

# Research on Pregnancy Disorders

Why do we need it?

What is going on here?

Where are the resources?

Peggy Neville

February 22, 2008

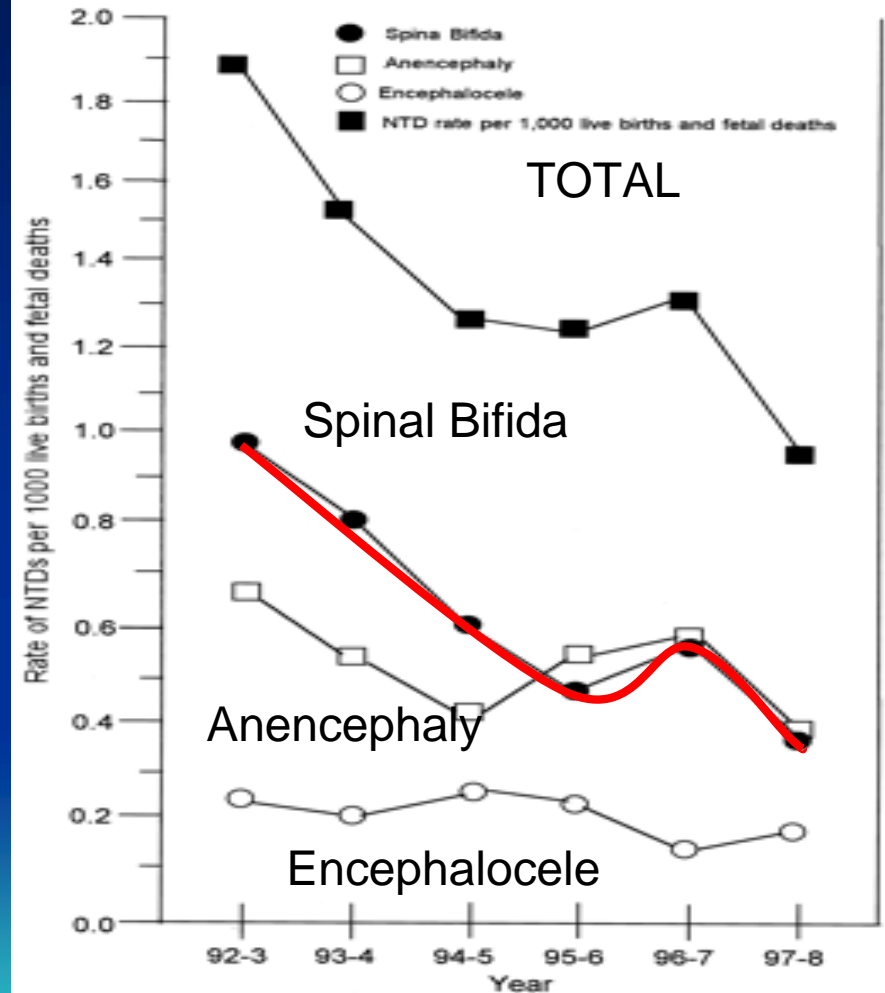
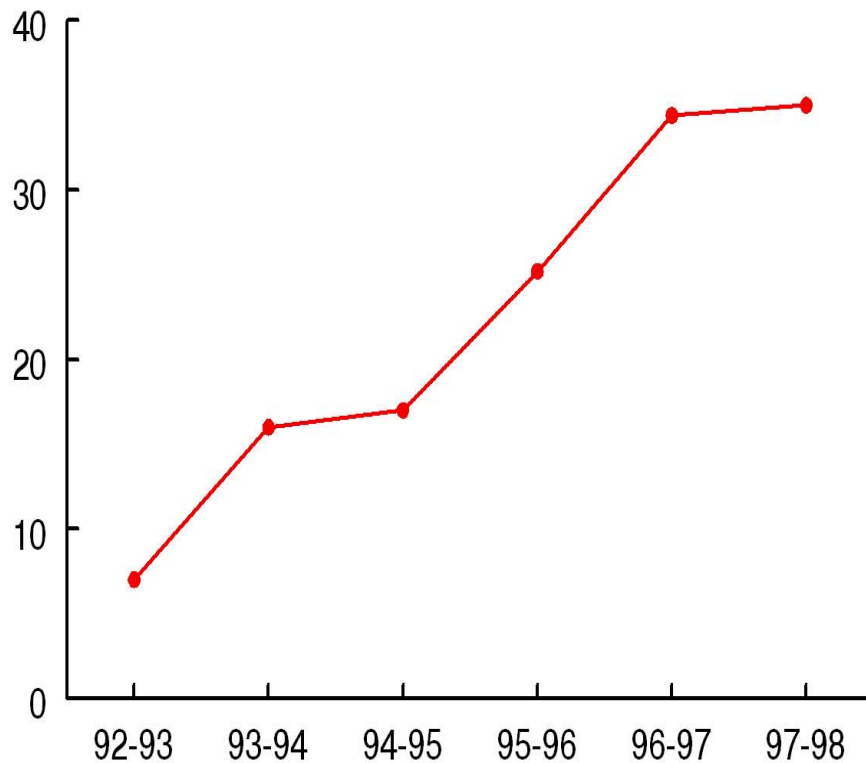


# A Success Story

- Neural tube defects (NTD, spina bifida and anencephaly) are among the most common birth defects (6/10,000).
- 1960's--understanding of relation of folic acid to anemia.
- 1964--Folic acid supplements to pregnant women seemed to decrease neural tube defects.
- 1991-- definitive epidemiological study showed that 400 micrograms a day of folic acid decreased spina bifida incidence by 70% in susceptible subjects.

