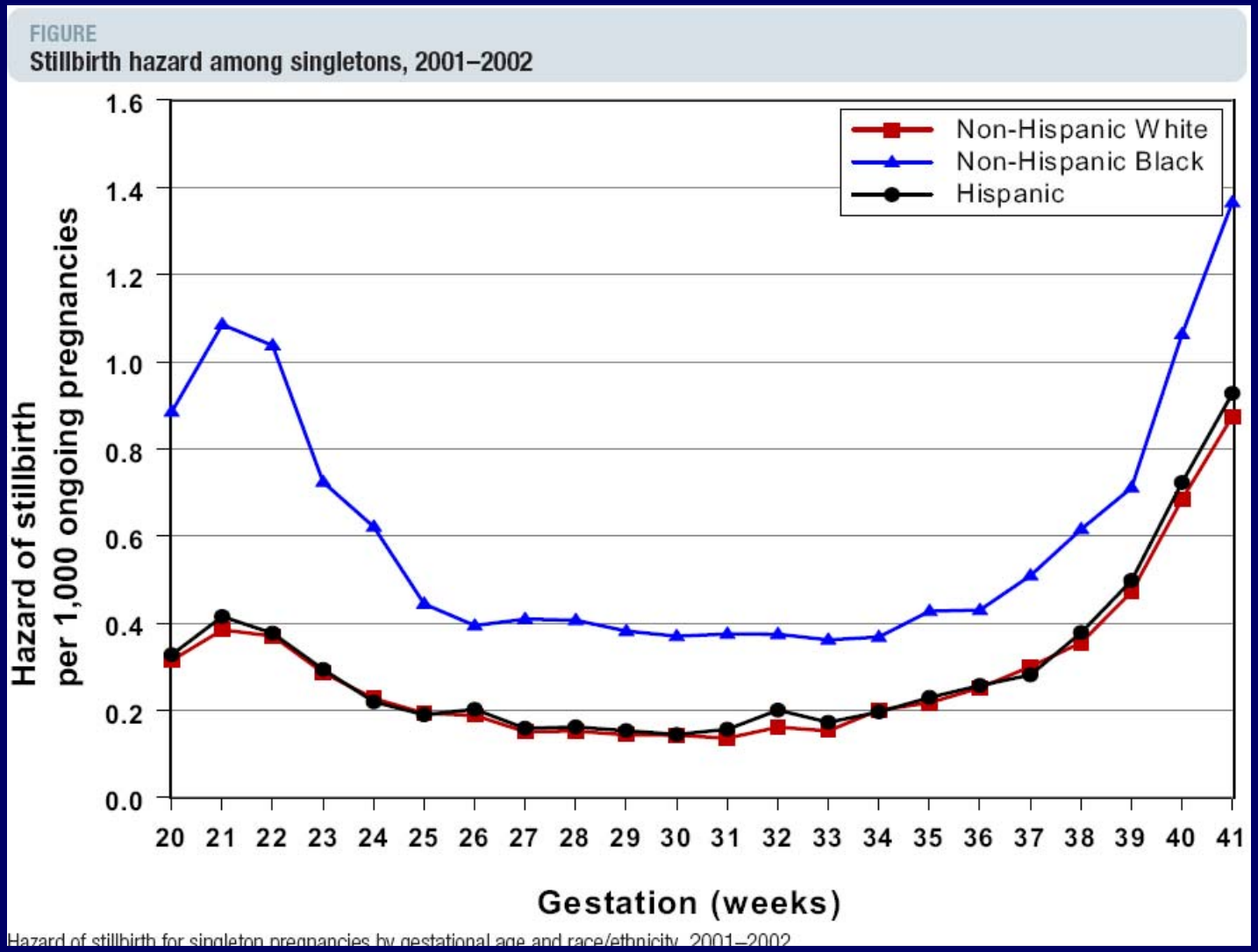
Source: MacDorman MF, Kirmeyer S. Fetal and perinatal mortality, United States, 2006. National vital statistics reports; vol 60 no 8. Hyattsville, MD: National Center for Health Statistics. 2012.

Stillbirth: Race

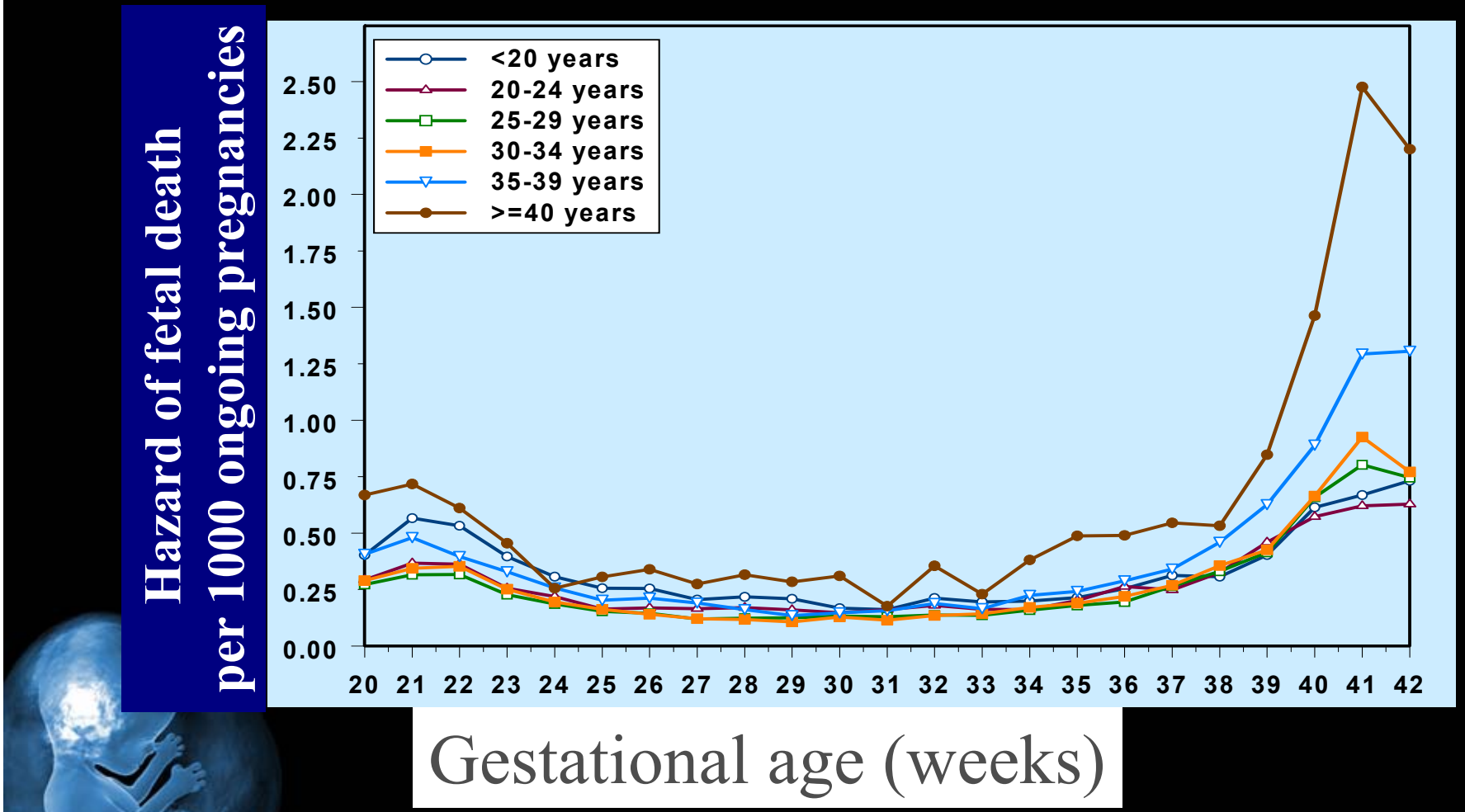
- Black women have >2X increase in stillbirth rate
  - 10.7 vs 4.8 per 1,000
- Secondary risk factors
  - Socioeconomic status
  - Access to prenatal care
- Increase persists even with prenatal care

Stillbirth Hazard Among Singletons, 2001 - 2002

Willinger et al., Am J Obstet Gynecol 2009;201:469.e1-8



Maternal age



Reddy, AJOG, 2006

Maternal age

- SB risk at 37 to 41 weeks:
  - 35-39 yo
    - 1 in 382 ongoing pregnancies
    - RR= 1.32 (95% CI 1.22, 1.43)
  - > 40 yo
    - 1 in 267 ongoing pregnancies
    - RR= 1.88 (95% CI 1.64, 2.16)

- Medical disease, parity, race/ethnicity controlled

Reddy, AJOG, 2006

Multiple

- 2.7-fold higher SB rate for twins
- 4.6-fold higher SB rate for ≥ triplets
- Increased rates
  - preterm labor
  - fetal growth restriction
  - maternal hypertension
  - placental and cord issues (especially with monochorionic twins)

Assisted Reproductive Technologies

- **Increased multiple gestation**
- **4 fold increased SB risk for singleton IVF/ICSI pregnancies vs spontaneous**
- **Reason for increased SB risk is unclear**
- **Risk: IVF/ICSI increased SB risk compared to women with time to pregnancy ≥ 1 year or use of non-IVF ART**

Obstetric History

- **Previous stillbirth**
  - **Recurrence risk is variable (2-10 fold increased)**
- **Previous preterm/ SGA**
  - **410,000 deliveries ≥ 28 weeks' gestation in Sweden**
  - **5-fold increased SB risk with previous live birth of a growth restricted infant before 32 weeks' gestation**
  - **SB hazard ratio of 5.65 in Australian cohort**

Surkan, NEJM, 2004

Gordon, Obstet Gynecol, 2012

Previous Cesarean Delivery

- **Association controversial**
- **No association in analysis of 11 million U.S. birth certificate and fetal death records**
  - **Limitations of birth certificate data**

Bahtiyar, Am J Obstet Gynecol 2006

- **Increased risk of stillbirth**
  - **1.6-fold increased risk of unexplained SB in 120,633 births (Scotland)**
  - **1.4-fold increased SB risk in 400,000 births in U.S. for African-American women but not among white women**

Smith, Lancet, 2003

Salihu, Obstet Gynecol, 2006

Obesity

- **Increased hypertension and diabetes**
- **Independent SB risk factor**
- **Increased pre-pregnancy weight**
  - **Overweight: 1.5 fold increased risk of stillbirth**
  - **Obesity: 2.1 fold increased risk of stillbirth**
- **Pre-pregnancy obesity: 3.5- 4.6 fold increased SB risk after 37 weeks**
- **Vascular, metabolic abnormalities inflammation are theorized mechanisms**

Nohr, Obstet Gynecol, 2005

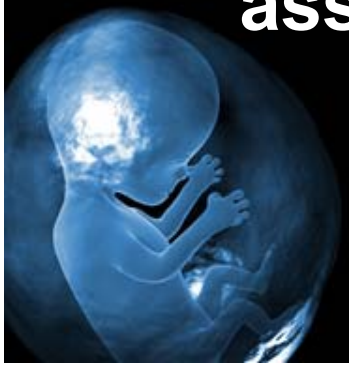
Chu, Am J Obstet Gynecol, 2007

Smoking

- **36% increase in the odds of stillbirth**
- **Women who quit smoking from first to second pregnancy reduce stillbirth risk to that of nonsmokers in the second pregnancy**
- **Alcohol use, illicit drug use, low maternal education level, lack of prenatal care or inadequate prenatal care all have been associated with increased stillbirth rates**

