Improving Outcomes of Pregnancy

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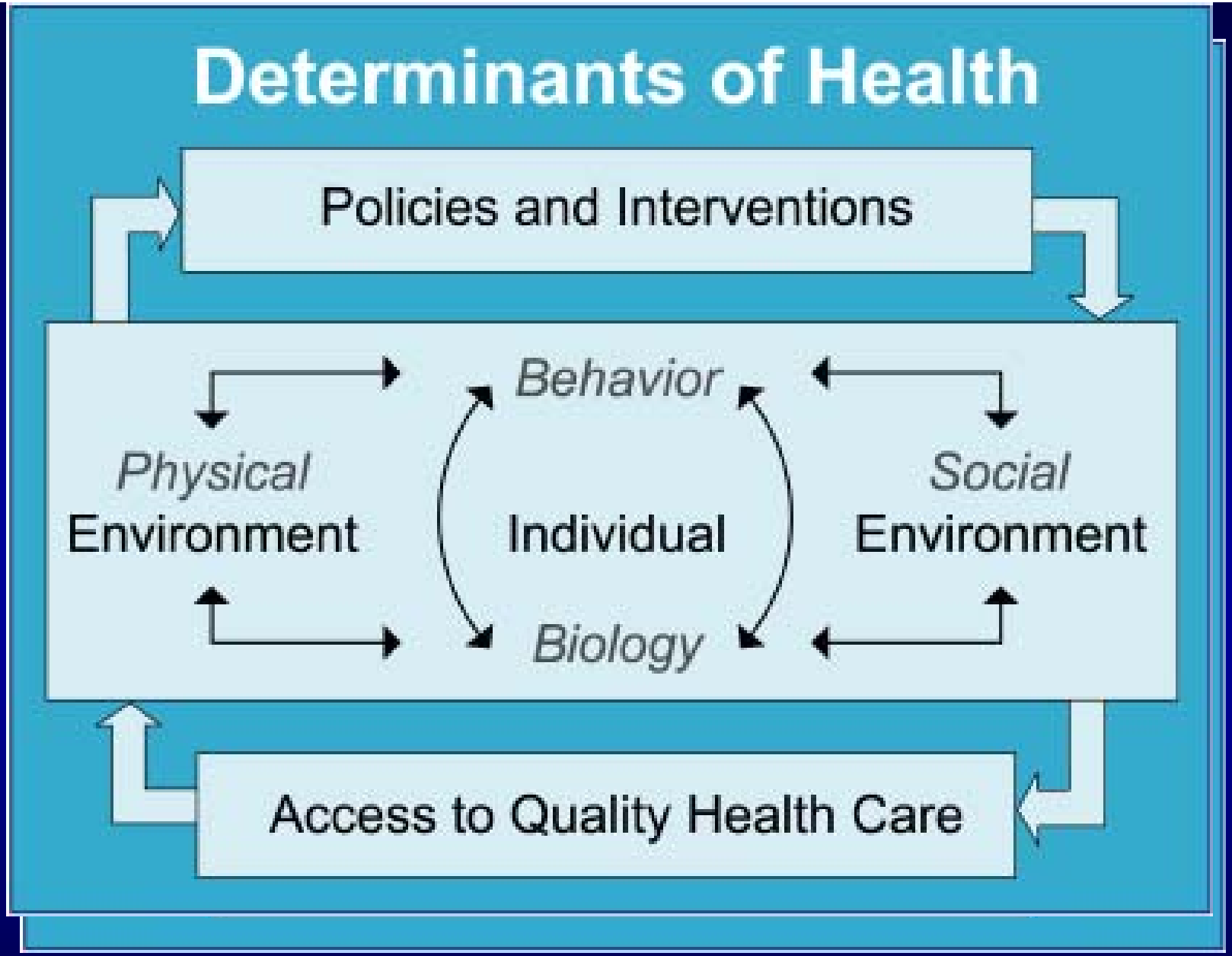

www.healthypeople.gov

PREEMIE Act (S. 707) Passes Congress

- December 2006
- Among it's most important provisions the bill authorizes:
  - a Surgeon General's conference at which scientific and clinical experts from the public and private sectors will formulate a national action agenda designed to speed development of prevention strategies for preterm labor and delivery
  - a consensus research plan for HHS on prematurity and LBW
  - a report to HHS Secretary and appropriate committees of Congress on current HHS activities relating to prematurity and LBW, and include the recommendations from Surgeon General's Conference, and the status of research activities

Preterm Birth

- #1 obstetric challenge in the US
- Major cause of loss
  - majority of all perinatal mortality
  - leading cause of neonatal mortality (since 1999)
  - leading cause of black infant mortality and second leading cause of all infant mortality in US?
- Leading problem in pediatrics
  - leading cause of neonatal morbidity
  - half of all neurodevelopmental conditions
- Associated with higher rates of chronic illness in adults
- Serious, common, and costly

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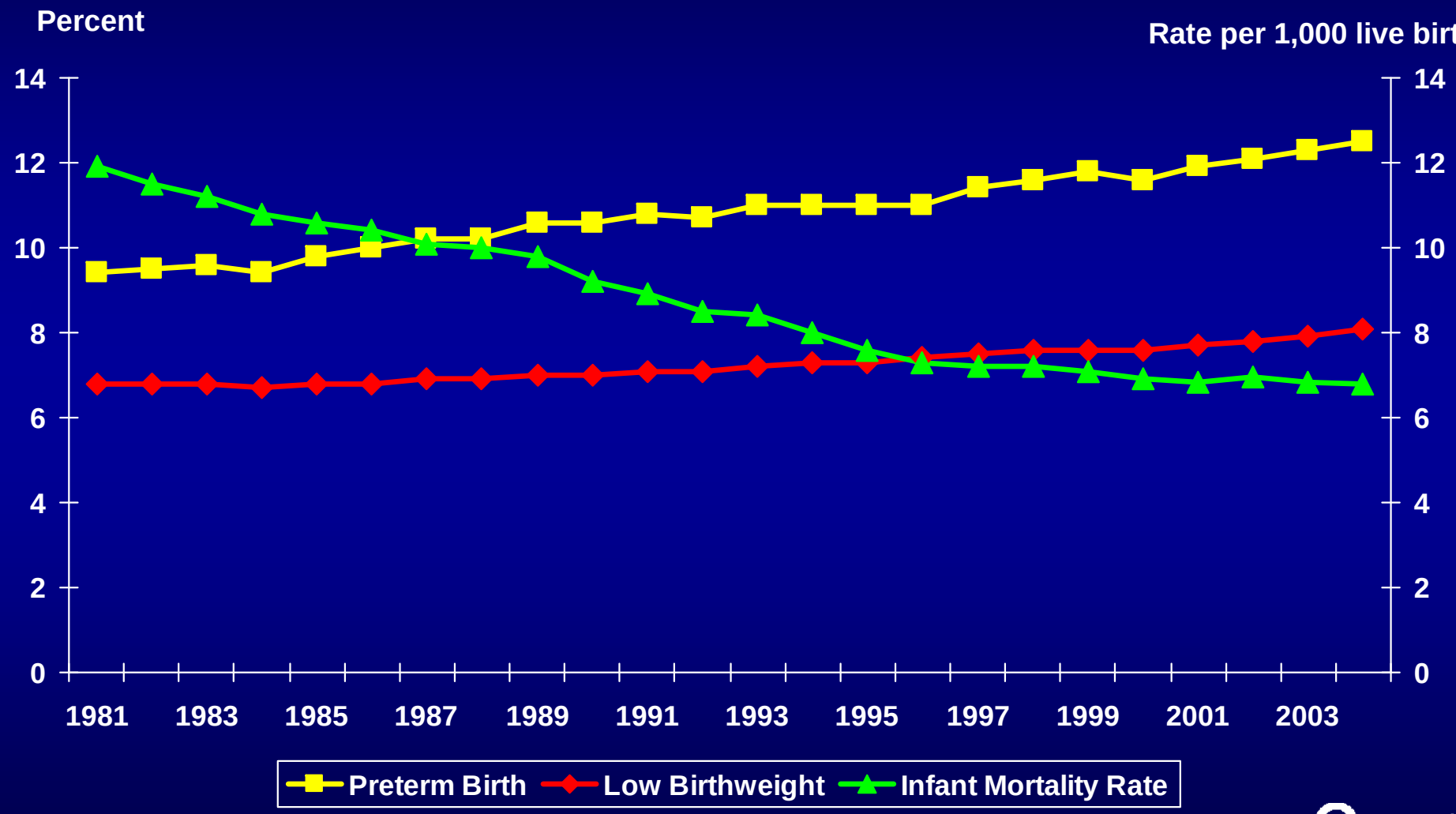
Preterm Births, Low Birthweight and Infant Mortality
United States, 1981 - 2004