# Rates of NTD in North Carolina

Prevalence of Folic Acid Use (%)  
North Carolina



# But....this success does not extend to other pregnancy problems

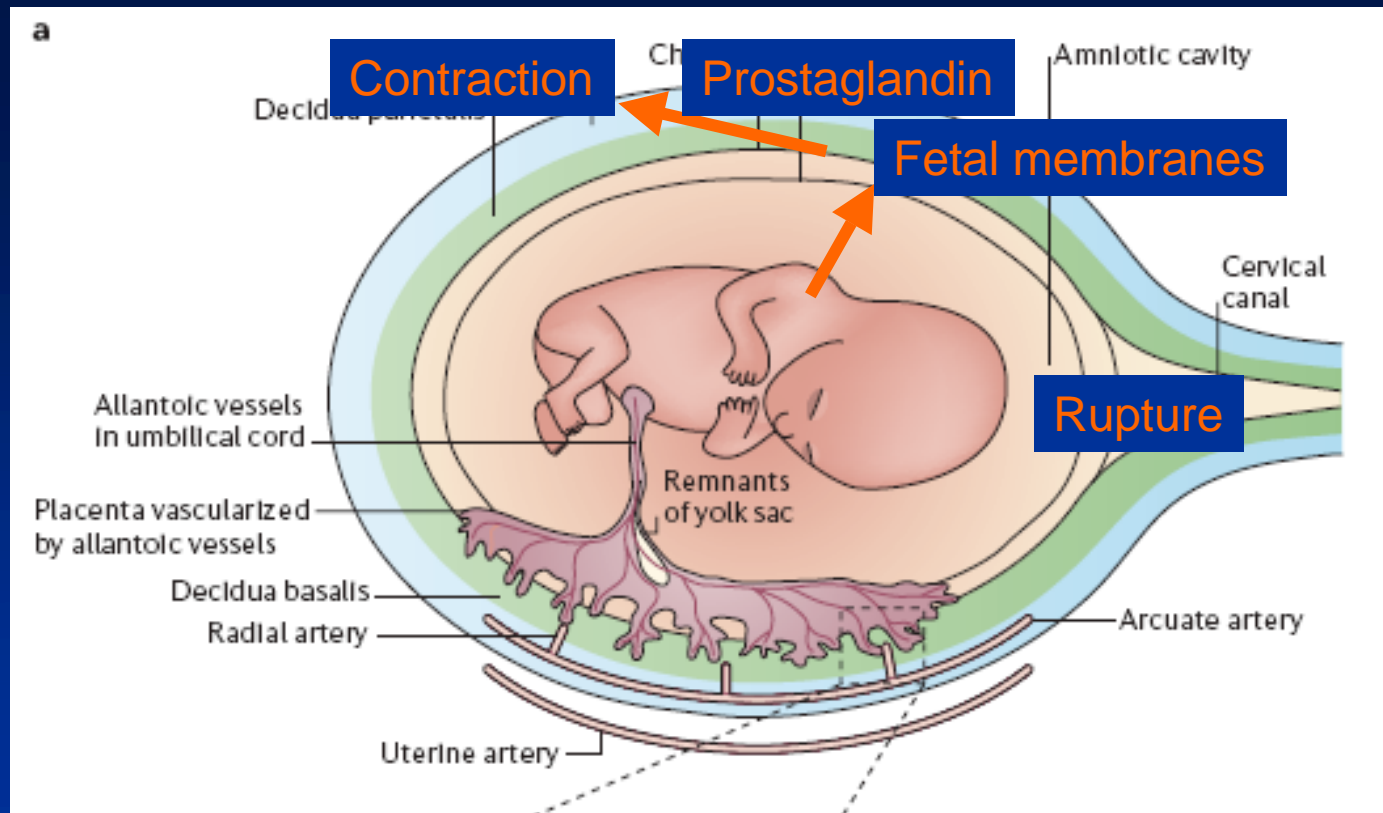
- Birth defects—4%
- Preterm birth—12.5%
  - Up from 8% 2 decades ago
- Low birth weight—8%
- Pre-eclampsia-- 5%
- Gestational diabetes—8%
  - Up from 4% a decade ago