Flenady, Lancet, 2011

Hogberg, BJOG, 2007



Flenady, Lancet, 2011

Maternal disease

- ~10% of SB associated with maternal conditions
- Late stillbirths are associated with maternal medical conditions that are potentially preventable

Stillbirth:
Fetal Conditions

- Genetic
- Infection
- Fetal growth restriction (FGR)

Genetic cause

- Stillbirth due to an alteration of the fetal, maternal or placental genome
- Probably the cause in a higher proportion of stillborn infants than presently understood

Stillbirth: Genetic Conditions

- Chromosomal abnormalities
- Syndromes / malformations
- Single gene disorders
- X-linked conditions
- Autosomal dominant mutations
- Confined placental mosaicism

Confined placental mosaicism

- Fetal karyotype is euploid but abnormal cell line in the placenta

- 1% - 2% of first trimester CVS
  - Most cases abnormal cell line has no phenotypic consequence
  - Increase risk of spontaneous abortion, stillbirth and fetal growth restriction

Confined placental mosaicism

- Factors that predict pregnancy outcome
  - specific chromosome (2, 3, 7, 8, 9, 16, 22)
  - persistence of the abnormal cell line
  - percentage of aneuploid cells in the placenta
- CPM of trisomy 16
  - high probability of fetal death, preterm delivery, fetal growth restriction, and fetal anomalies
  - < 1/3 of affected pregnancies deliver a full term normally grown infant

Genetic Conditions
Chromosomal Abnormalities

- 6-13% of stillbirths
  (10 times the rate in liveborn)

- Same distribution as live births
  - Monsomy X - 23%
  - Trisomy 21 - 23%
  - Trisomy 18 - 21%
  - Trisomy 13 - 8%

Genetic Conditions
Chromosomal Abnormalities

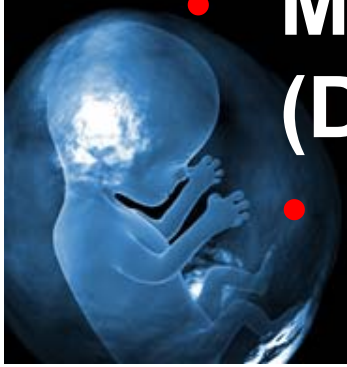
- Karyotype higher yield if:
  - Early loss
  - History of recurrent losses
  - Family history of abnormal offspring
  - IUGR
  - Malformations
  - Hydrops

Stillbirth
Infections

- 10 – 25% of fetal deaths
- Higher in developing countries
- More common at early gestational ages (developed countries)

Stillbirth
Viral infections

- Uncertain proportion of stillbirth
- Lack of a systematic approach
- Difficult to culture
- ? Causation
  - Positive serology
  - Positive viral nucleic acid
- Molecular diagnostic technology (DNA and RNA PCR)
  - Improved diagnosis

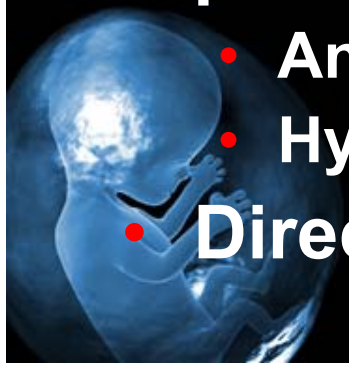


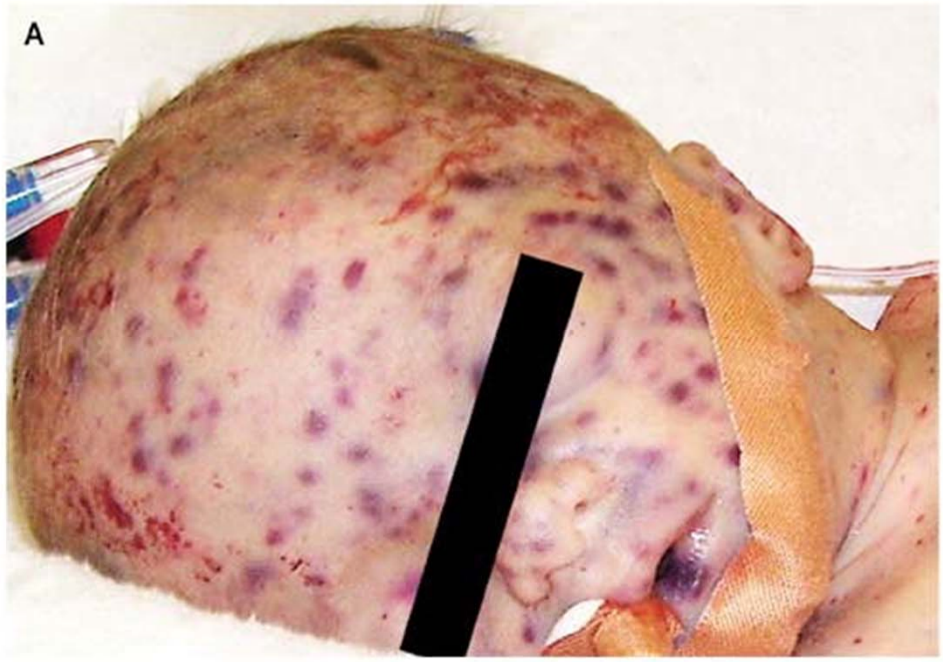
Stillbirth
Enteroviruses

- Coxsackie viruses
  - ✓ Villous necrosis
  - ✓ Inflammatory cell infiltration
  - ✓ Calcific pancarditis
  - ✓ Hydrops
  - ✓ Cardiovascular defects
- ✓ Polio, enterovirus, echovirus

Parvovirus B19

- 8% of stillbirths by PCR in Sweden Skjoldebrand, BJOG, 2000
- < 1% of all SB in U.S Goldenberg, AJOG, 2003
- Proportion of SB may be underestimated
- Erythema infectiosum or fifth disease, ("slapped cheek" rash) in children
  - Adults: arthritis / no symptoms
- Virus trophic for fetal red blood cell precursors and cardiac cells
  - Anemia
  - Hydrops
- Direct myocardial damage

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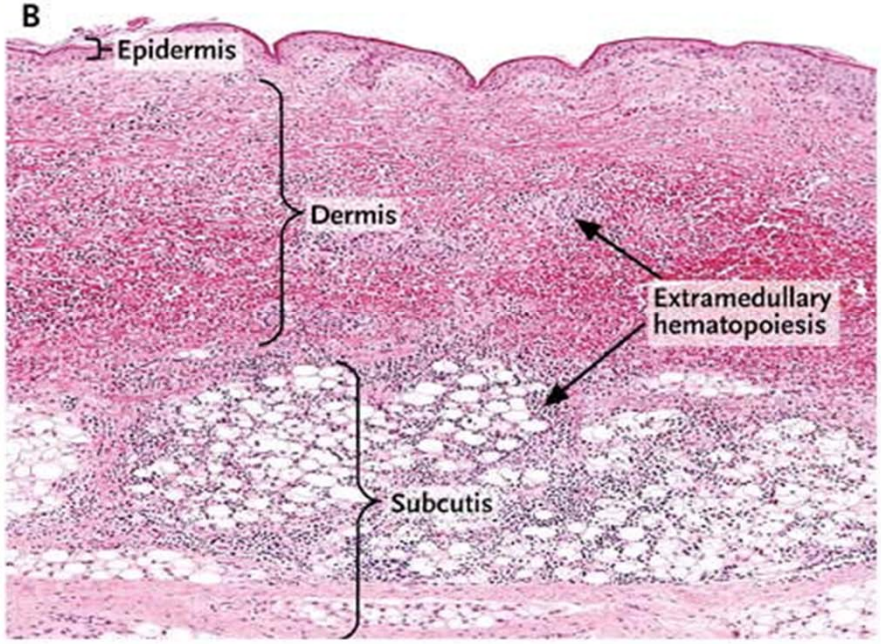
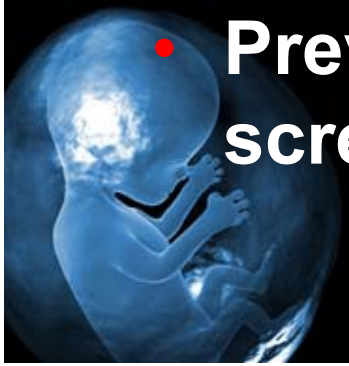

B
Epidermis
Dermis
Extramedullary hematopoiesis
Subcutis

Stillbirth
Cytomegalovirus (CMV)

- Most common congenital viral infection
- 1% of pregnant women acquire primary CMV during pregnancy
- Primary CMV
  - Highest rate of transmission
  - Most severe consequences
- Placental damage
- IUGR
- Direct fetal effects

Stillbirth Syphilis

- Treponema pallidum (spirochete)
- 25 - 50% of stillbirths in some African populations
- Direct fetal and placental infection
- 50% rate of stillbirth (untreated)
- 30% rate of congenital syphilis
- Over 1 million cases of congenital syphilis per year
- Preventable cause of stillbirth through screening and treatment in pregnancy!



Stillbirth
Transplacental Bacterial Infection

- Listeria monocytogenes
  - Unpasteurized soft cheese
  - Undercooked meat
  - Villous necrosis and microabscesses in the placenta
  - Direct fetal infection
- Many other rare causes such as TB, tularemia, clostridia, anthrax, typhoid fever, brucellosis, haemophilus influenza, etc.