Source: National Center for Health Statistics, final natality and mortality data
Prepared by March of Dimes Perinatal Data Center, 2007

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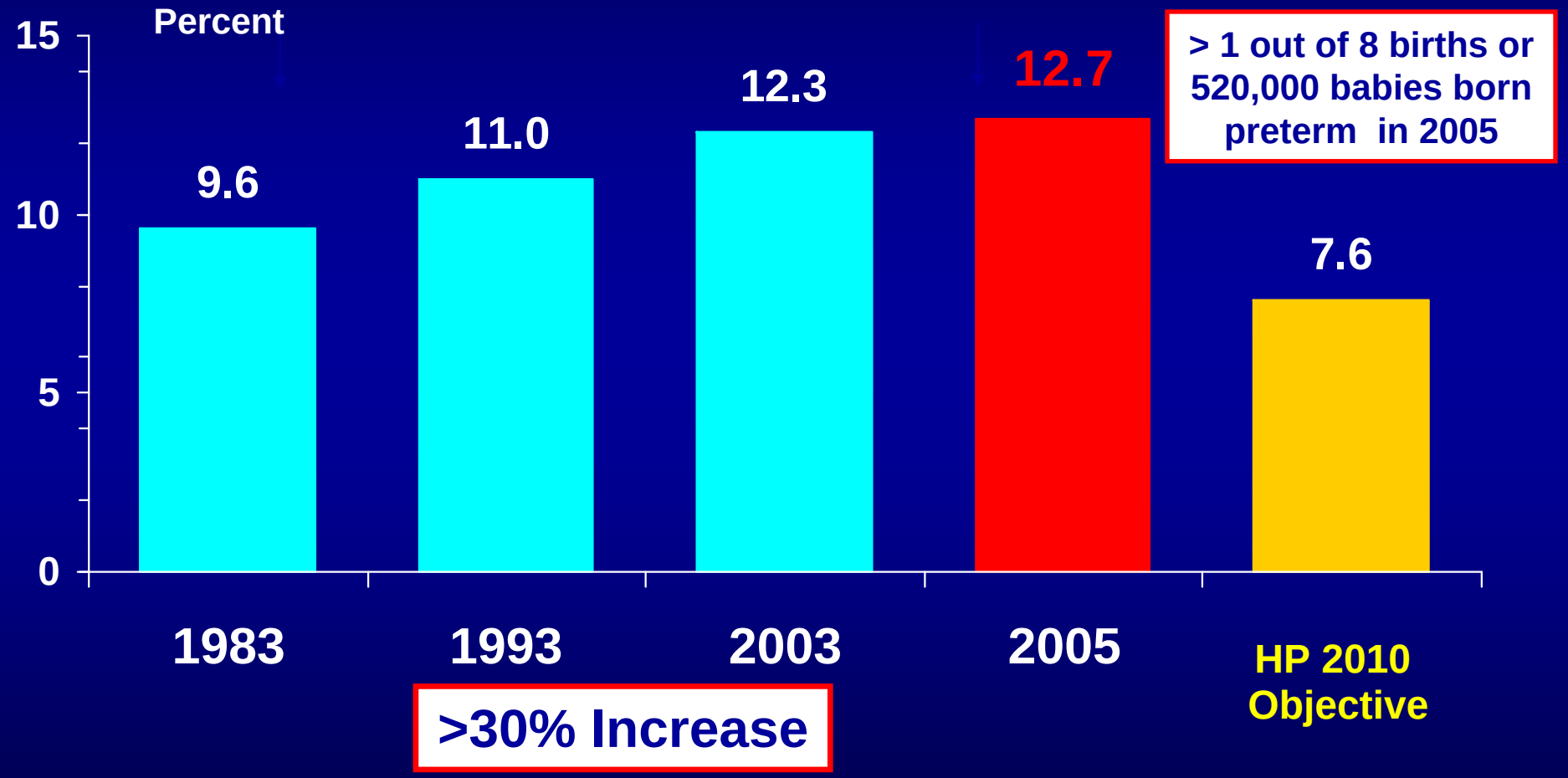
Preterm Birth Rates
United States, 1983, 1993, 2003, 2005*



Preterm is less than 37 completed weeks gestation.
Source: National Center for Health Statistics, final natality data
Prepared by March of Dimes Perinatal Data Center, 2005
*preliminary

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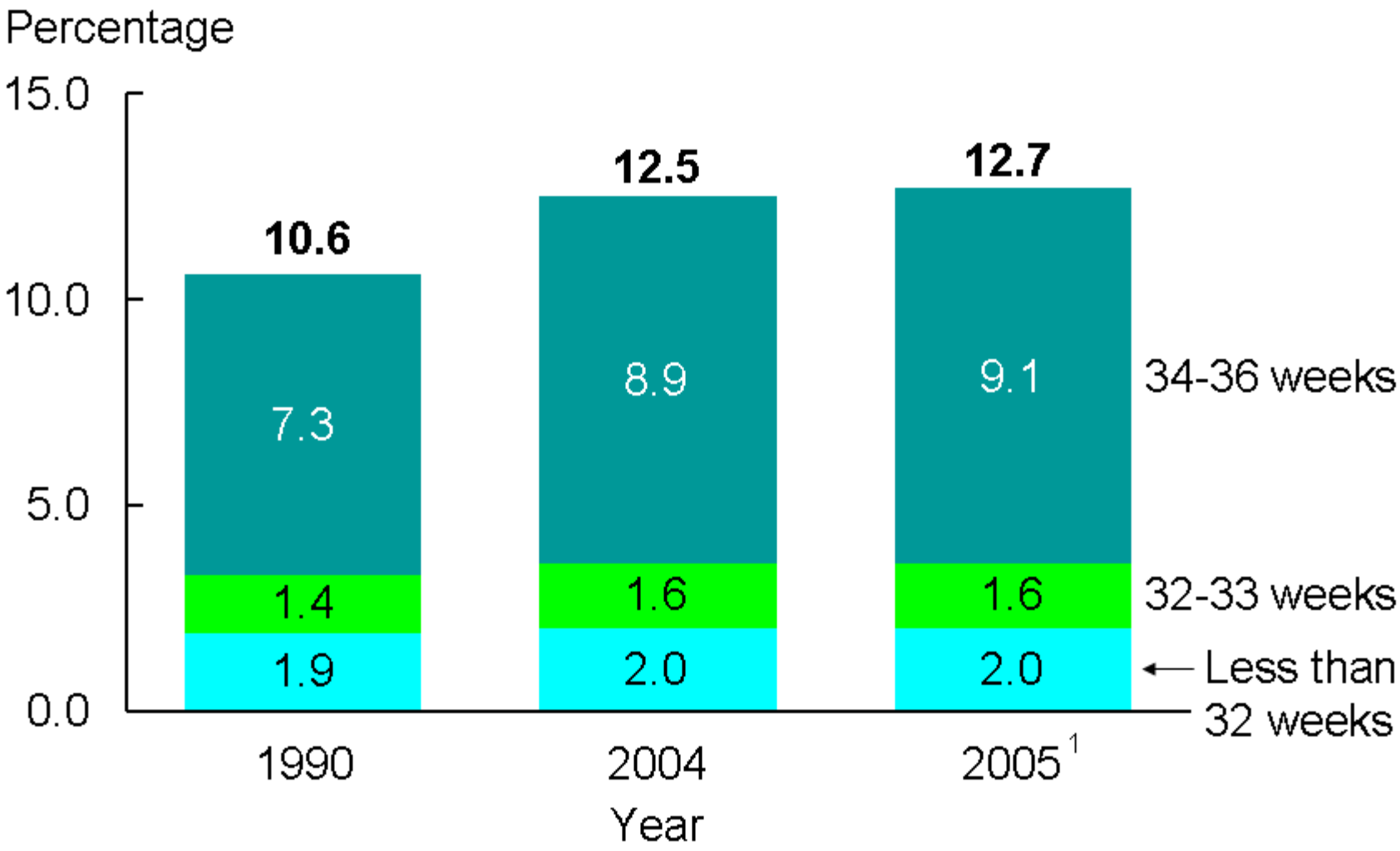
Preterm Birth Rates by Race and Education, IOM 2006

