

## THE OB-PEDS INTERFACE: “GOT ISSUES?”

George J. Gilson, M.D.  
Loma Linda University  
March 2009

## Faculty Disclosure

- I have no relevant financial relationships with the manufacturer(s) or any commercial product(s) and/or provider of commercial services discussed in this CME activity.
- I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

## THE OB-PEDS INTERFACE OBJECTIVES

- > PPROM: What gestational age to deliver?
- > GBS: Where does controversy remain?
- > Antenatal Corticosteroids: Should you repeat the course?
- > Meconium: To suction or not to suction?
- > Oxygen: Does it really help resuscitation?
- > Apgars: What do they really mean?
- > Cord clamping: Early vs. late?

## PPROM:

### What gestational age to deliver?

- The longer the latent period, the more mature the baby, and the less time and effort it will require in the nursery.
- Versus*
- The longer the latent period, the more likely that infection will occur, and that the baby will have a longer LOS.

## PPROM: When to deliver? What does the evidence show?

- Mercer (1993) - RCT @ 32-36 wks (n=93)
- | Management:         | Expectant | vs. | active |
|---------------------|-----------|-----|--------|
| • Latency (hrs)     | 36        |     | 14*    |
| • Chorio (%)        | 28        |     | 11*    |
| • Suspect sepsis(%) | 60        |     | 28*    |
| • Confirmed sepsis  | 4.3       |     | 6.8    |
| • Antibx tx (%)     | 79        |     | 35*    |
| • Home w/mom(%)     | 4         |     | 30*    |

## PPROM: When to deliver Incidence of IRDS

- 28 weeks 65%
- 30 wks 50%
- 32 weeks 40%
- 34 weeks 13%\*
- 35 weeks 7%\*
- 36 weeks <1%\*

\* majority needed suppl O2, 1.3% ventilator

## PPROM: When to deliver?

- As-Sanie (2003)-CCS @34-36 wks (n=1544)
- Non-pulmonary morbidity if no IRDS?

	IRDS (n=75)	Controls
NICU admit (%)	100	36*
PDA	8.1	1.3
IVH	6.8	1.3
NEC	0	0
Confirmed sepsis	0	0

## PPROM: When to deliver?

- As-Sanie (2003)-CCS@34-36 wks (n=1544)
- Non-pulmonary morbidity if no IRDS?

	IRDS (n=75)	Controls
Hyperbili-UVL(%)	57	29*
Hypoglyc-OGT	45	21*
Hypothermia	98	57*
Apnea/brady	30	5*

## PPROM: When to deliver?

- (3) smaller studies: (n=485) @ 32-36 wks
- Expectant vs. active management:
- More chorio and longer maternal LOS
- More sepsis and suspected sepsis
- Latency: 10%>48 hrs, 2.5%>7days
- Incidence of IRDS: 1.5-13%
- Cut off for IRDS and infant LOS: 34 wks

## PPROM: When to deliver?

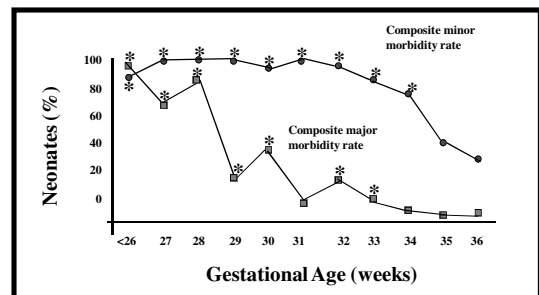
- Leiman (2005) –retrospective (n=430):
- Latency: 3.3 ± 6.8 days overall
- No improvement in either major or minor neonatal morbidity after 34 weeks
- Both maternal and neonatal LOS longer after 34 weeks with expectant management

## PPROM: When to deliver?

### At 34 weeks (n=58):

- IRDS 5.2%
- IVH 1.7%
- NEC 0
- Sepsis 1.7%
- Hyperbili-UVL 72%
- Hypoglyc-OGT 8.6%
- LOS 8.1 ± 5.8 days

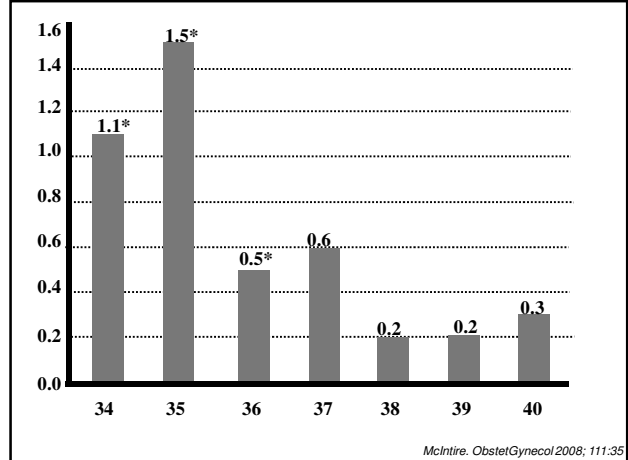
## PPROM: When to deliver?