Stillbirth
Ascending Bacterial Infection

- Very common
- The same organisms that cause chorioamnionitis
  - Mycoplasma / ureaplasma
  - Group B streptococcus
  - E. coli
  - Klebsiella
  - Enterococcus
  - Bacteroides

Stillbirth
Protozoal Infections

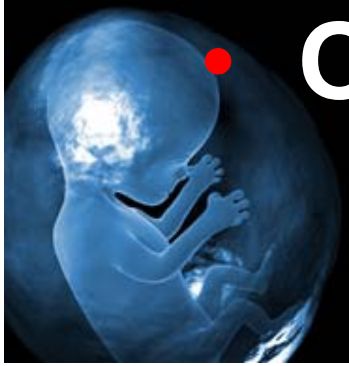
- Malaria (Plasmodium falciparum)
- 14 million pregnant women exposed per year – sub-Saharan Africa
- Outcome is worse if nulliparous or if first exposure to malaria
- Stillbirth related to placental involvement (16 – 63% of cases)
  - Lymphocyte and macrophages
  - Thickened basement membrane
  - Impedes placental blood flow

Stillbirth
SGA Fetus

- Difficult to ascertain
  - Serial growth
  - Growth potential
- Risk factor or clue (Not a diagnosis)
- Major risk factor
- OR 6.1 for stillbirth

Stillbirth:
Obstetric Conditions

- Fetal-maternal hemorrhage
- Multiple gestation
- Placental abnormalities
- Cord accidents
- Other disorders

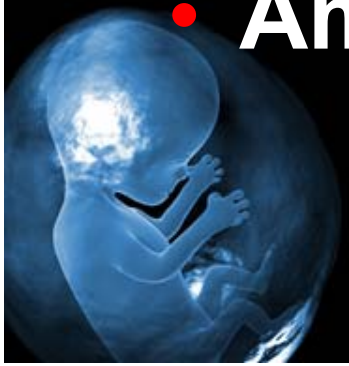


Stillbirth
Fetal-Maternal Hemorrhage

- 4 % of all stillbirths
- Volume of blood transfused
  - ~ 30% -75% of total fetoplacental blood volume
- Reliable method for identification and quantification of FMH (prior to labor induction)
- Evidence of hypoxia and anemia on autopsy

Stillbirth
Placental Abnormalities

- Umbilical cord thrombosis
- Villamentous cord insertion
- Vasa previa
- Amniotic band syndrome

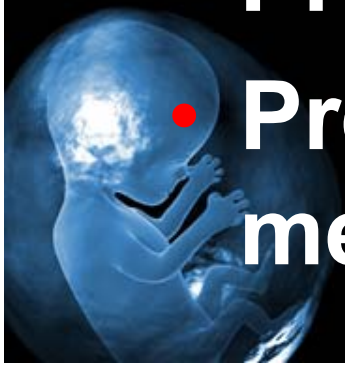


Stillbirth
Umbilical cord accidents

- Many cases attributed to cord accident
- Possible mechanisms:
  - ✓ Cessation of blood flow
  - ✓ Intermittent disruption of blood flow
  - ✓ Fetal blood loss and disruption of flow
  - ✓ Cord entanglement
- ✓ Cord entanglement
  - ✓ 30% of normal pregnancies
- Causality: Cord occlusion and hypoxic tissue injury on autopsy, and exclude other accepted causes of stillbirth.
- True knots also common in live birth

Stillbirth
Other Obstetric Conditions

- Abruption
- Preeclampsia
- Cord prolapse
- Cervical insufficiency
- Preterm labor
- Preterm premature rupture of membranes



Stillbirth
Other Obstetric Conditions

Spontaneous Preterm Birth

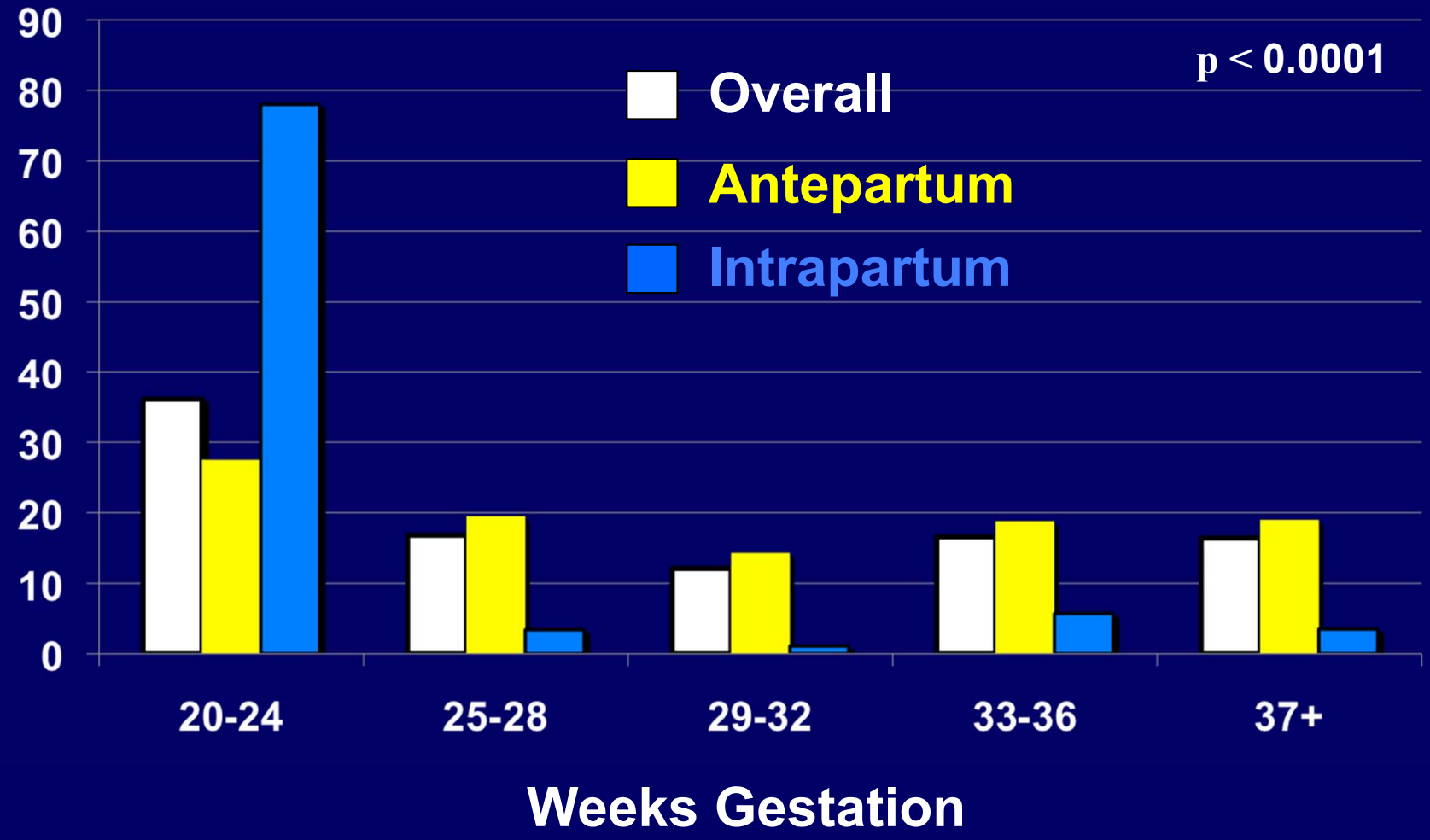
Stillbirth

Stillbirth Collaborative Research Network (SCRN)

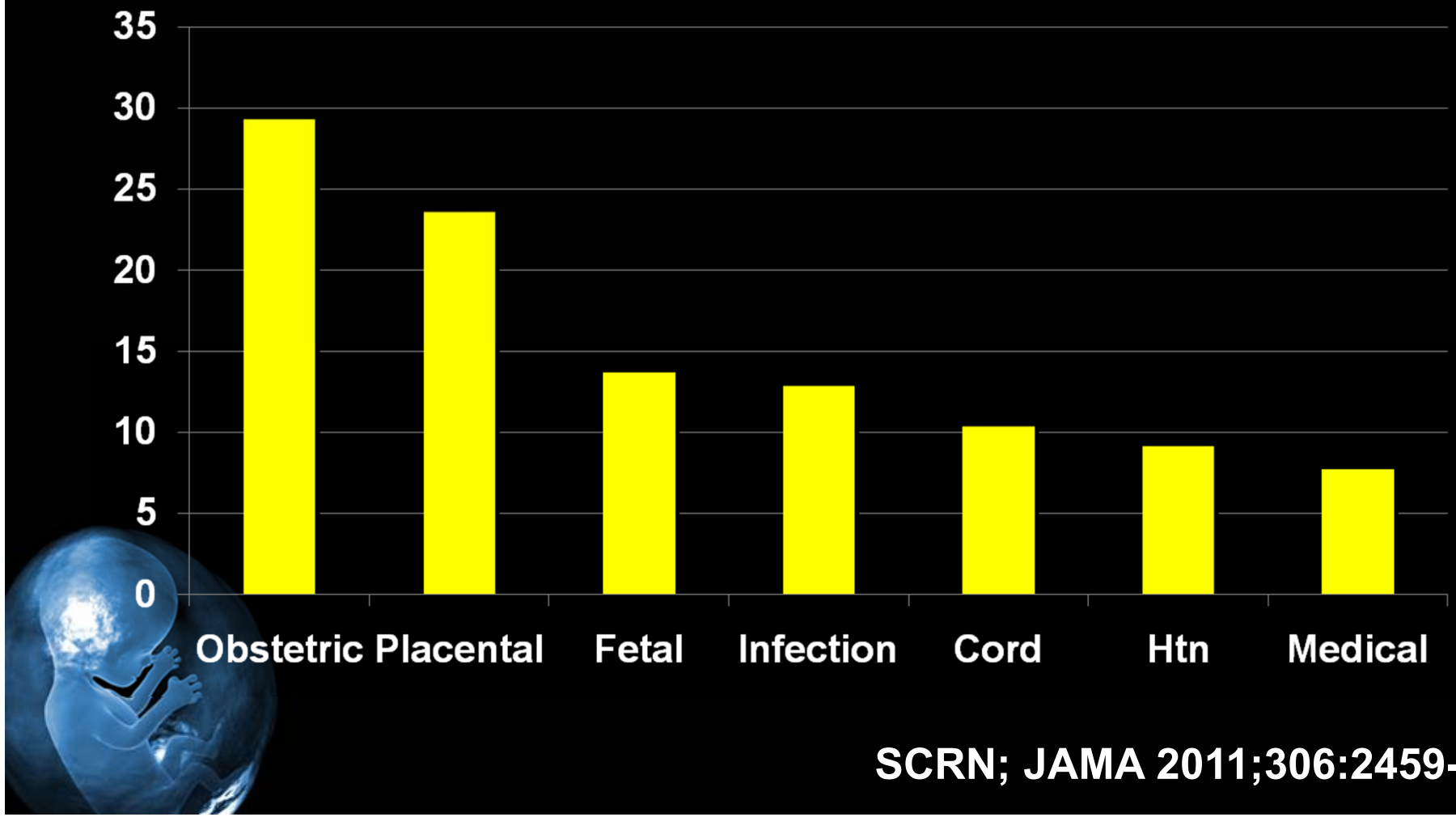
- NICHD – 2001 workshop
- Population-based study
- 5 geographic catchment areas defined *a priori* by county lines
- 59 hospitals averaging > 80,000 deliveries per year
- ≥ 90% of stillbirths (SBs) and live births (LBs) born to residents of the catchment areas are delivered in these 59 hospitals