Years of Ed	NonHisp Black	NonHisp White	Asian Pacif Isl	Amer Indian	Hispanic
< 8	19.6	11.0	11.5	14.8	10.7
8-12	16.8	9.9	10.5	11.8	10.4
13-15	14.5	8.3	9.1	9.9	9.3
≥16	12.8	7.0	7.5	9.4	8.4

Definitions

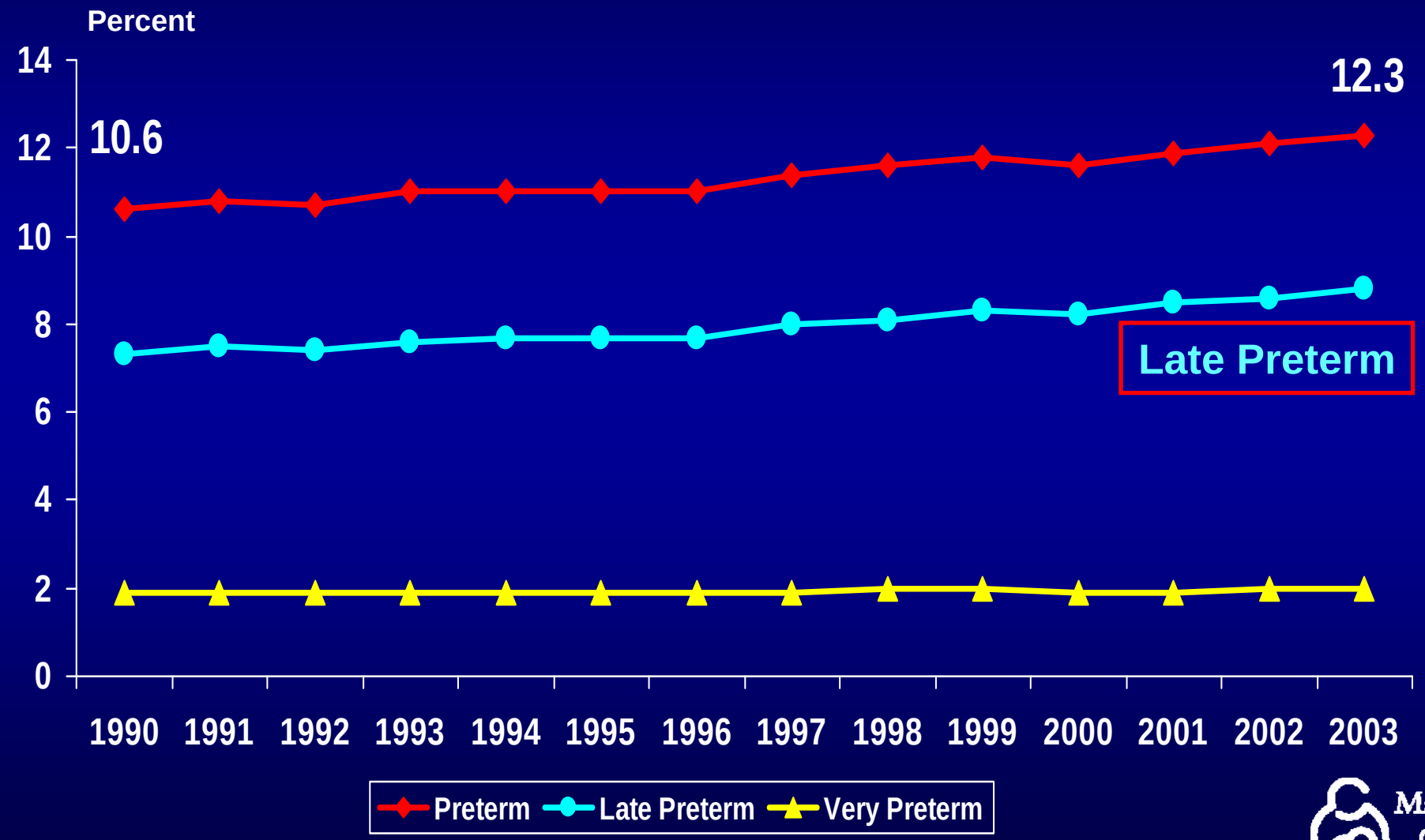
- Preterm birth:
  - < 37 completed weeks gestation
- Late preterm (or Near-Term):
  - 34-36 completed weeks
- Very preterm:
  - <32 completed weeks

Figure 5. Percentage of preterm births: United States, 1990, 2004, and 2005



[1] Based on preliminary data.
SOURCE: CDC/NCHS, National Vital Statistics System

Total (<37 weeks), Very (<32 weeks) and Late Preterm Births (34-36 weeks) U.S., 1990- 2003



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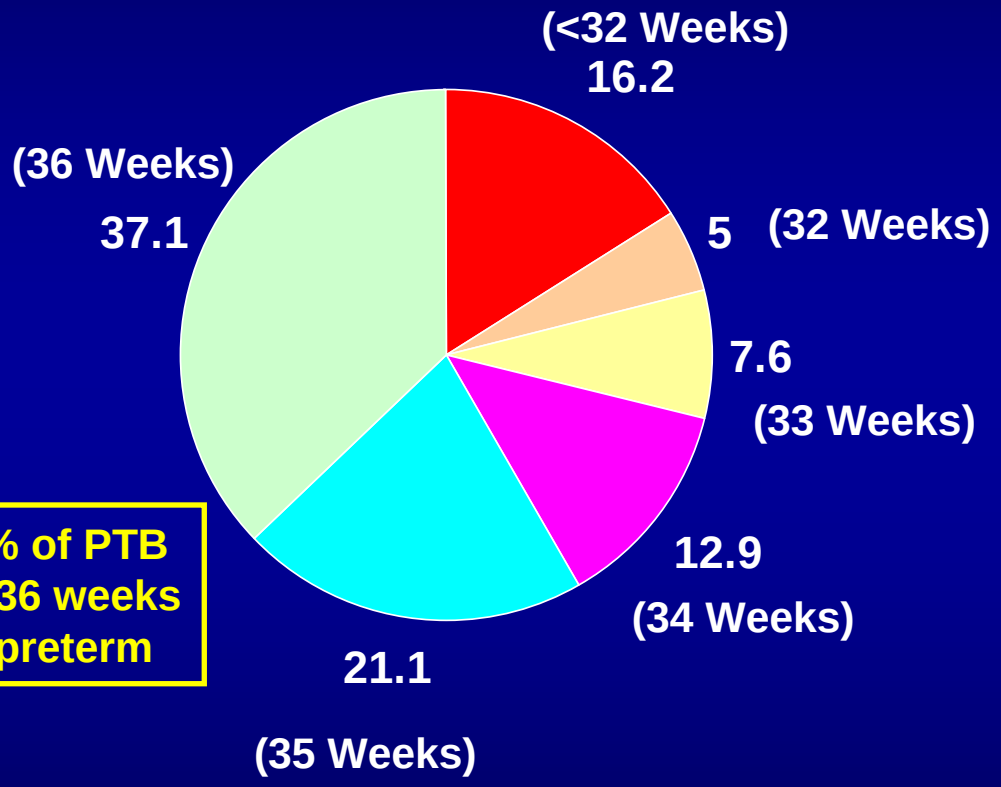
Why are Late Preterm Rates Rising?