# Major diseases of pregnancy affect about 20% of live births each year or more than 800,000 babies

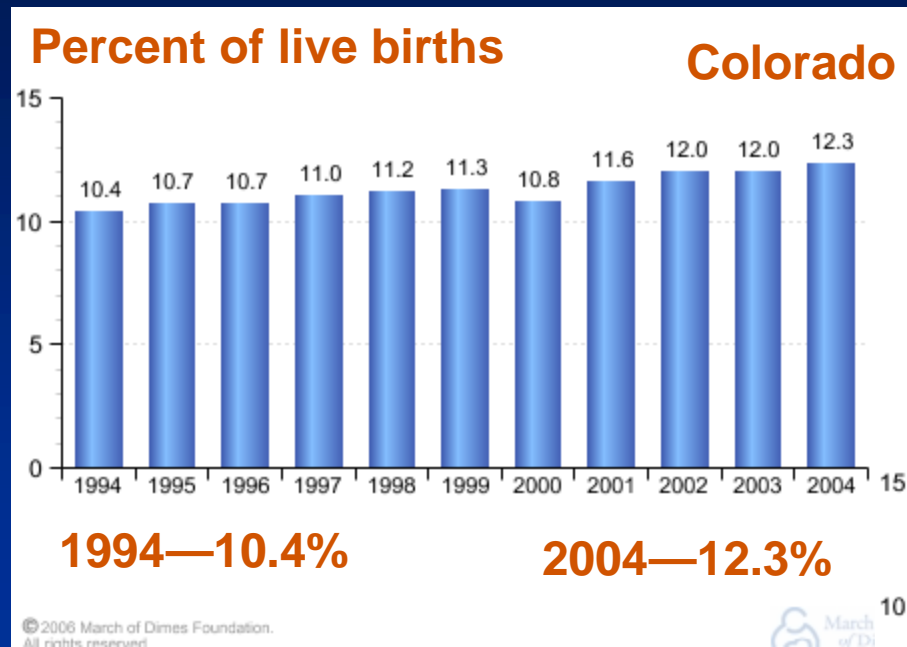
- All of these have a significant potential for long term effects on the offspring
  - Preterm birth—cerebral palsy, cognitive impairment
  - Gestational diabetes—diabetes, heart disease
- Although good data are lacking long term disability can affect up to 25% of these births or about 200,000 babies per year
- The cost for Preterm Birth alone is estimated at more than **\$26 billion** a year.



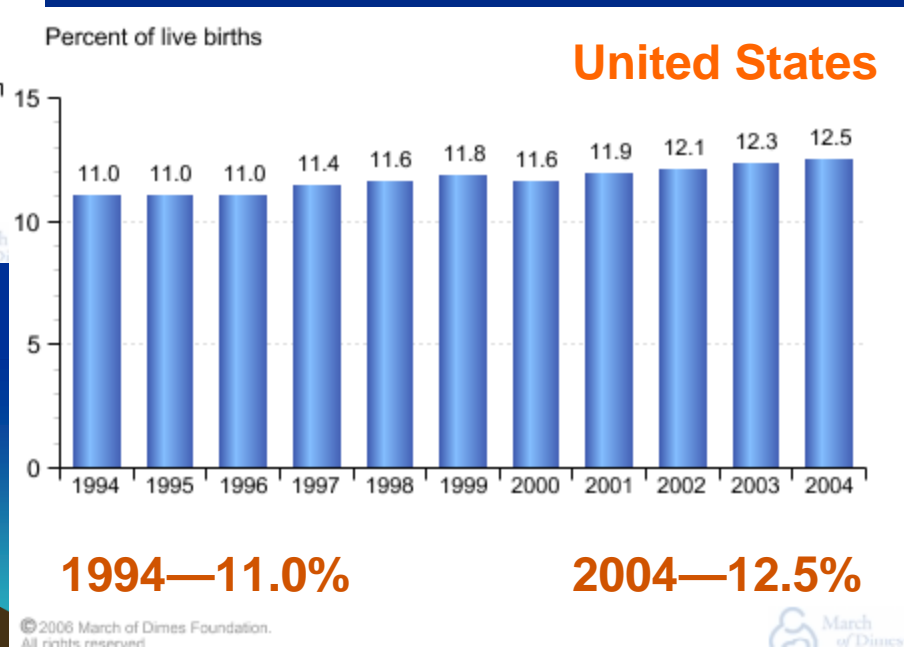


# Let's look at Preterm Birth

# Preterm Birth--Colorado



**NOTE:**  
Frequency of PTB in other developed nations is 5 – 9%



# What do we need to know?

- The biology of labor
- The risk factors that increase PTB
- Need early biomarkers so that early interventions can be designed
- Development of interventions
- Strategies for prevention