Timing in Gestation of Stillbirths

SCRN; JAMA 2011;306:2459-68



Probable / Possible Cause of Death Broad Categories



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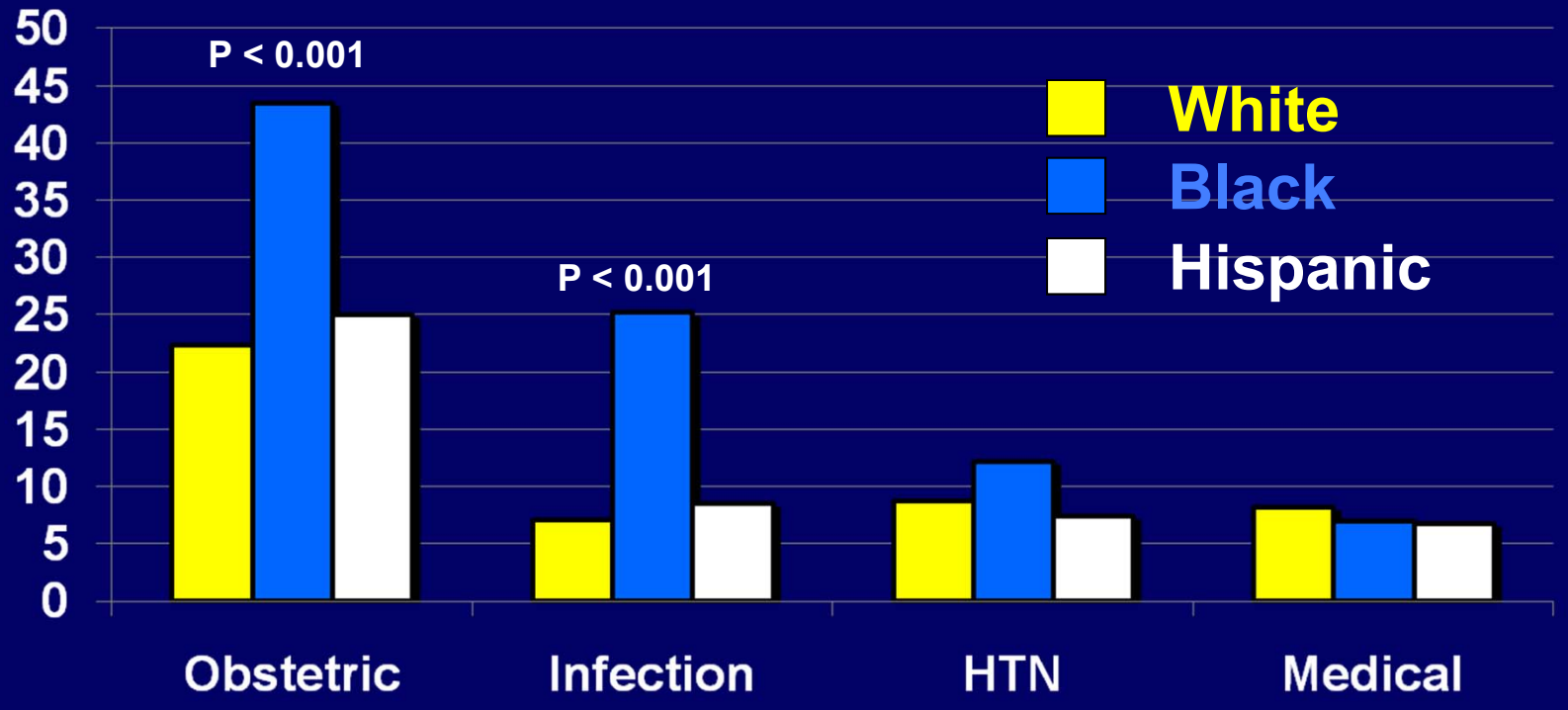
Probable / Possible Cause of Death by Race / Ethnicity



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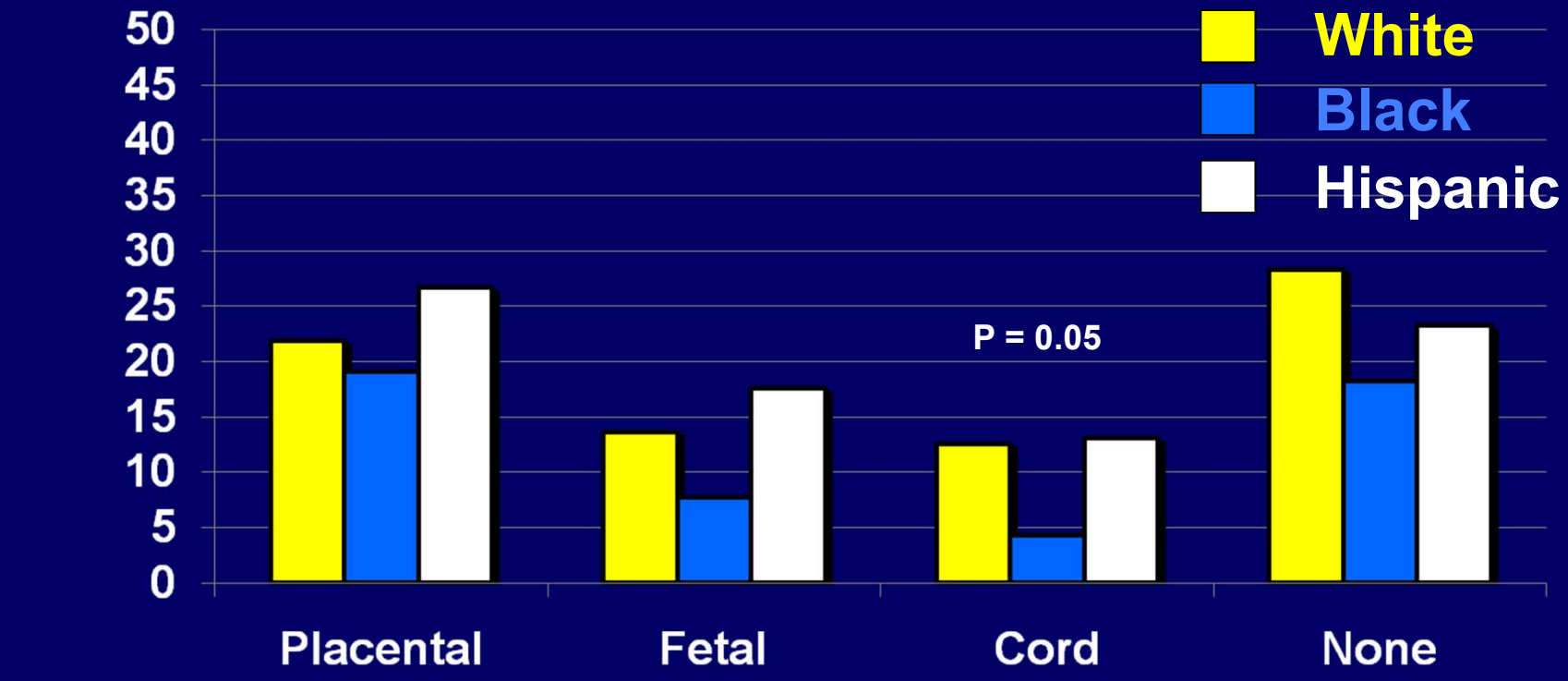

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Summary

- Systematic and thorough evaluation leads to a probable or possible cause in a majority of cases
- The most common causes of stillbirth were placental and obstetric conditions
- A higher proportion of stillbirths in non-Hispanic Blacks are intrapartum and due to obstetric complications and infections
- Proportion of stillbirths due to various causes differ by race / ethnicity and may contribute to racial disparity for stillbirth

Evaluation of Stillbirth: Why?

- Facilitates grieving and “closure”
- Recurrence risks
- Sporadic cause- reassurance
- May improve subsequent outcome
- Fewer unexplained cases with systematic evaluation

Optimal Evaluation of stillbirth

- CONTROVERSIAL
- Cost versus yield
- Focus on common causes
- Focus on recurrent conditions
- Pay attention to clues
- Emotionally challanging:
  - Varied levels of comfort with autopsy or genetic testing

Autopsy

- Single most useful step in evaluation
- Autopsy cause of death differed from the fetal death record in 55% of cases
- New information in 26-51% of cases
- Birth defects and morphologic abnormalities-genetic or developmental abnormalities
- Confirm infection, anemia, hypoxia, and metabolic abnormalities

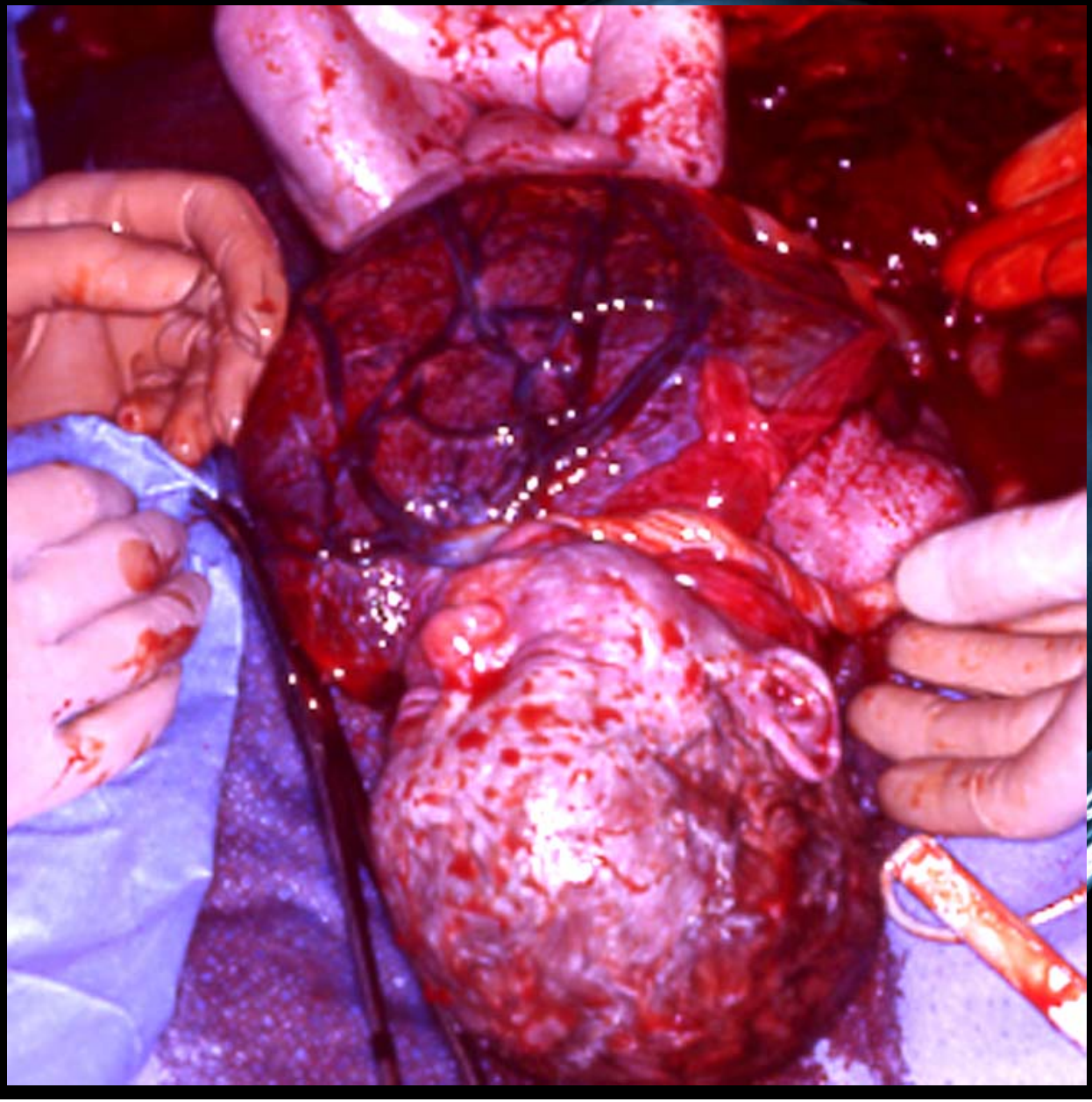
Autopsy

- Limited use in U.S.
  - Cost
  - Lack of trained pathologists
  - Discomfort by physicians
  - Discomfort by patients
- Work with families
- Partial autopsy, X-rays, and / or post-mortem MRI