Lieman. Preterm PROM and Neonatal Morbidity. Obstet Gynecol 2005.

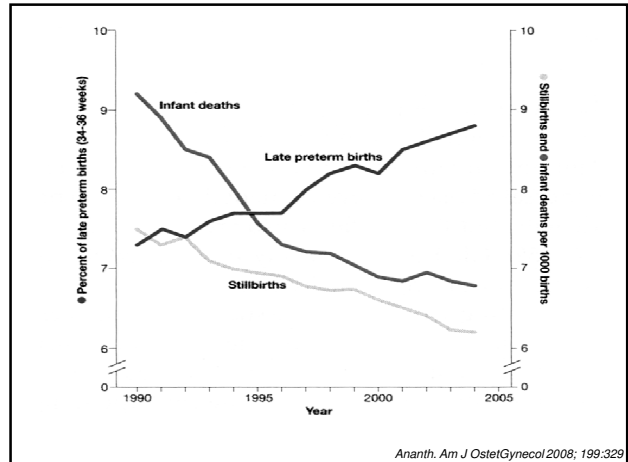
## LATE PRETERM BIRTHS: Mortality Compared to Term

- McIntyre –OG 2008-(n= 21,771)
- Late preterm = 34, 35, 36 wks
- 76% of all preterm births
- Neonatal mortality:
  - 34 wks 1.1/1000
  - 35 wks 1.5/1000
  - 36 wks 0.5/1000
  - 39 wks 0.2/1000\*



## LATE PRETERM BIRTHS: Morbidity Compared to Term

- McIntyre- OG 2008-(n=21,771):
- 
- 
- IRDS (vent) 3.3 1.7 0.8 0.3 %\*
- Sepsis (cult+) 0.5 0.4 0.2 0.1 %\*
- Phototherapy 6.1 3.5 2.0 1.0\* %
- IVH (gr 3-4) 0 1 1 3
- NEC 3 1 1 1\*
- \*Bottom line: there is a difference, but it is small
- If you don't need to deliver early, don't!



## GBS: Remaining Controversies

### Alaska GBS EONS 2000-2004:

- 21 cases (incidence: 0.42/1000)
- (Pre-1996 guidelines incidence = 1-2/1000)
- 8/21 mothers had an indication for IAP:
  - 3 preventable (2 no abx, 1 wrong abx)
- 13/21 mothers did not have an indication:
  - 9 preventable (not screened...)
  - 5 mothers delivered in <4 hours...

## GBS Controversies: IAP for elective cesarean?

### NO:

- Ramus et al (1998) n=3590 elective C/S
- 20% carrier rate
- Attack rate = 0 (95% CI-0.0-0.7%)
- No benefits to IAP if NIL and no ROM

**GBS Controversies:  
How about PPROM and PTL?**

YES (initially):

- Culture and treat x 48 hrs
- If GBS (-): stop abx, no IAP when in labor
- If GBS (+): may continue abx x 5-7 d, but will need IAP when in labor
- If GBS (-) and more than 5 wks until labor, repeat the culture and tx if now (+) (5%+)

**GBS Controversies:  
What about PCN allergy?**

- 15% of GBS are resistant to clindamycin
- 21% of GBS are resistant to erythromycin
- Always request sensitivities if allergic
- Cefazolin if no hx anaphylaxis
- Vancomycin if hx anaphylaxis
- To date no reports of resistant GBS

**GBS Controversies:  
Indications for IAP**

- Prior GBS affected infant
- GBS bacteriuria during this pregnancy
- Positive GBS culture 35-37 wks
- Unknown GBS status AND:
  - Delivery <37 wks
  - ROM >18 hrs
  - Temp >100.4 in labor