- Changing culture of childbearing
  - more high risk pregnancies (AMA, chronic/developing problems, multiples, infertility management, obesity, GDM)
  - public preference/autonomy (induction and CDMR)
  - changes in clinical management (more interventions)
    - litigious environment, fear of suit, defensive medicine
      - 2006 ACOG liability survey 89.2% (79.1% in 2003) named in a claim, avg 2.6/career
    - reimbursement system changes
    - window to administer antenatal steroids 24-34 weeks
    - increase in survival to almost 100% at 34 weeks
    - change in 'risk tolerance'

      Ecker JL, Frigoletto FD Jr. NEJM; 356:885-8, Mar 1, 2007
    - increasing rates of elective inductions and section before 39 weeks despite ACOG guidelines

Distribution of Preterm Births by Gestational Age, US, 2002



~71% of PTB 34 - 36 weeks late preterm

"Near term infants had significantly more medical problems and increased hospital costs compared with contemporaneous full term infants

Near term infants may represent an unrecognized at-risk neonatal population."

Wang, et al. Clinical Outcomes of Near-Term Infants, Pediatrics (114) 372-6, 2004.

Source: National Center for Health Statistics, 2002 natality file
Prepared by the March of Dimes Perinatal Data Center, 2004

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Morbidities associated with Late PTB?

Need to separate causes and effects

- Increased immediate morbidities:
  - Respiratory distress
  - Jaundice
  - Feeding difficulties
  - Hypoglycemia
  - Temperature instability
  - Sepsis
- Increased NICU use (and re-admissions)
- Increased cost
- Long term outcome - *??* - **NO DATA!**

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NICHD Invitational Conference , July 2005

Late Prematurity Facts

- Late preterm delivery is increasing
  - up at least 16% from 1993
  - straining the Public Health system
  - 52% of late preterm infants are delivered by cesarean, a much higher rate than term infants
- Late-Preterm infants are:
  - a majority of NICU admissions
  - the greatest percentage of NICU patients to receive respiratory support
  - the majority of NICU economic costs

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Late Prematurity Facts

- often the sickest babies in a NICU
- more likely than a full term baby to be rehospitalized in the first year of life
- twice as likely to die in the first year of life as a full term baby
- at risk for long term health issues

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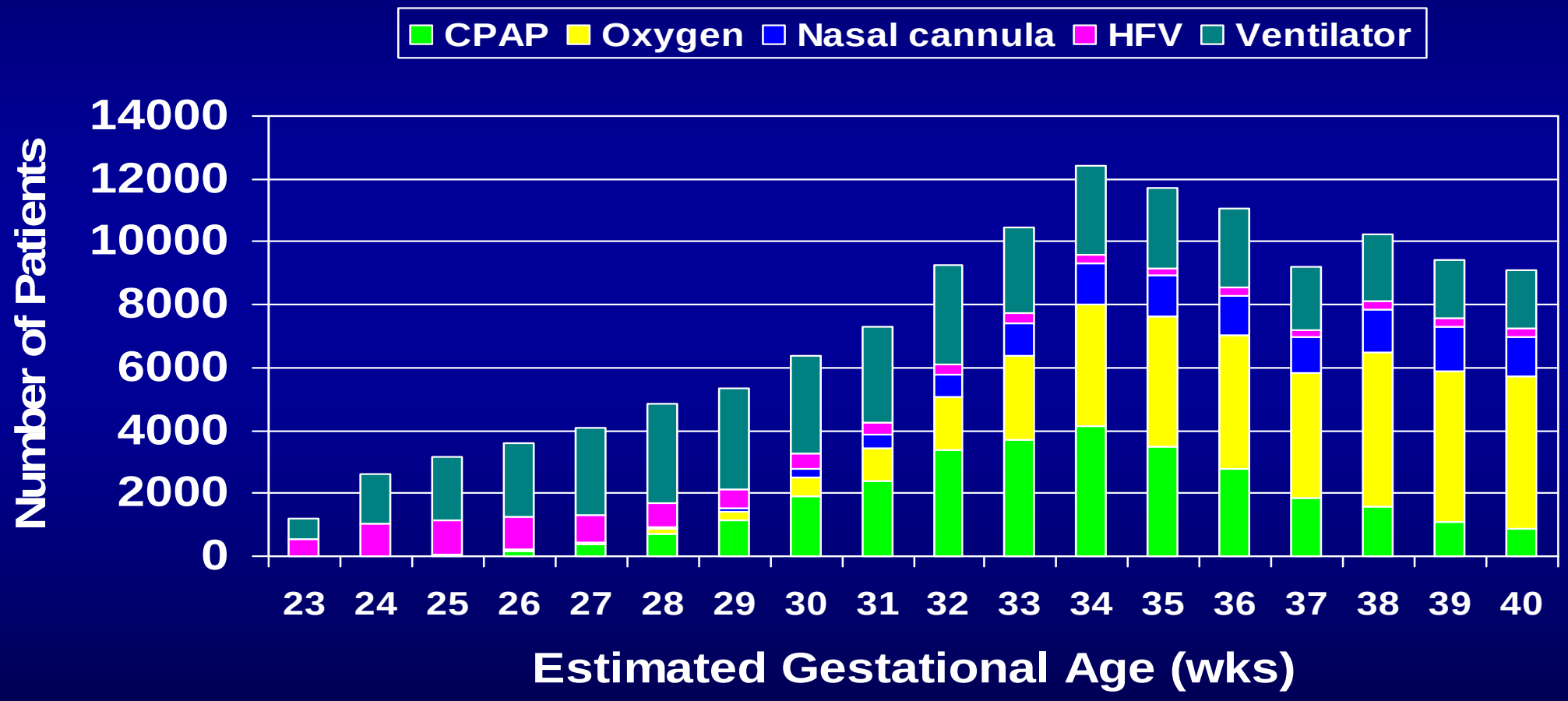
NICU Admissions Requiring Respiratory Support by Gestational Age



Clark RH 2006

The Late Preterm Birth
Fetal Lung Fluid Clearance

- Disruption of hormonal and maturational changes:
  - Lack of surge in endogenous steroids and catecholamines that accompany normal labor
  - Immaturity of transepithelial sodium resorption to create osmotic gradients and promote fluid clearance
    - Antenatal Steroids for Term Cesarean Section study--steroids mature the sodium channels in alveolar epithelium – Emory
- Alveolar hypoventilation
- Inadequate surfactant
- Persistent Pulmonary Hypertension and shunting

The Late Preterm Infant - Hypoglycemia

- Unlike term infants, late preterm and IUGR infants are incapable of mounting an adequate mature counter-regulatory response to hypoglycemia.
  - Glycogen reserves build up only in late gestation
  - Peripheral adipose tissue builds up only in late gestation
  - Ketogenic respose to mobilize alternate fuels is inadequate
  - In brain, astrocytes are still growing during late gestation
    - provide an immediate store of glycogen;
    - Alternate fuels like lactate and ketones are actively transported into astrocytes
- Hypoglycemia with hyperinsulinemia is more likely to cause adverse neurologic outcome because what stores there were are already used up from the hi insulin levels, so alternate substrates (ketones) are lacking

Garg M, Devaskar SU. Glucose metabolism in the Late Preterm Infant. Clin Perinatol 33 (2006):853-70.