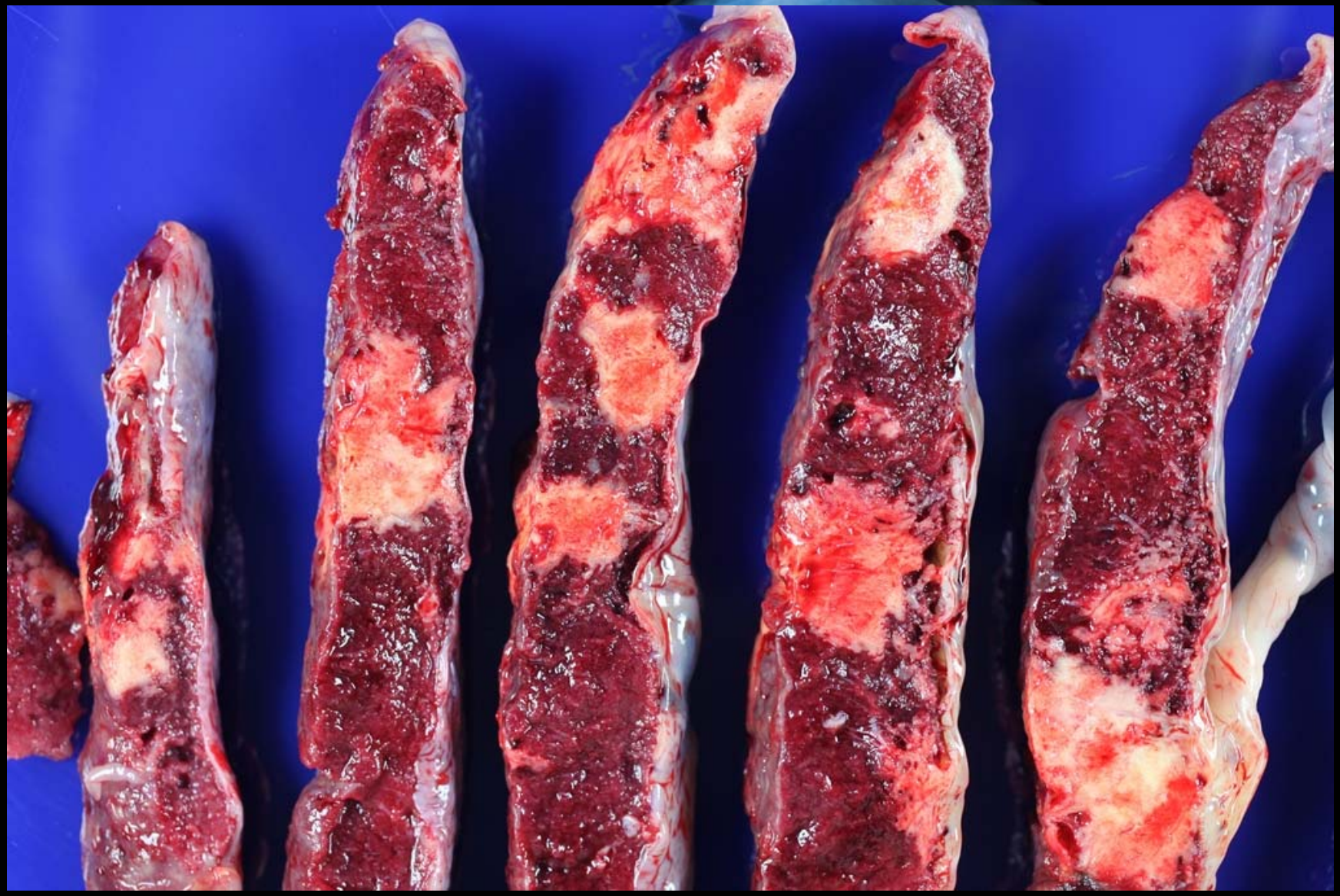
Placental, membranes, umbilical cord evaluation

- Infection, genetic abnormalities, anemia
- Trained pathologists
- Scientific, systematic evaluation
- Advised for medico-legal purposes in all cases of adverse pregnancy outcome

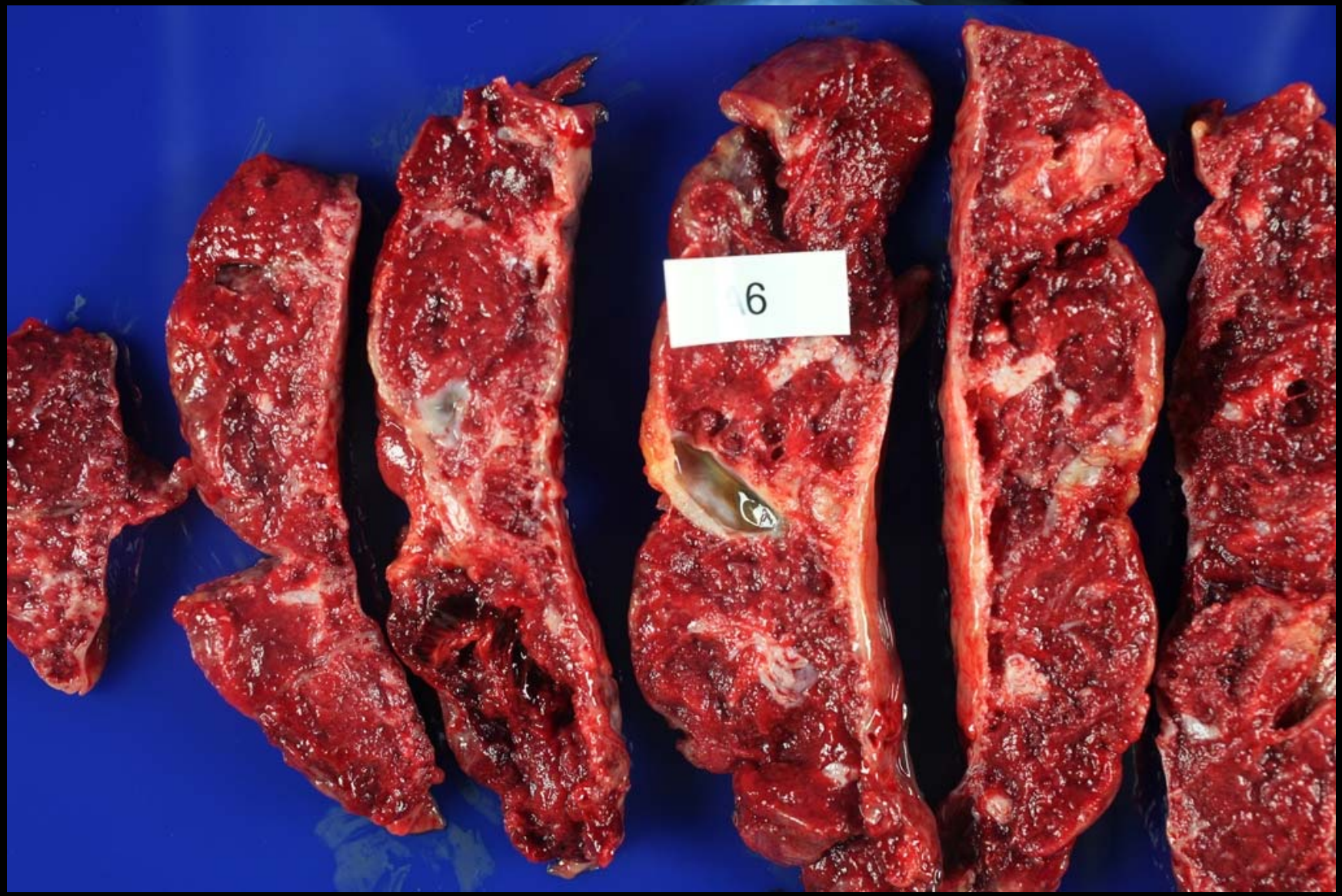
Abruption



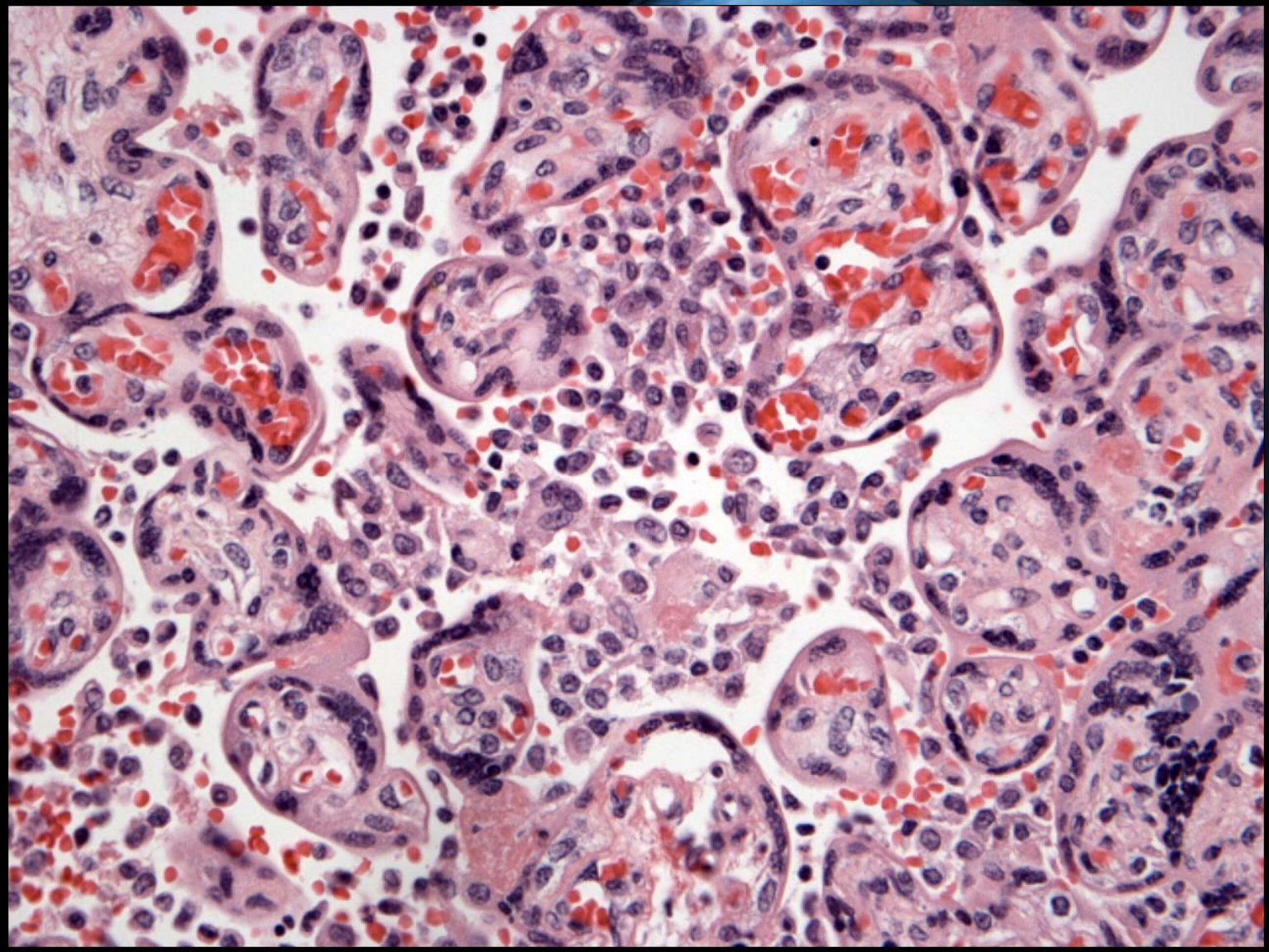
Multiple Infarcts



Massive Fibrin Deposition



Histiocytic Villitis



Karyotype

- Trained pathologist- tissues for karyotype after evaluation of the fetus and placenta.
- DO NOT put placental / fetal tissues in formalin