**GBS Controversies:  
IAP NOT indicated**

- GBS (+) in a prior pregnancy
- GBS (-) and SROM x >18 hours
- GBS (-) and fever in labor
- Planned cesarean (NIL, I-BOW)
- GBS (-) at 35-37 wks this pg (despite having a risk factor)

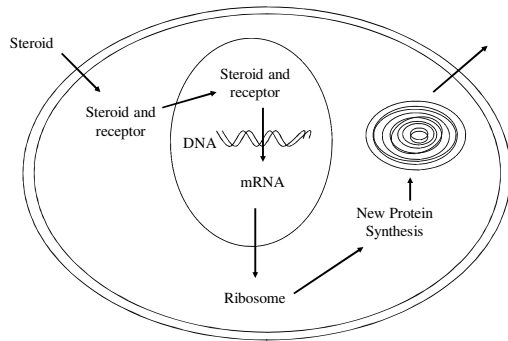
**GBS:  
Newborn Management after IAP**

- Maternal chorio or signs of NN sepsis:  
Full diagnostic evaluation:  
-CBC, BC, CXR, LP
- GA <35 wks –or- IAP for <4 hrs:  
Limited diagnostic evaluation:  
-CBC, BC, 48 hr obs
- IAP for >4 hrs:  
No eval, no tx, 48 hr (24 hr?) observation

**Antenatal Corticosteroids:  
A Single Course REALLY Works!**

<u>Single Course</u>	<u>OR</u>	<u>CI</u>
• Reduction in IRDS	0.49	(.41-.60)
• “ “ IRDS after 7 d*	0.69	(.50-.94)
• “ “ Neonatal death	0.59	(.47-.75)
• “ “ IVH	0.45	(.21-.97)
• “ “ NEC	0.37	(.17-.69)
• “ “ Neuro abn	0.61	(.34-1.08)

## Steroids: Mechanism of Action



## Antenatal Corticosteroids: REPEAT Courses: Is More Better?

- Meta-analysis of 8 observational studies:
- Aghajafari – 2001: n=1682 (24-34 wks):
  - Reduction in IRDS OR=.79\*
  - Reduction in PDA OR=.56\*
  - No difference in IVH, NEC, sepsis, NND
  - Trend to increased BPD OR=1.30
  - Selection bias

## Antenatal Corticosteroids: Repeat Courses: Is More Better?

### Retrospective studies of multiple courses:

- Thorp (2002): n=14,338 (23-34 wks)  
Decrease in BWt (63g) and HC (3.1mm)
- French (2004): n=541 (23-32 wks→6 y/o)  
Decrease in IVH and PVL: OR=.40\*  
Decrease in CP (n=22): OR=.31\*  
Increase in ADD (n=31): OR=2.39

## Antenatal Corticosteroids: Repeat Courses: Is more better?

- 3 RCT: n=561
- Guinn (2001): n=502 (23-32 wks)
- No difference in composite outcome of IRDS, BPD, IVH, PVL, NEC, NND
- OR=.80 (CI: .59-1.10)
- No difference in BWt or HC
- Insufficient evidence to recommend

## Antenatal Corticosteroids: Repeat Courses: Is More Better?

- ACOG Committee Opinion – 2008:
- A single course of steroids between 24-34 wks is the standard of care
- Insufficient data regarding safety and efficacy to recommend repeated courses
- Need more RCT (currently 3 in progress)
- “If a little is good, more may NOT be any better”

## Meconium Happens!

- Meconium happens in 7-22% of all births
- Meconium happens >30% in postterm birth
- MAS occurs in 2/1000 births (8% postterm)
- Meconium is found below the cords in 21-58% of births thru mec stained fluid
- Only 5-10% of infants with mec below the cords will develop MAS

### Meconium Happens What are the risk factors for MAS?

- NOT correlated w/ decels, low pH, 5 min Apgar or other markers of acute hypoxia
- IS correlated w/ oligo, elevated cord EPO, postmaturity, muscularization of the pulmonary arterioles (chronic hypoxia)
- Fetal breathing vs. fetal gasping (>pCO<sub>2</sub>)
- MAS is the result of in-utero gasping

### Meconium Happens Is MAS Preventable?

AMNIOINFUSION: YES?