Poor Feeding

- Feeding is most complex activity a newborn infant must master
  - Coordination of suck-swallow-breath rhythms
    - Swallow rhythm develops first
    - Suckle is developing from 32-40 weeks
      - Usually reaches 1:1 ratio 34 weeks
      - Variation can occur in Late Preterm infants

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Temp Instability

- The Late Preterm infant is more likely than term infants to have temperature instability
  - 10% vs 0% in term
  - Wang et al. *Pediatrics* 2004;114:372-376
- Due to
  - Immature epidermis
  - Higher ratio of surface area to birthweight
  - More frequent delivery room interventions
- If untreated, infant can loose 2-3°C in the first 30 minutes

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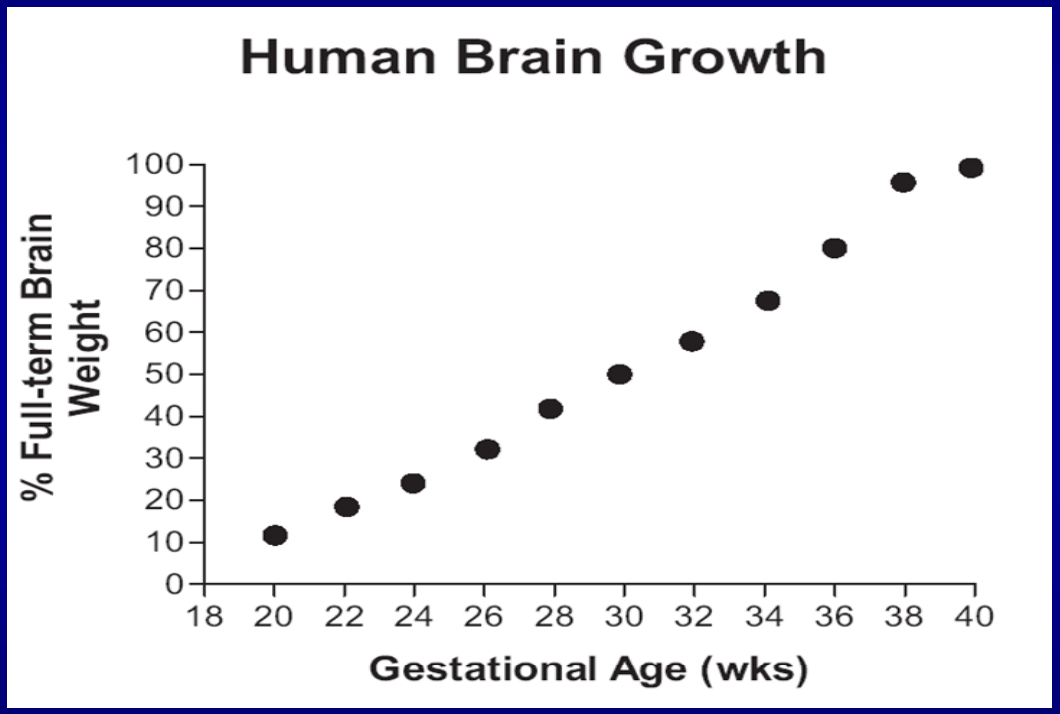
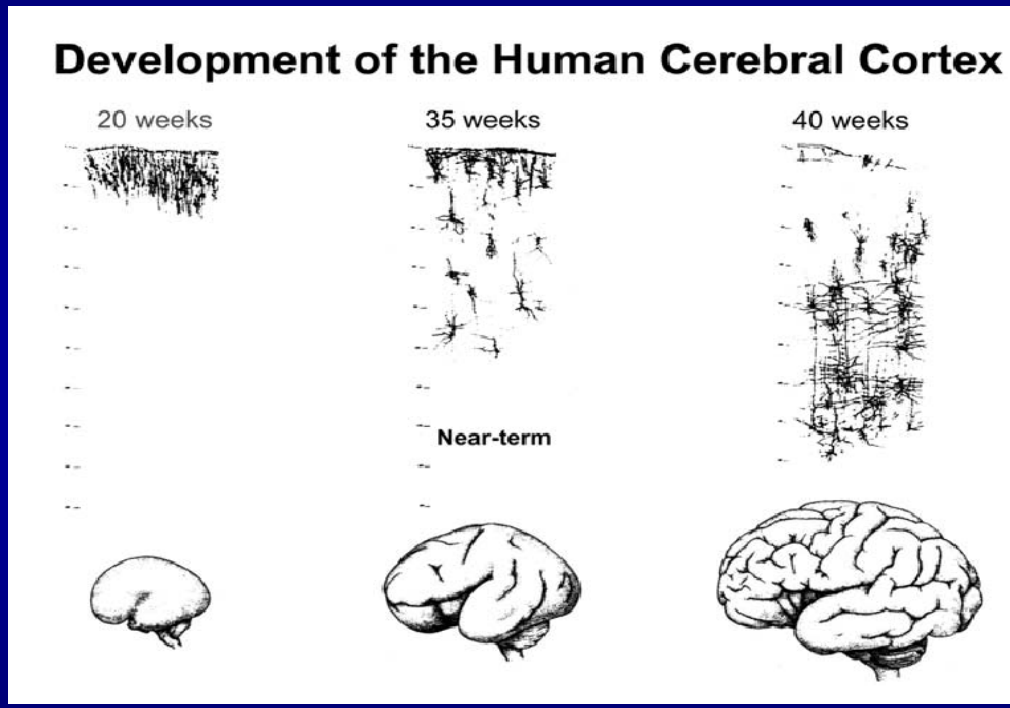
Human Brain Growth in Gestation





Kinney, 2006

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Development of the human brain through gestation

- Lower functions mature first
- Cortex is last to develop
- Brain at 35 wks weighs only 2/3 what it will weigh at term

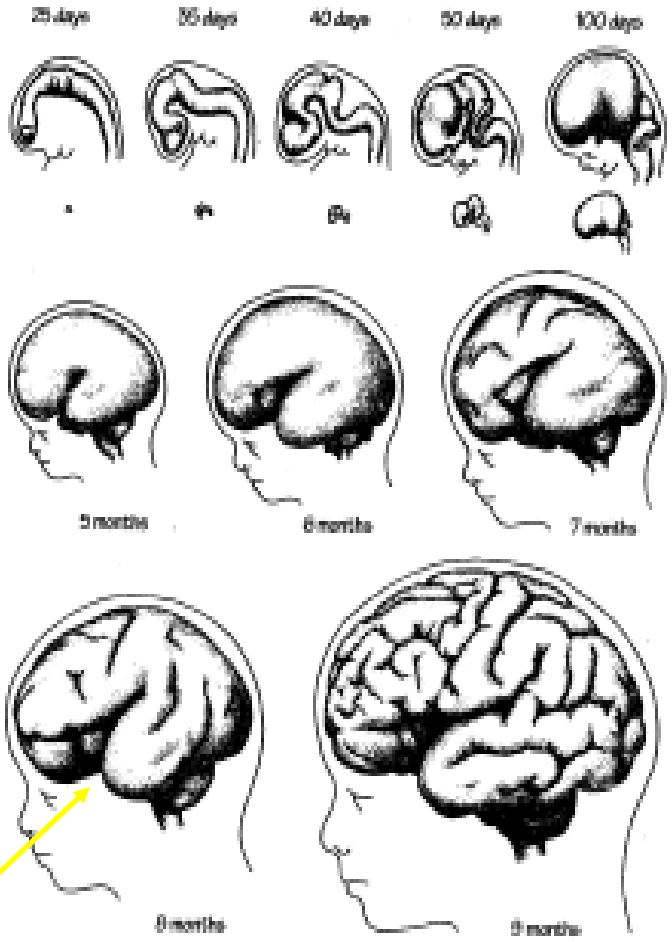


FIGURE 2-3

Prenatal growth of the brain. Drawings are enlarged to show detail between twenty-five and one hundred days postconception. Actual sizes (proportional to lower drawings) are shown in the second row.