Genetic Conditions Microarray

- The "future" of genetic testing for pregnancy loss (and everything else)
- Does not require live cells!
- Identification of abnormalities not ascertained by conventional cytogenetics

Array vs. Karyotype

- Unexplained developmental delay/ intellectual disability, autism spectrum disorders, or multiple congenital anomalies
  - Array: 15 - 20%
  - Karyotype: ~3%

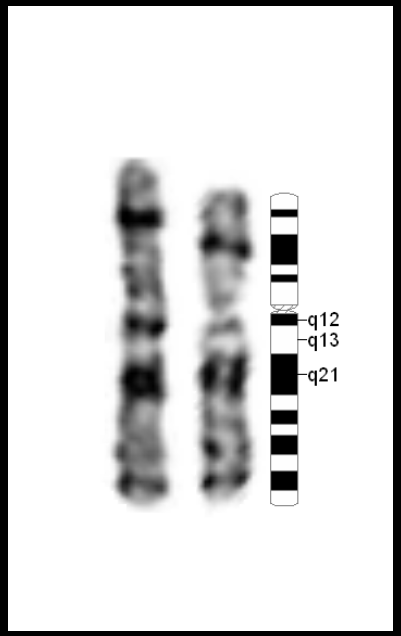
The American Journal of Human Genetics 86: 749-764, 2010

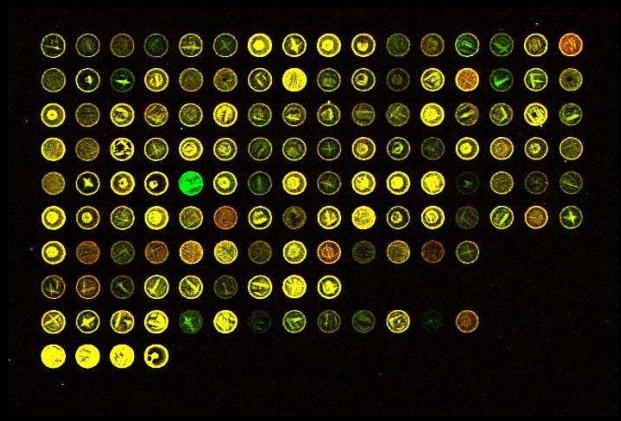
- Pregnancy loss
  - Array successful when cytogenetic evaluation has failed

Genetic Analysis
Karyotype - Microarray

- **Karyotype**
  - 5 – 10 megabase
  - Losses and gains
- **Microarray**
  - Coverage at a higher density
  - 50 – 100 kilobase
  - Losses and gains

  (Copy number variants)





Results

- Overall success rate
  - Karyotype: 70.5%
  - Array: 87.4% (p<0.001)
- Abnormal (aneuploidy + pathogenic CNV)
  - Karyotype: 5.8%
  - Abnormal Array: 8.3% (p=0.007)
  - 42% increased detection rate with array

SCRN, NEJM 2012;367:2185-2193

Results

- 157 Cases with failed karyotype
  - 74% normal array
  - 5.7% abnormal array

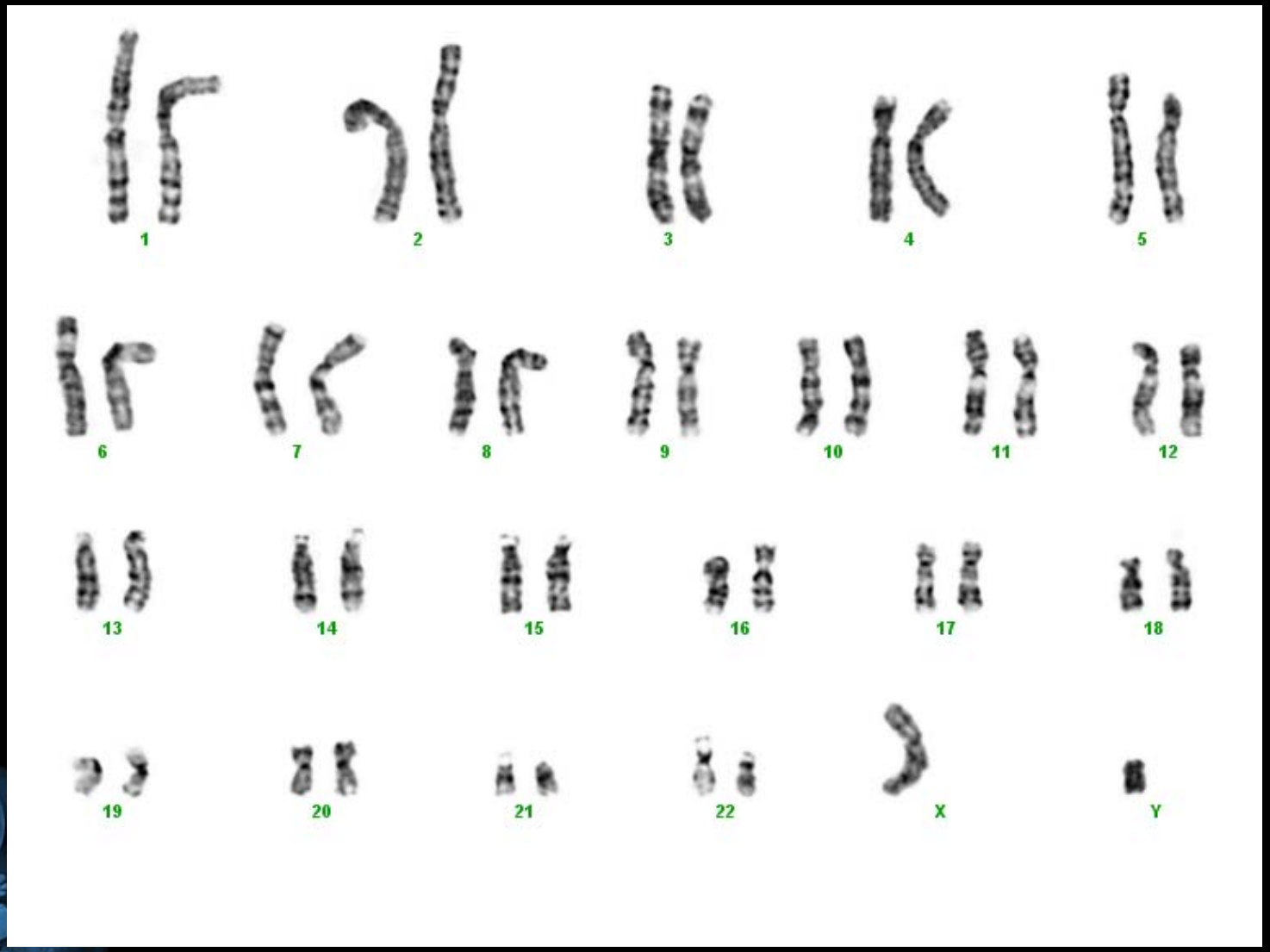
- Stillbirths with major anomalies (n=472)
  - 19.4% abnormal karyotype (13/67)
  - 30% abnormal array (20/67)
  - 53.8% increased detection rate with array

SCRN, NEJM 2012;367:2185-2193

Case #2

- 27 week stillbirth, 746 grams (AGA)
- Multiple congenital malformations
  - Cranio-facial dysmorphism
  - Cleft soft palate
  - Limb deficiencies
  - Multiple cardiac defects

Case #2



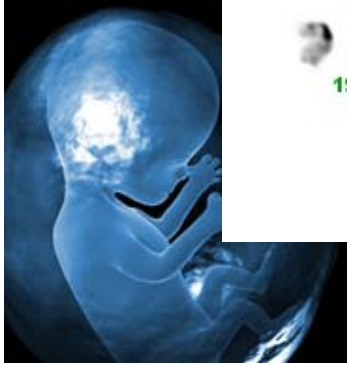
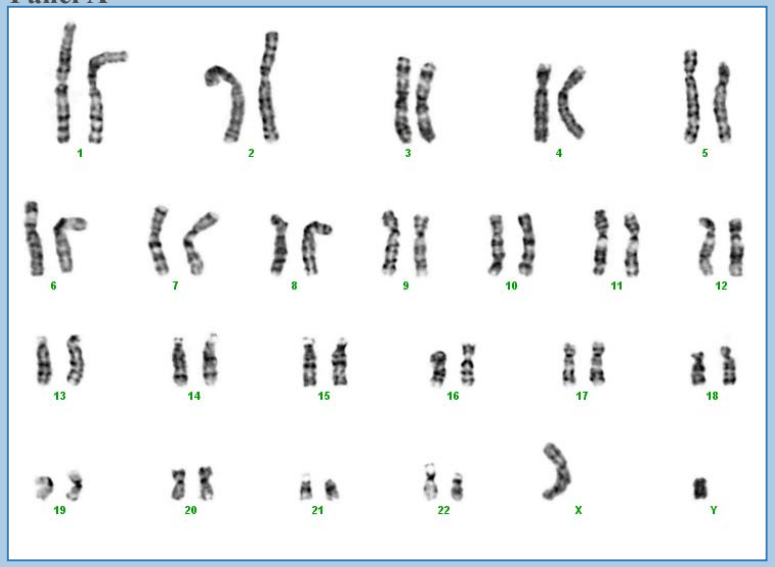