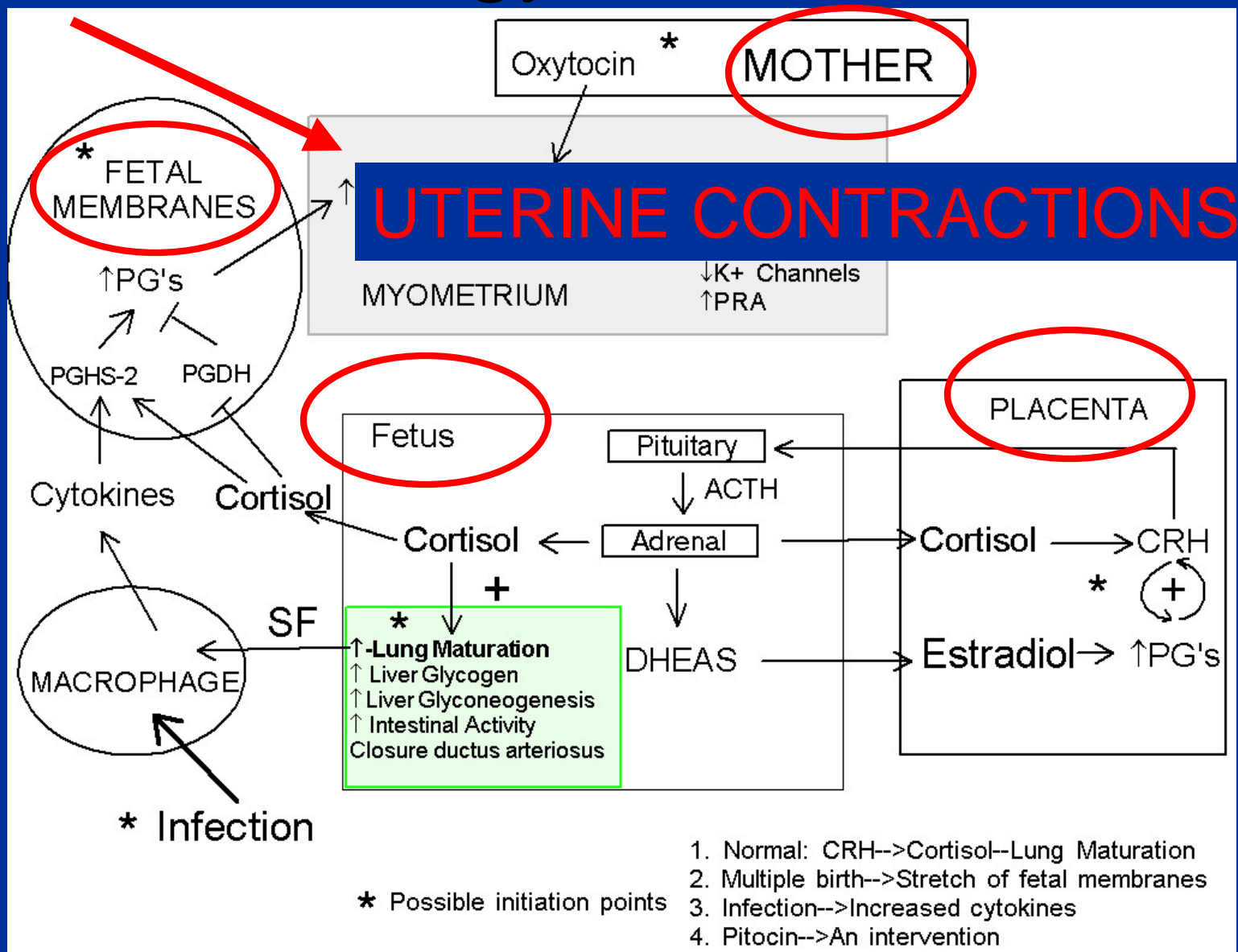


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# The Biology of Parturition