Modified from W.M. Cowan, "The development of the brain," Scientific American, September 1979 by permission of Nature Publishing.

The Late Preterm Infant – Brain Development: Brainstem

- BRAINSTEM –

Vital Functions

  - –Respiration, rhythmic
  - –Heart rate variability
  - –Homeostatic mechanisms
  - –Sleep
  - –Coordination of suck/swallow/breathing

- Immature Control in LPTB Evidenced by
  - Periodic breathing, apnea
  - Decr HR variability
  - Immature responses to hypoxia, CO_2
  - REM sleep
  - Feeding difficulties

The Late Preterm Infant – Brain Development: Cerebellum

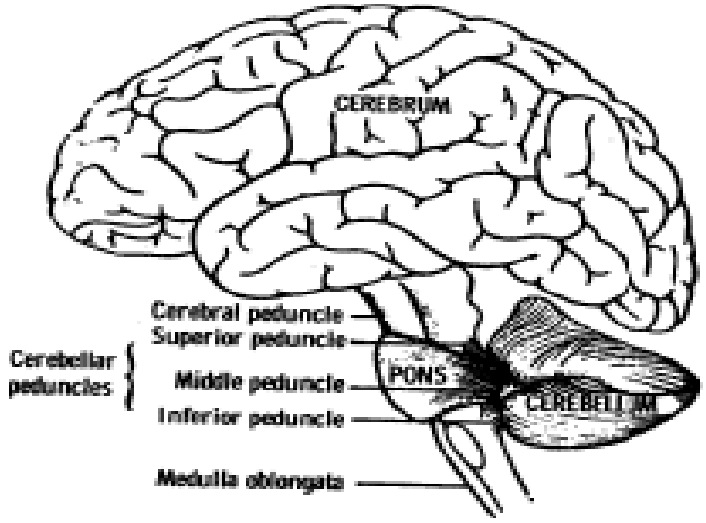


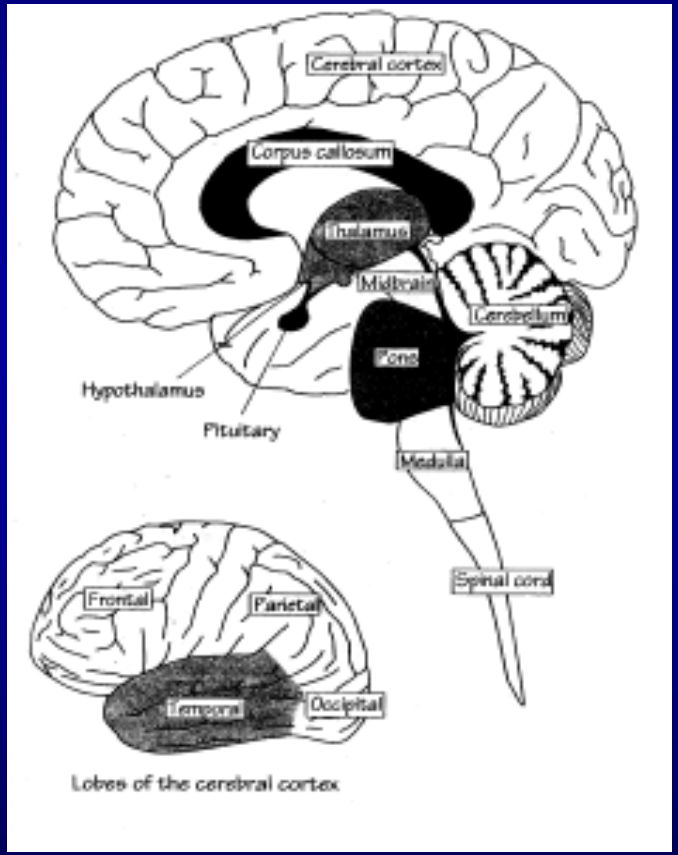
FIG 12–10. Diagrammatic representation of the principal parts of the brain. The parts are distorted to show the cerebellar peduncles and the way the cerebellum, pons, and middle peduncle form a napkin ring around the brain stem. (Reproduced, with permission, from: *Gray's Anatomy of the Human Body*, 27th ed. Goss CM [editor]. Lea & Febiger, 1959.)

CEREBELLUM

- –Volume of the cerebellum at 34 weeks is only 55% of that at term
- –Function related to
  - •Fine motor control
  - •Coordination
  - •Motor sequencing
  - •Cognition & language
  - •Social function & learning
- –PTB alters cerebellar growth and autoregulation

The Late Preterm Infant – Brain Development: Cerebral Cortex

- **CEREBRAL CORTEX Volume at 34 weeks is only 53% of term volume**
- Volume of the white matter increases 5-fold from 35-41 weeks
- **Cortex is seat of higher order functions – cognition, perception, reason, motor control**
- **Functional processing units form in columns; more surface area allows more functioning units**
- **Brain organizes during late preterm period –huge development of synapses, axon growth, dendrites, neurotransmitters**
- **Myelination does not begin in the cortex until the late preterm period**



Lobes of the cerebral cortex

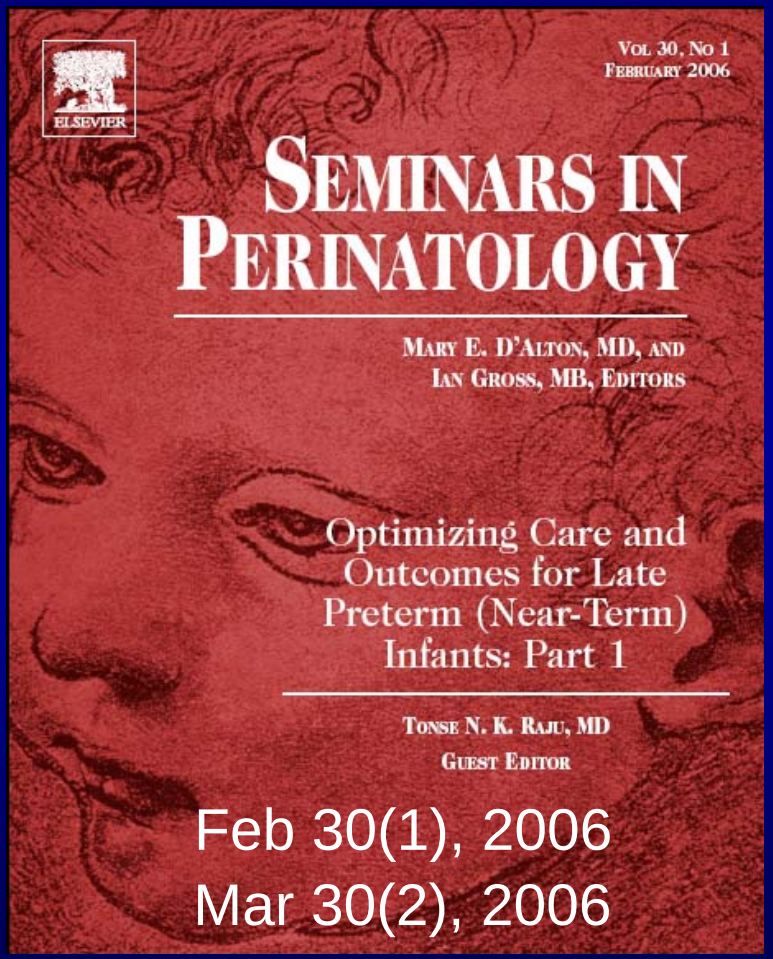
Brain Development in the Late Preterm Infant- Outcomes