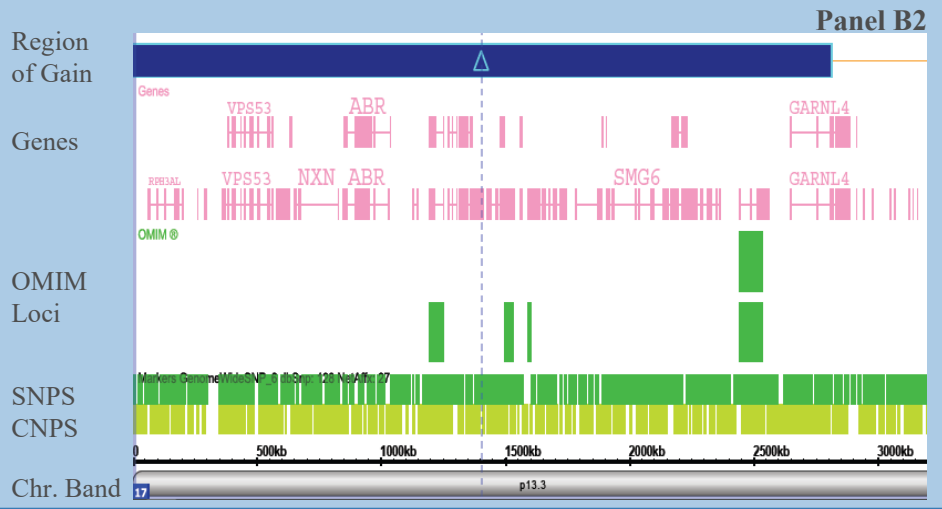
Figure 3a: Case 1

Panel A

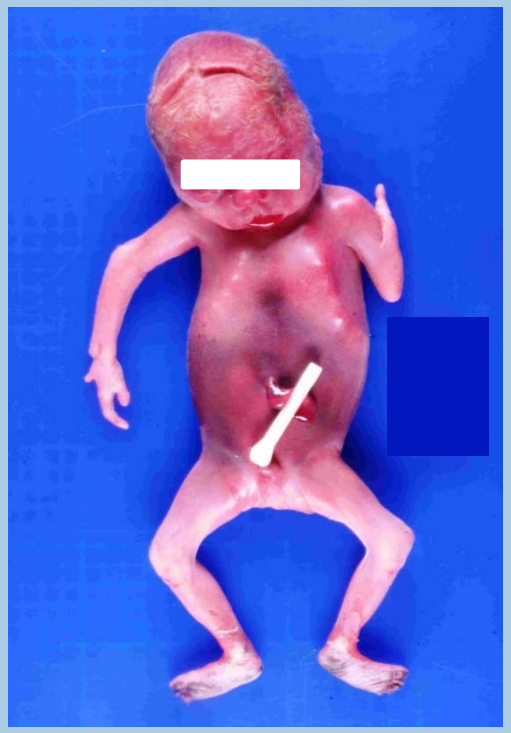


Panel B1

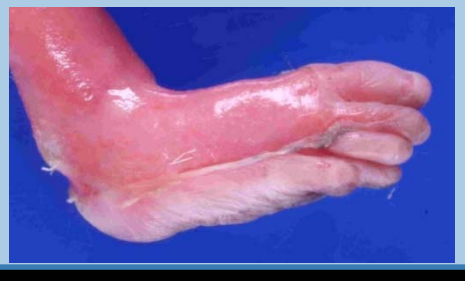
Panel B2



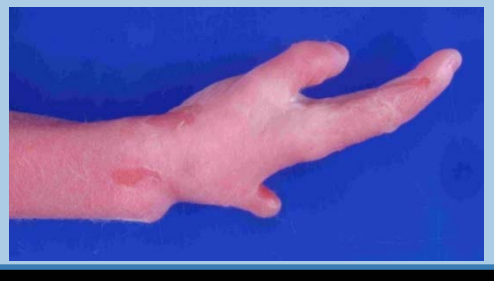
Panel C1



Panel C2



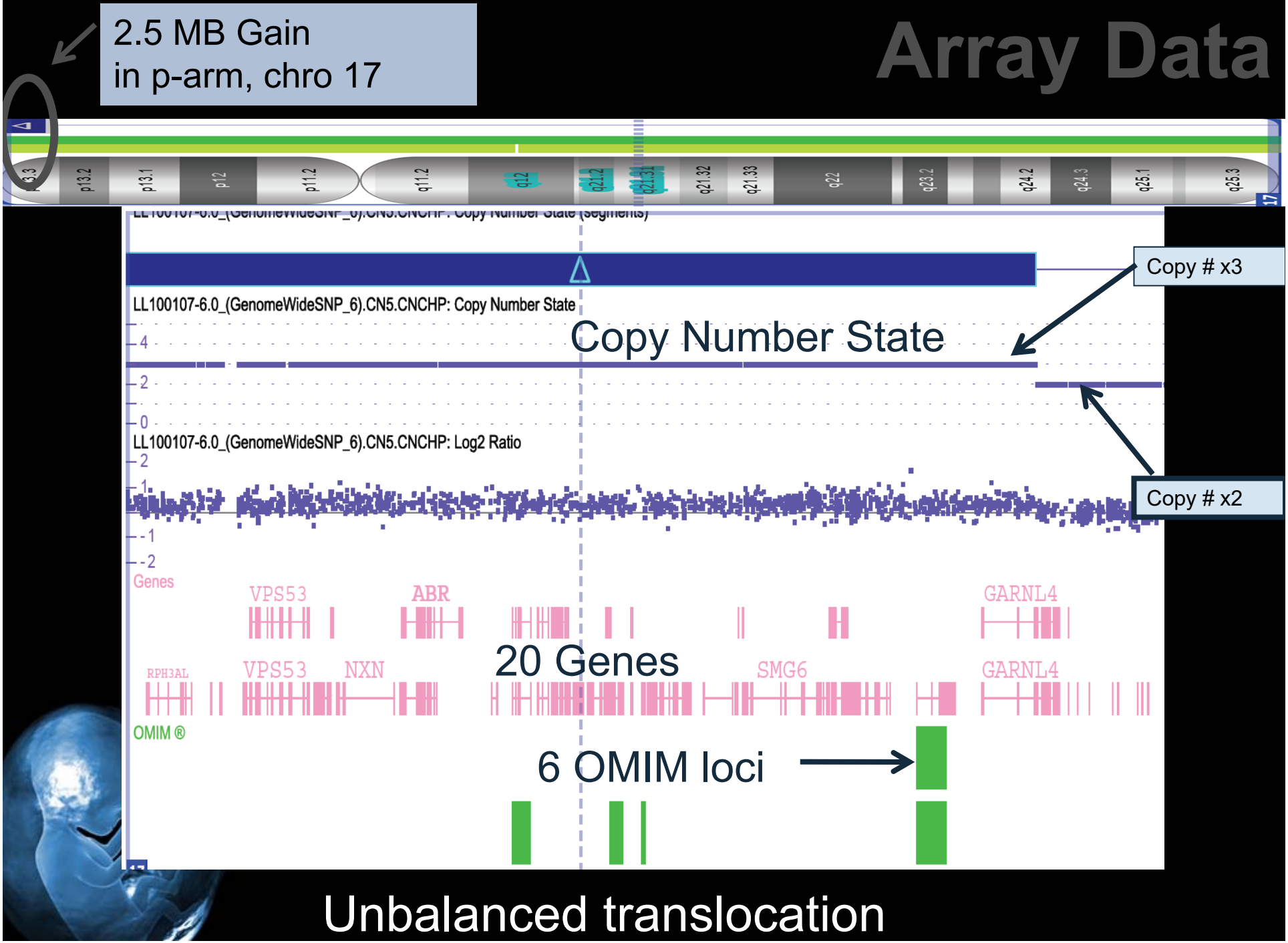
Panel C3



Array Data

25 MB Deletion
in q-arm, chro 4

Array Data

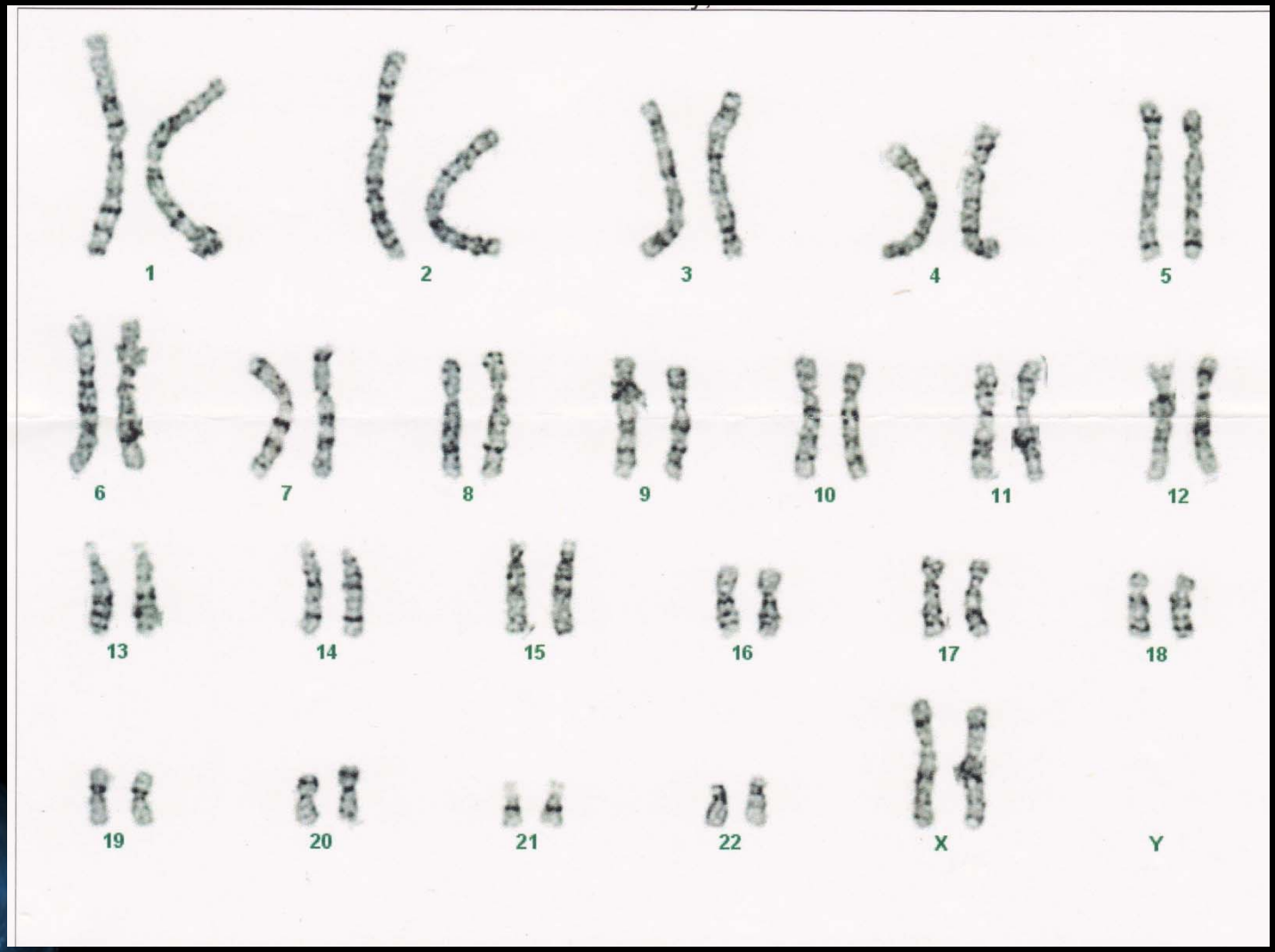


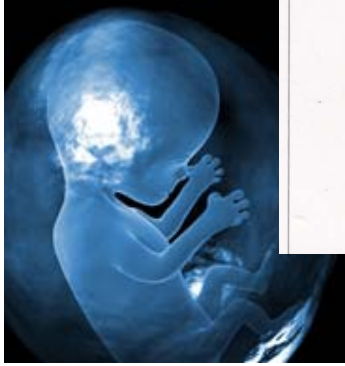
Unbalanced translocation

Case #3

- 37 week stillbirth, 2490 grams (AGA)
- Multiple minor facial and lower extremity anomalies, no clear recognized syndrome