Pierce – OG 2000

- Meta-analysis: 13 studies (n=1,924):
- Reduced MAS (8.5 vs 2.5%) OR=.30\*
- “mec below cords (23% vs 5%) OR=.18\*
- “acidemia (25% vs 12%) OR=.42\*
- “cesarean (19% vs 24%) OR=.74

### Meconium Happens Is MAS Preventable?

- AMNIOINFUSION: NO
- Fraser – NEJM Sept 2005
- International multi-center RCT(n=1,998)

	<u>Amnioinfusion</u>	<u>Control</u>	
• MAS	4.5%	3.1%	NS
• NND	0.5	0.5	NS
• C/S	32	29	NS

- Does a large RCT trump a meta-analysis?

### Meconium Happens Is MAS Preventable?

- AMNIOINFUSION: NO
- Xu – BJOG 2007 – 15 trials (n= 4,070)
- Amnioinfusion vs. Control
- MAS RR = 0.59 (.28-1.25)
- Apgar<7 RR = 0.90 (.58-1.41)
- Cesarean RR = 0.89 (.73-1.10)
- Conclusion: the evidence does not support

### Meconium Happens Is MAS Preventable?

ORO-PHARYNGEAL SUCTIONING: “MAYBE”

- YES: Wiswell (2000) - RCT - n=2094  
Reduced MAS (8.5 vs. 2.7%)
- NO: Vain (2004) – RCT - n=2514  
No reduction in MAS (4 vs 3.8%)  
“ “ mech vent (2 vs 1%)  
“ “ NN death (0.7 vs 0.3%)

### Meconium Happens Is MAS Preventable?

Tracheal suctioning: NO

- Meta-analysis of 4 RCT (2000) n=2,884  
No decrease in MAS (2.5 vs 2.0%)  
No decrease in NN death (0.3 vs 0.1%)  
No decrease in pulm prob (3.8 vs.4.5%)
- 3.8% incidence of stridor, bradycardia, etc in the *intubated* infants....

## Meconium Happens Recommendations

- Amnioinfusion in the presence of meconium and decels may be helpful
- Oropharyngeal suctioning may be helpful, and is not harmful
- Tracheal suctioning is not indicated in vigorous infants, and may or may not be helpful in depressed infants
- (Inducing labor at 41 wks is probably the biggest factor in reducing MAS and PNM as meconium is probably aspirated before presentation...)

"THE ENEMY OF GOOD IS BETTER!"

## When should we clamp the cord?

- Animal evidence: the "barker foal"
- Women in developing nations normally squat (gravity) and delay cord clamping
- When is clamping "early" vs. "late"?
- Is there a difference in term vs. preterm?
- What are the concerns?

## When should we clamp the cord?

- Why is "stat" clamping current practice?
- Concerns:
  - hyperbilirubinemia
  - polycythemia
- Desire to obtain cord blood for gases
- Desire to minimize PPH
- Pediatricians want to begin immediate resuscitation

## When should we clamp the cord? Full-term Infants

Hutton - JAMA (2007) – 15 RCT (n=1912)

	Early	Late	RR
Hematocrit (%)	54	59*	
Ferritin (ug/L)	56	74*	
Anemia (at 2 mos)			0.53*
Polycythemia(>65%)			3.82*
Jaundice			1.35
Phototherapy			1.78

Conclusion: The only benefit to late clamping is less anemia, but there were downsides...

## When should we clamp the cord? Full-term Infants

- Cochrane (2008)-11 RCT (n=2989):
- Early vs. Late                      RR
- RDS    1.01
- Jaundice/UVL                              0.59\*
- Polycythemia (>65%)                  0.40
- Anemia (at 2 mos)                        -0.3g/dL\*
- Ferritin (' ')                                +17.9 ug/L\*
- Conclusion: "mixed benefits"

## When should we clamp the cord? Preterm Infants

- Mercer – (2001) 9 RCT (N=531)
- Improved mean BP
- Higher hematocrit
- Fewer transfusions
- Less need for ventilation and supplemental O2
- No difference in hyperbilirubinemia

## When should we clamp the cord? Preterm Infants

- Rabe (2008) 10 RCT (n=454)
- Improved early cardiovascular stability w/ less need for pressors
- Increase in hematocrit
- Less need for transfusion
- Lower incidence of IVH

## When should we clamp the cord? CONCLUSIONS

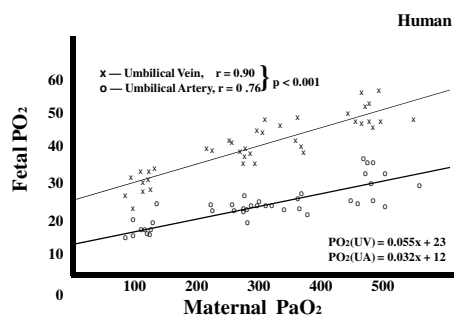
- In term infants at risk of nutritional anemia, delayed cord clamping is advantageous
- Infants with IUGR or IDDM are at risk of hyperviscosity and hyperbilirubinemia, and should have *early* cord clamping
- Rh(-) mothers will have less FMH if cord clamping is delayed
- Preterm infants will have improved CNS oxygenation and less need for transfusion if delayed cord clamping is practiced
- "WAIT 'A MINUTE'!"