- Compared to term infants, late preterm infants:
  - Are twice as likely to die of SIDS
  - Have an 80% increased risk of ADHD
  - Have a 20% risk of clinically significant behavior problems
  - Are more likely to be diagnosed with Developmental Delay in the first 3 years
  - Are more likely to be referred for special needs in pre-school
  - Are more likely to have problems with school readiness
  - Are more likely to have severe hyperbilirubinemia and neurologic consequences from it

Singletons by Birth Category

	1992	1997	2002
• Spontaneous:	68.1%	63.4%	56.8%
• PROM:	3.0%	2.7%	2.2%
• Intervention:	28.9%	33.9%	41.0%

July 2005- Invitational NICHD Workshop on Near Term/Late Preterm births (34-36 weeks)



Feb 30(1), 2006
Mar 30(2), 2006

SPECIAL ARTICLE

Optimizing Care and Outcome for Late-Preterm (Near-Term) Infants: A Summary of the Workshop Sponsored by the National Institute of Child Health and Human Development

Tonse N. K. Raju, MD[a], Rosemary D. Higgins, MD[a], Ann R. Stark, MD[b], Kenneth J. Leveno, MD[c]

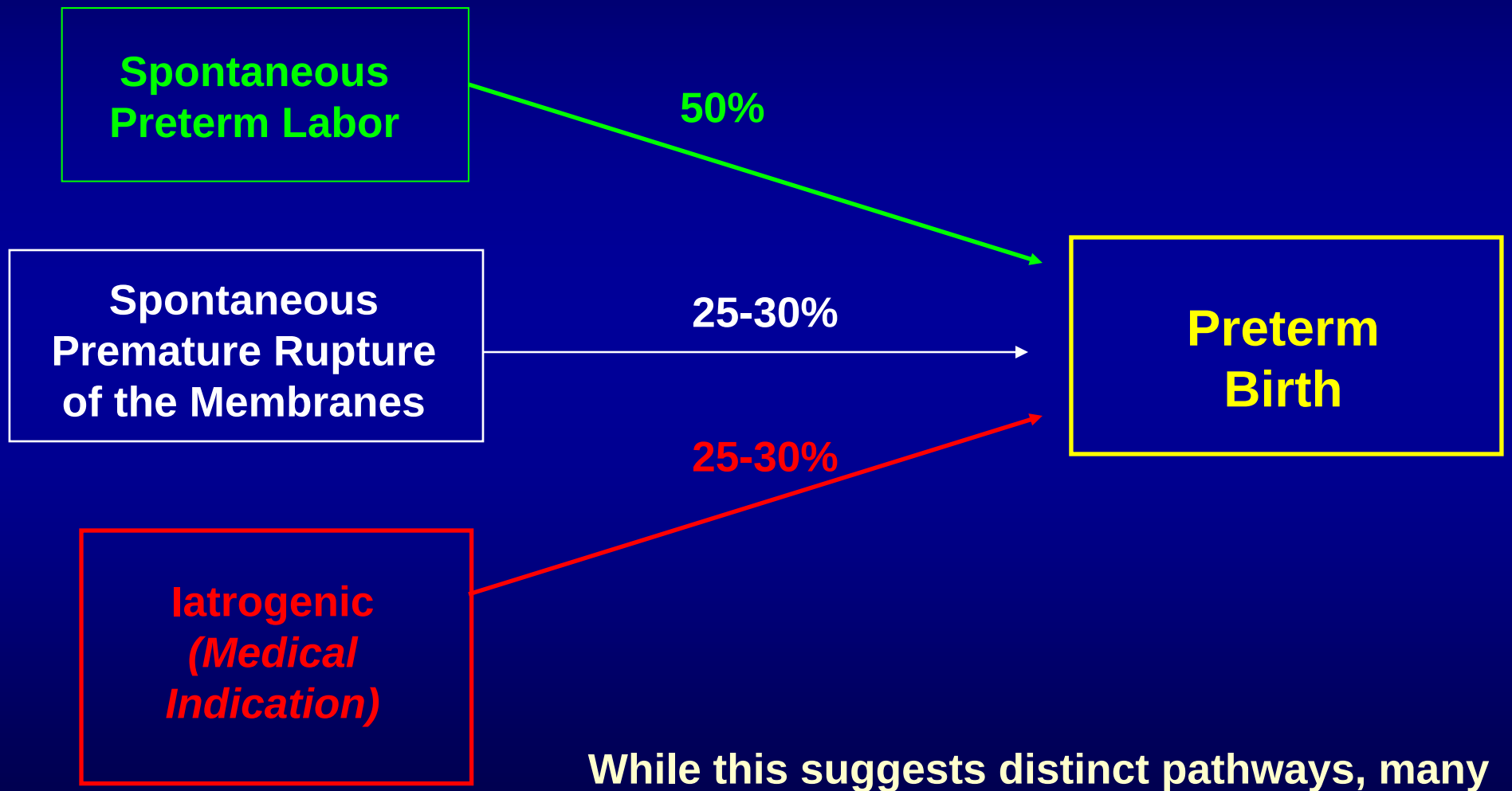
[a]National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland; [b]Division of Neonatology, Department of Pediatrics, Baylor College of Medicine, Houston, Texas; and [c]Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, Texas

The authors have indicated they have no financial relationships relevant to this article to disclose.

Peds, 118(3):1207-14, 2006

Clinics in Perinatology, Dec 2006

TYPE of Preterm Birth



While this suggests distinct pathways, many of the risk factors for all 3 are similar

Prevention of Preterm Labor, Preterm Delivery and Prematurity

- Primary prevention
  - identifying and managing risks
  - risk reduction approach and strategies to reproductive health
  - prevent PTL
- Secondary prevention
  - prevent preterm delivery
- Tertiary prevention
  - prevent/minimize complications of prematurity