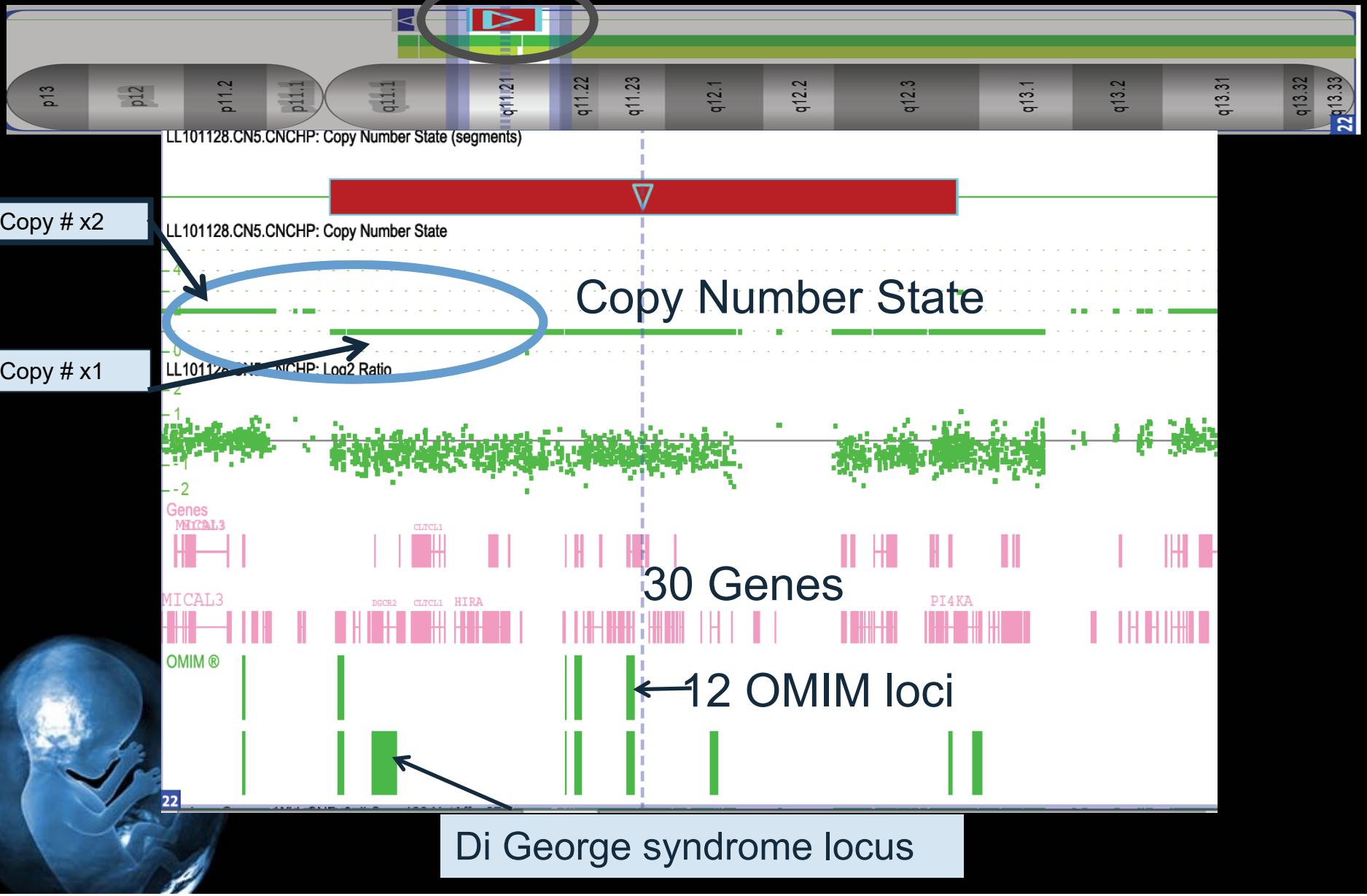
Case #3





Array Data

2.5 MB Deletion
in q-arm, chro 22



Array- Conclusions

- Primary benefit of array is the greater likelihood obtaining a result
  - Ability to analyze non-viable tissue
- Higher resolution allowing for detection of copy number changes not visible on karyotype

SCRN, NEJM 2012;367:2185-2193

Array- Conclusions

- Array should be considered in cases of karyotype failure or major anomalies
- Array may prove useful as a first line screen for genetic abnormalities in stillbirth given higher yield of abnormalities as cost decreases

SCRN, NEJM 2012;367:2185-2193

Fetal-maternal hemorrhage

- **Kleihauer-Betke test (KBT)**
  - ✓ Elution of adult hemoglobin (HbA) from adult red cells, more acid-resistant fetal hemoglobin (HbF) remains intact in fetal RBC.
  - ✓ Remaining hemoglobin is subsequently visualized by staining with erythrosin.
- **Flow cytometry**
  - ✓ May be more accurate
  - ✓ Used by some centers

Stillbirth: Infection Evaluation

- Clinical history
  - Maternal illness / obstetric complications
- Placental histology
- Fetal autopsy
- Routine cultures NOT useful
  - Vaginal delivery – contamination
- Routine serology NOT useful
- Routine TORCH titers NOT useful
- Targeted studies based on clinical history, placenta and autopsy

Generally accepted tests:

- Clinical history
- Fetal autopsy
- Placental evaluation
- Karyotype/Microarray
- Screen for fetal-maternal hemorrhage

Korteweg; Am J Obstet Gynecol 2012;206:e1-12

SCRN; JAMA 2011;306:2459-68

Useful in some cases (If “clues” present)

- Testing for specific organisms
- Screening for diabetes
- Toxicology screen
- Assessment of thyroid function
- Antibody screen
- Syphilis serology

Korteweg; Am J Obstet Gynecol 2012;206:e1-12

SCRN; JAMA 2011;306:2459-68

Useful in some cases (If “clues” present)

- Lupus anticoagulant screen
- Anticardiolipin antibodies
- Factor V Leiden mutation?
- Prothrombin G20210A mutation?
- Protein C, protein S, and antithrombin III deficiency screen?

Korteweg; Am J Obstet Gynecol 2012;206:e1-12

SCRN; JAMA 2011;306:2459-68

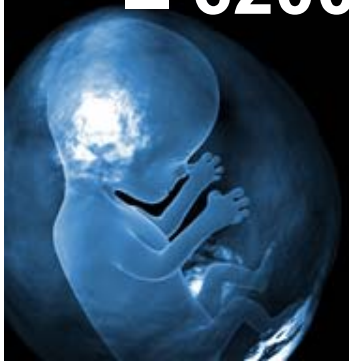
Not Useful

- Placental cultures
- Routine TORCH titers
- ANA testing
- Testing for large numbers of thrombophilias
  - MTHFR mutations
- Bile acids / glycohemoglobin / thyroid function if no features of disease

Hospital Care for Parents After Perinatal Death

Gold KJ, Obstet Gyencol 2007

- 1,100 articles from 1966-2006 on fetal death in second or third trimester, neonatal death in first month
- 60 eligible studies were included
- 6200 parents



Recommendations for Improving Hospital Care After Perinatal Death

- Allow parents to help decide when to deliver
- Provide parents the option for post-delivery care on or off a maternity floor
- Be sensitive to physical pain during delivery and offer adequate pain control. Avoid over sedation
- Encourage parents to see and hold their infants for extended periods and at multiple sittings and offer who initially decline additional chances later.

Recommendations for Improving Hospital Care After Perinatal Death

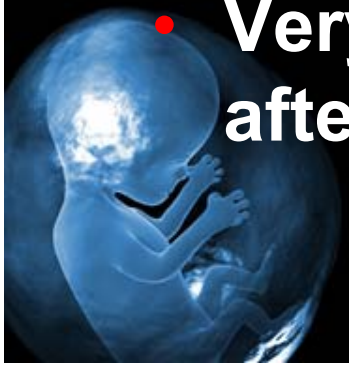
- Take nonclinical photographs of cleaned-up infants as soon after delivery. Include a photograph of multiples together even if one or more babies has died
- Collect memorabilia about the baby. If the parents decline these items initially, offer them again later or hold the materials for a future time
- Discuss options for burial with both parents, allow parents to participate in final decisions.

Recommendations for Improving Hospital Care After Perinatal Death

- Ensure autopsy results are provided to parents promptly
- Educate other members of a patient's obstetric team about interventions valued by bereaved parents
- Ask other team members to perform key tasks (collecting memorabilia or taking pictures)

The subsequent pregnancy after stillbirth

- Difficult for couple
  - ✓ Anxiety, failure, personal guilt, apprehension
  - ✓ Lack of closure- cause of stillbirth remains unknown (50%), never counseled postpartum
- Difficult for clinicians to optimally counsel, evaluate and manage
- Very little is known about pregnancy after experiencing stillbirth



Stillbirth
Recurrence risk (summary)

- Risks known for a few conditions
  - Diabetes / Some genetic conditions
- Overall rates:
  - 0-8%
  - Increase: 2 to 10 fold
- Higher risk of loss:
  - Earlier losses
  - Recurrent losses
  - Non-Hispanic Black
  - Fetal growth impairment
- Lower risk of loss:
  - ? Unexplained stillbirth

Stillbirth: Transient Risk Factors

- Biochemical markers
  - Low PAPP-A
  - High MSAFP
  - High β-hCG
  - High inhibin A
- Uterine artery Doppler velocimetry
- Relatively poor predictive values

Stillbirth: Recurrence risk

Condition	Adjusted OR	95% CI
Stillbirth	1.6	(1.1, 2.3)
Abruption	9.4	(4.5, 19.7)
Preterm birth < 37 wks	7.5	(5.9, 9.4)
Low birthweight	6.7	(5.3, 8.4)

Bhattacharya S et al, Br J Obstet Gynecol 2010; 117:1243

Stillbirth: Risk Factors

- Many associations with stillbirth
  - Obesity, HTN, Diabetes, Nulliparity, prior pregnancy loss, prior stillbirth, AMA, non-Hispanic black race, AB blood type
- Risk factors explain very little of the variance in stillbirth
- Target entire population
- Better methods to identify high risk patients

SCRN, JAMA 2011;306:2469-79

Stillbirth
Recurrence risk

- Most cases are sporadic
- Recurrence risk is low for most families
- In cases at higher risk:
  - ✓Medical interventions
  - ✓Prenatal diagnosis

Stillbirth
Subsequent pregnancies

- Emotional management
- Reassurance
- Serial sonograms
- Antenatal surveillance
- Fetal kick counts
- Delivery (at 39 weeks)
- Medical interventions for selected cases

Thank You!