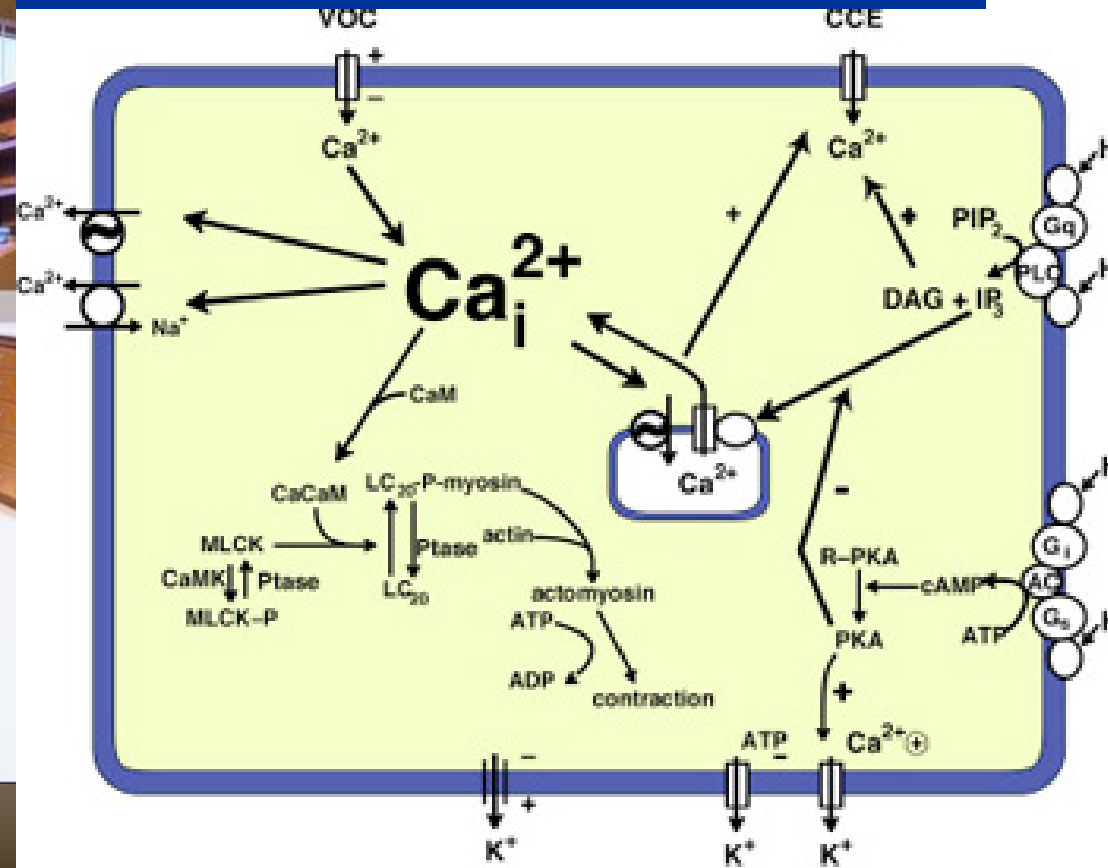


# Wet Lab Research



Dr. Barbara Sanborn, Chair, Biomedical Sciences  
College of Veterinary Medicine, CSU

## Control of uterine contraction and relaxation



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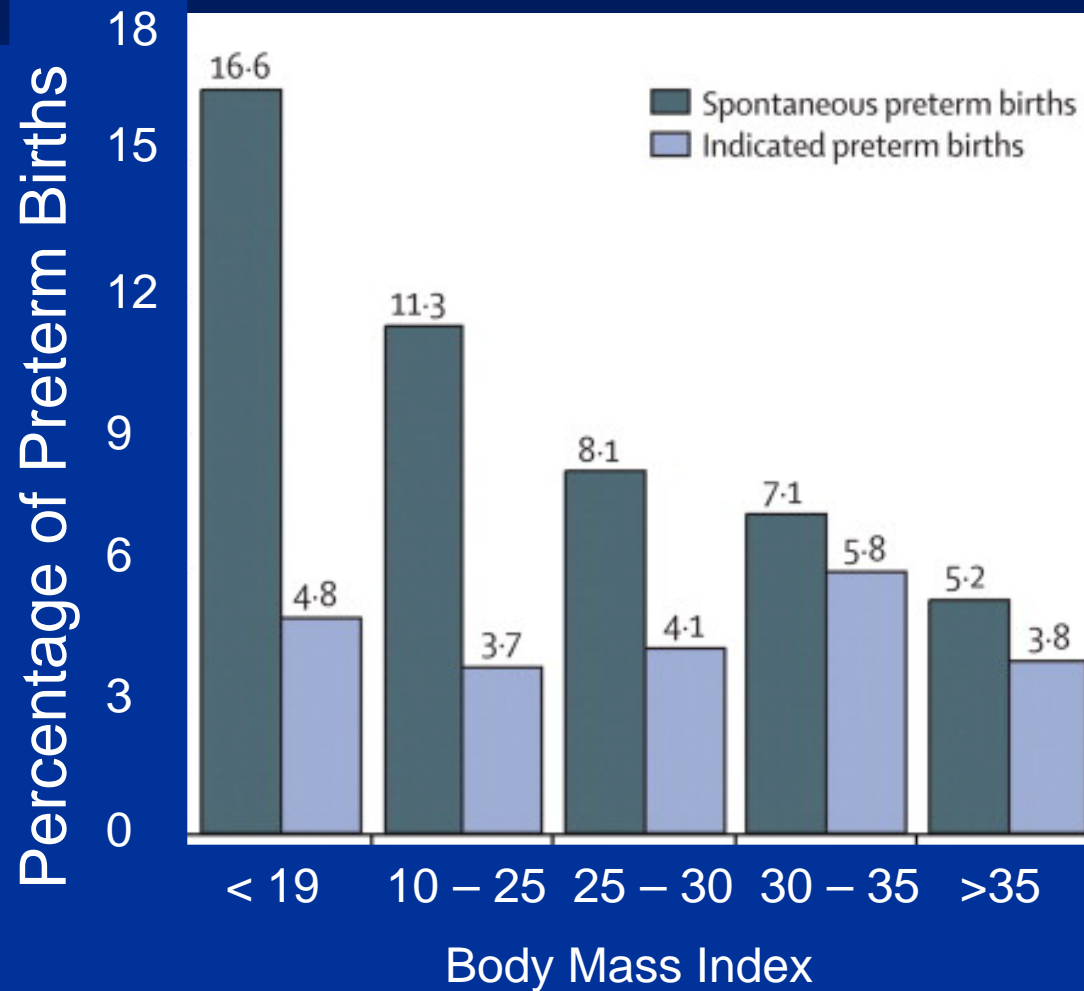