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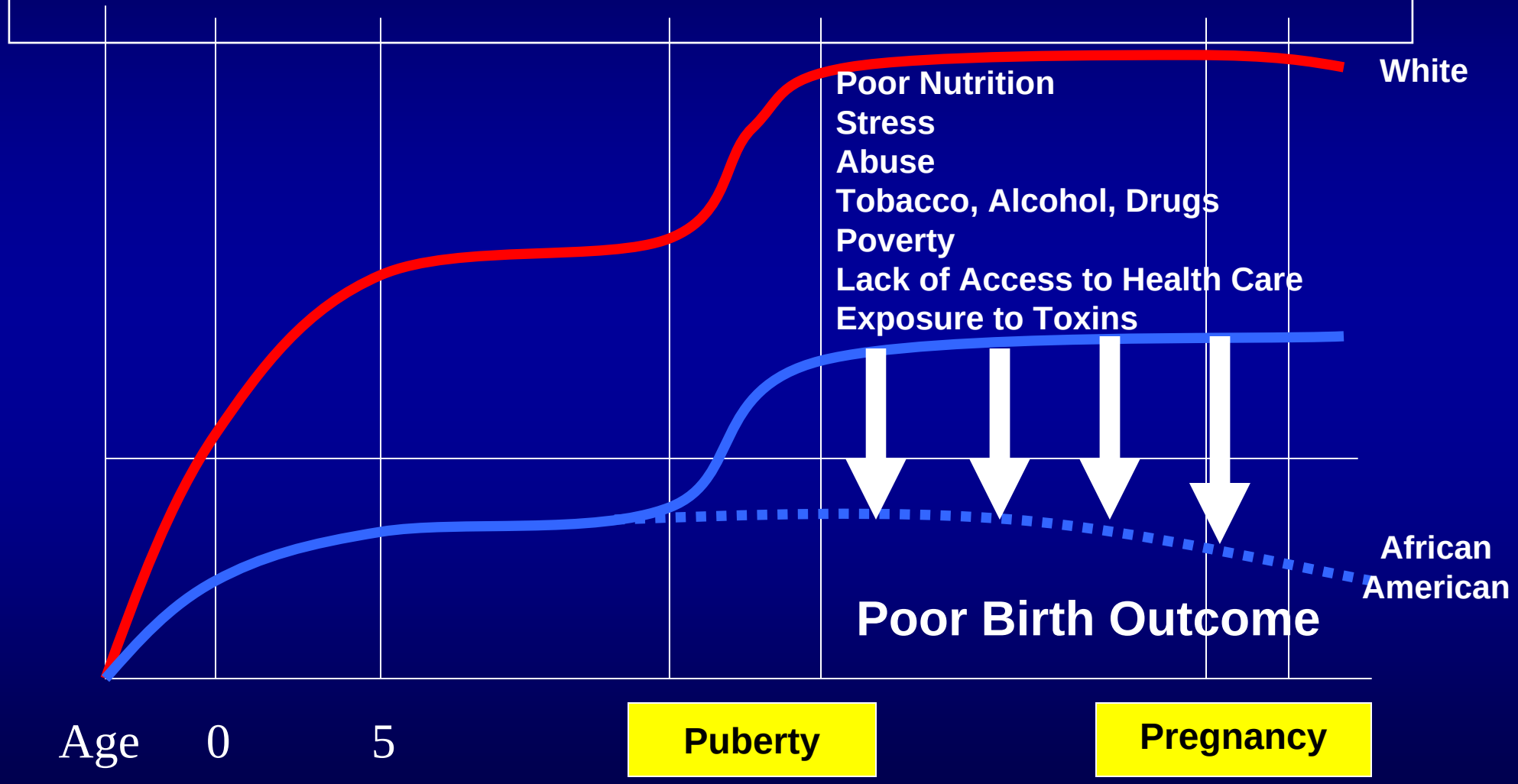
Life Course Perspective



Major Pathways to Preterm Labor

- **Inflammation/infection (ascending), 40%**
  - **cytokines**
- **Stress (maternal/fetal), 25%**
  - **CRH**
- **Bleeding (decidual hemorrhage, abruption), 25%**
  - **thrombin**
- **Stretching (uterine distention), 10%**

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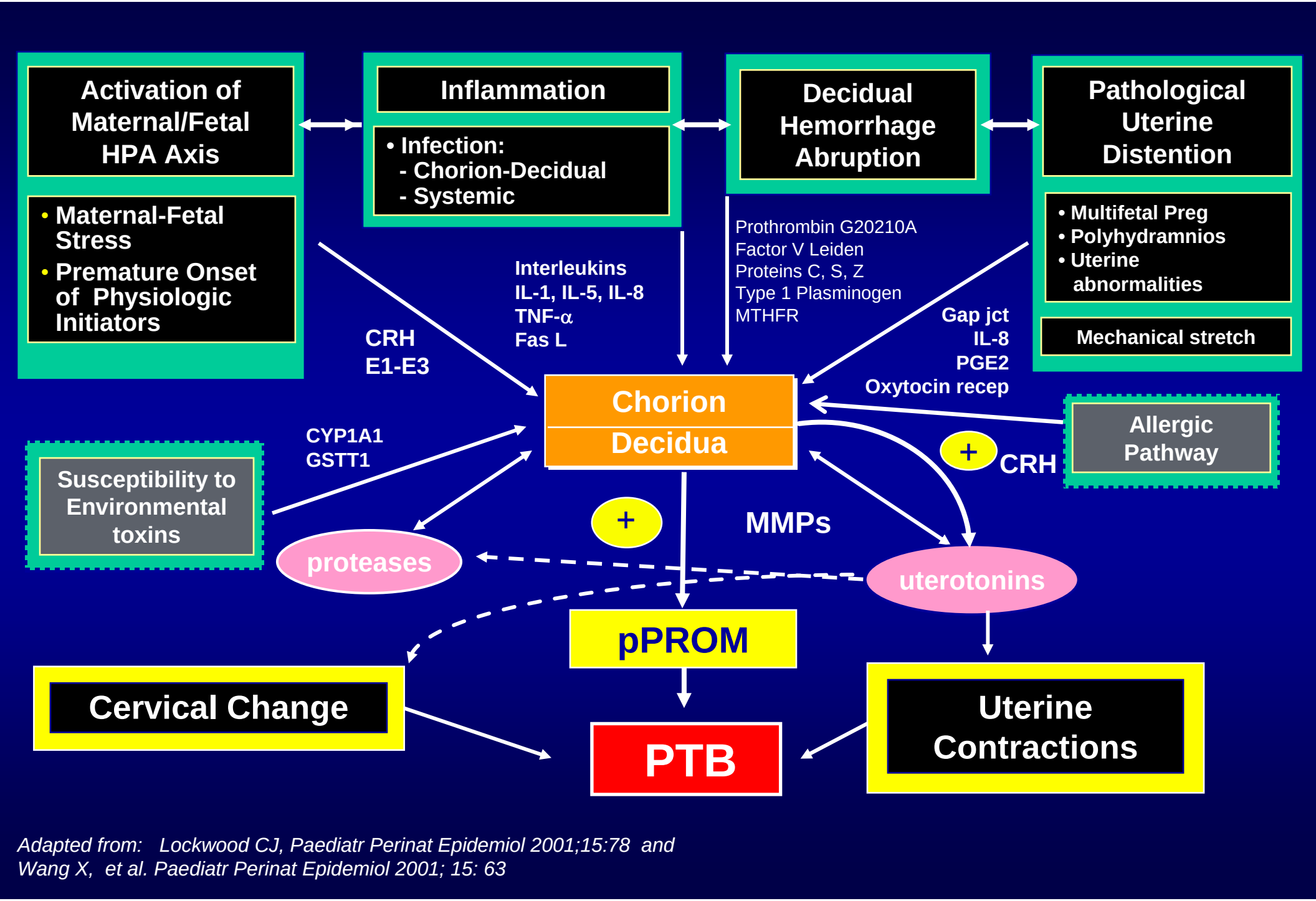

Adapted from: Lockwood CJ, Paediatr Perinat Epidemiol 2001;15:78 and Wang X, et al. Paediatr Perinat Epidemiol 2001; 15: 63

Prevent the Preventable

- Ø Unintended pregnancies
- Ø Folic acid deficiency
- Ø Alcohol
- Ø Tobacco
- Ø Illicit drugs
- Ø Infections (UTIs, STIs, periodontal disease)
- Ø Extremes of weight
- Ø Some medications (Rx, OTC, home remedies)
- Ø Environmental toxins
- Ø Known genetic/familial risks
- Ø Unnecessary interventions resulting in preterm birth
- Promote appropriate level designation and regionalization

at least--

do no harm

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