# Major Risk Factors for Preterm Labor

- Multiple Pregnancy
  - 60% of twins are born preterm
- Smoking
- Inadequate Maternal weight gain or low BMI
- Premature Rupture of Membranes
- Infection

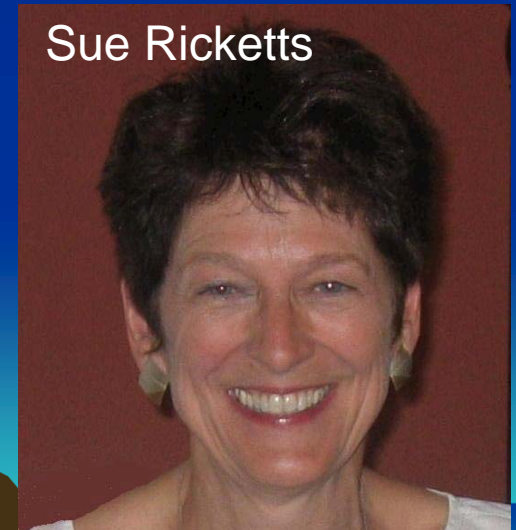


# Low BMI is a Significant Risk Factor for Preterm Labor



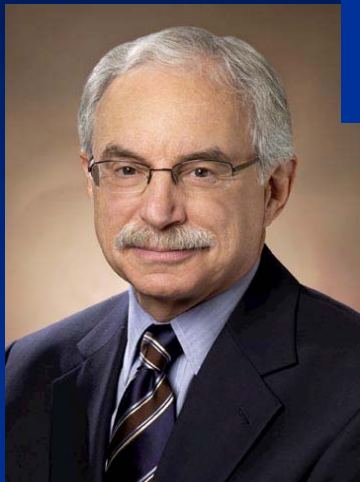
Researchers at the Colorado Department of Health and the Environment showed that low BMI and/or low weight gain in pregnancy was a significant risk factor for low birth weight.

Sue Ricketts



# Infection is a Significant Risk Factor for Preterm Labor

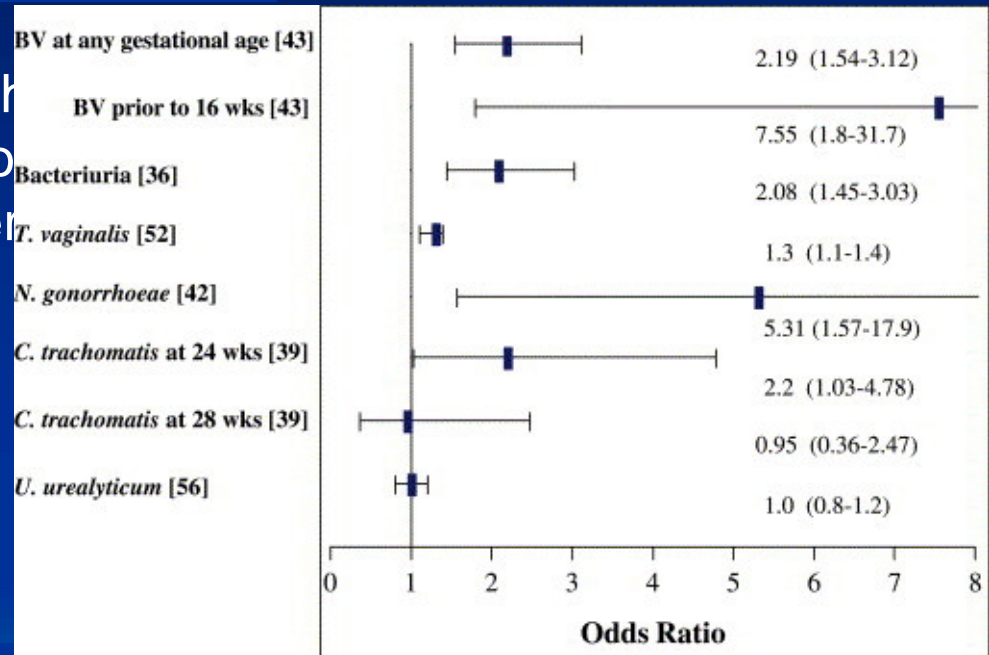
Dr. Ronald S Gibbs, Chair, OB/GYN  
UCD-School of Medicine



Studies in rabbits show that bacteria can lead to preterm labor only when given very early.

Studies in humans:

Show the same thing



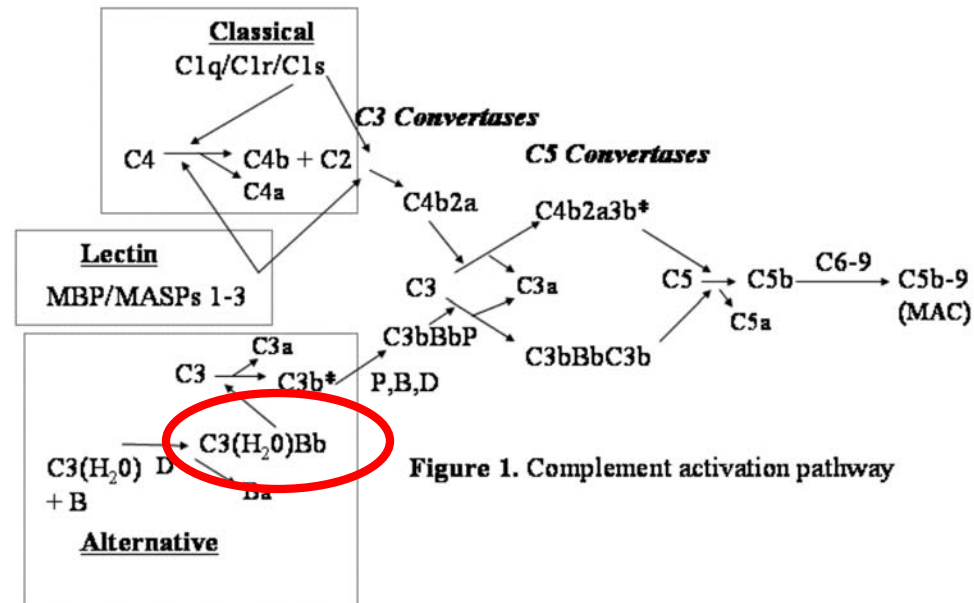
- But antibiotics given when labor is threatened do not help.
- Do they help when given early in pregnancy?

# Early biomarkers of disease would help us predict who needs intervention



Dr. Anne Lynch, Assistant Professor, Basic Reproductive Sciences OB/GYN, UCD-School of Medicine

## Complement Activation Pathway



# Early biomarkers of disease would help us predict who needs intervention



Dr. Anne Lynch, Assistant Professor, Basic Reproductive Sciences  
OB/GYN, UCD-School of Medicine

Epidemiological study on ~800 women  
Blood drawn between 10 and 20 weeks of pregnancy  
Analyzed for Activated Complement Bb

Finding: Elevated Bb predicted a 3 fold increased risk of  
PTB

Thanks to [Newborn Hope](#) for financial assistance to perform  
these assays

# Early biomarkers of disease would help us predict who needs intervention



Dr. Jim McManaman, Associate Professor, Basic Reproductive Sciences, OB/GYN, UCD-School of Medicine

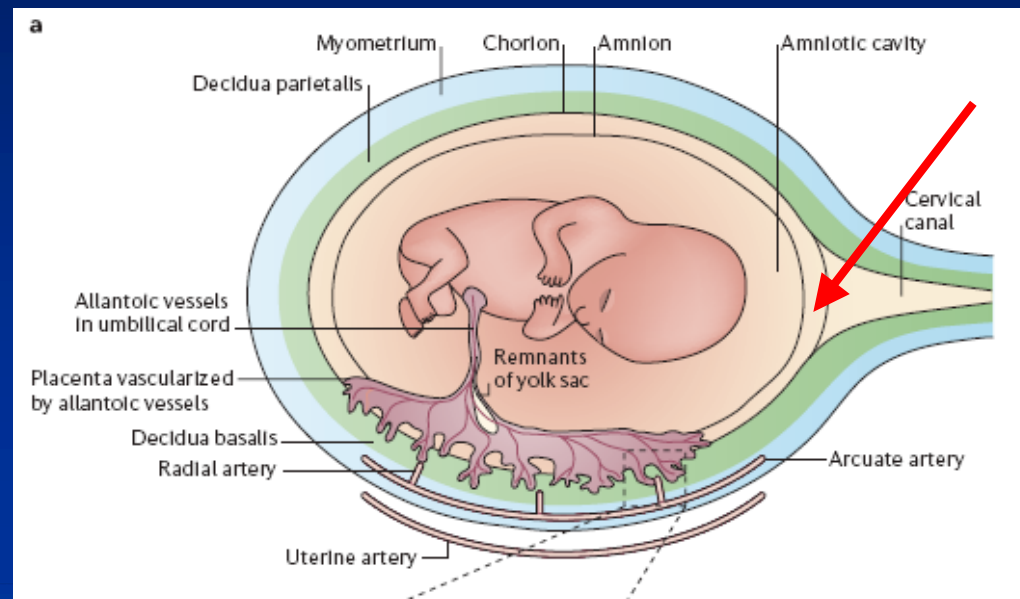
Longitudinal study of ~150 women  
Vaginal proteomics throughout pregnancy  
Expectation: inflammatory markers will be elevated in women who have preterm birth

Study supported by the **March of Dimes**

# Finally, premature rupture of fetal membranes (PPROM) often accompanies preterm birth



Dr. Ginger Ferguson, Assistant Professor, Mechanical Engineering, UC-Boulder



Question: Are the biomechanical properties of the fetal membranes different in women with PPRM?

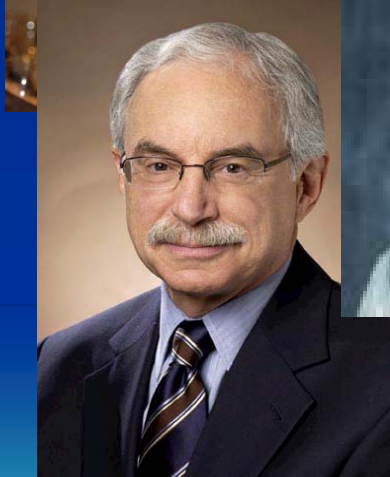
# Finally, premature rupture of fetal membranes (PPROM) often accompanies preterm birth

Question: Are the biomechanical properties of the fetal membranes different in women with PPRM?

Dr. Ginger Ferguson, Assistant Professor,  
Mechanical Engineering, UC-Boulder

**“We need to understand what leads to early structural failure”**

Grant submitted to the **Butcher Foundation**



# Other Active Research Areas

- The Placenta



Virginia Winn, MD/PhD  
OB/GYN, UCD-SOM



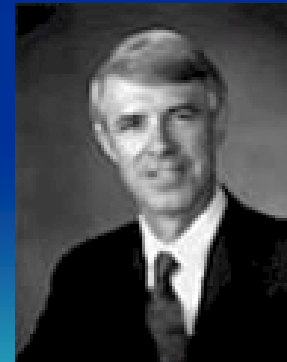
Henry Galan, MD  
OB/GYN, UCD-SOM



Lorraine Dugoff, MD  
OB/GYN, UCD-SOM



Russ Anthony, PhD  
Biomedical Sciences  
CSU



Bill Hay, MD  
Pediatrics, UCD-SOM

Henry Galan, MD  
OB/GYN, UCD-SOM

# Other Active Research Areas

- Diabetic Pregnancy



Lynn Barbour, MD/ MsPH  
OB/GYN and Medicine  
UCD-SOM



Jed Friedman, PhD  
Pediatrics, UCD-SOM

Dana Dabelea, MD  
Epidemiology  
UCD-School of Public Health

# Other Active Research Areas



Lee Niswender, PhD  
Pediatrics  
Birth Defects



Jess Tyler, PhD  
Molecular Genetics  
Genetics of Birth Defects

Patti Thureen, MD  
Pediatrics, UCD-SOM  
Neonatal nutrition

# In Sum...

- Problems of pregnancy are complex and multifactorial
- There are more questions than answers at the moment
- Teams will have to work together to answer these questions
- Increased research funding will be necessary



# Economic and Societal Impact

- Excess hospital costs for PTB in the US were estimated as ~\$18 billion in 2005.
- Special education costs, lifelong loss of productivity, and increased susceptibility to adult diseases such as cardiovascular disease and diabetes increase the economic impact of PTB and low birth weight several fold.



# Cost to Business

- Direct health care costs to employers for a premature baby average \$41,610 —15 times higher than the \$2,830 for a healthy, full-term delivery.
- Additional costs to employers in lost productivity average \$2,766.
  - [http://www.marchofdimes.com/prematurity/15341\\_15349.as](http://www.marchofdimes.com/prematurity/15341_15349.as)
- Average additional cost to employer per premature birth vs. full-term birth (when mother is an employee)  
**\$41,546**
- In 2002, approximately \$7.4 billion in hospital charges for premature infants, almost half the U.S. total, were billed to employers and other private insurers (5).
- These estimates do not include the cost of long-term disability of the child.

# NIH Funding for Prematurity compared to Funding for Cancer Research

- All cancers:
  - 1.35 million new cases/year
  - NCI funding is \$2.1 billion
  - Research funding \$1555/case
- Breast cancer
  - 200,000 new cases/year
  - 1800 NIH grants in 2007 at \$300,000 / grant
  - Research funding \$2700/case
- Prematurity
  - 400,000 preterm births per year
  - 104 grants in 2007 at \$300,000/grant
  - Research funding is < \$100/case

# SUMMARY

- Preterm birth and low birth weight are significant societal problems
- We have a poor understanding of how to prevent these increasingly prevalent conditions.
- Very inadequate funding for research
  - MOD provides excellent small grants for start-up programs.
  - CDC is fostering a program on healthy preconception weight
  - NIH funded about 100 grants for causes and prevention of preterm birth in 2007 (1871 grants for breast cancer, a condition with similar prevalence, were funded in 2005)

# THE BOTTOM LINE

If we are to make a dent in the serious life long consequences of preterm birth and other adverse pregnancy outcomes, we must, as a society, foster much more research