## Perinatal Resuscitation Is Room Air or 100% O2 Best?

- Does O2 actually help?
- Might O2 actually be harmful?
- Availability and cost in rural settings
- Some thoughts about:
  - pO2
  - O2 saturation (SaO2)
  - O2 content (CaO2)
  - O2 delivery (DO2)

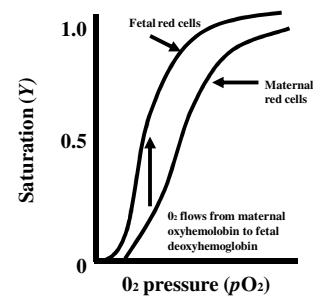
## Perinatal Resuscitation Room Air or 100% O2?

- pO2 = concentration of O2 x tot pressure
- SaO2 = O2 combined w/ Hb x 100
- CaO2 = 1.39 x Hb x O2 sat/100 + .003 pO2
- DO2 = CO (Hb x O2 sat/100)
- CO = HR x SV
- Ventilation responds to pO2
- O2 delivery depends on CaO2

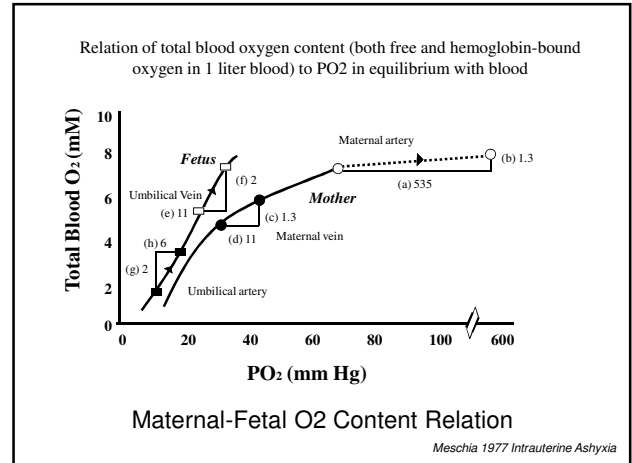
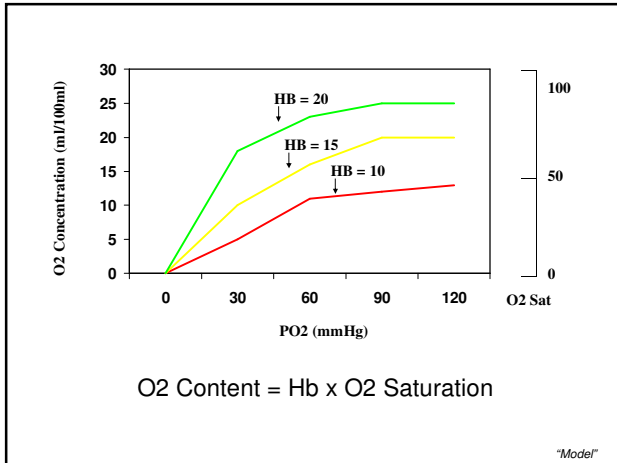


Maternal-Fetal pO2 Relationship

Ramanathan Anesth Analg 1982; 63:69



Maternal-Fetal O2 Saturation Relation



### In-Utero Resuscitation Room Air or 100% O<sub>2</sub>?

- Cochrane – 2005
- No trials of O<sub>2</sub> for fetal distress
- 2 RCT of prophylactic O<sub>2</sub> in normal labor
- Abnormal cord pH (<7.2) more frequent in the O<sub>2</sub> group (RR=3.51, CI 1.34-9.19)
- O<sub>2</sub> may cause placental vasoconstriction
- Conclusion: the evidence does not support the use of O<sub>2</sub> in labor....

### Neonatal Resuscitation Room Air or 100% O<sub>2</sub>?

- Davis (2004) meta-analysis (n=1302):
- Infants still cyanotic and bradycardic switched to O<sub>2</sub> at 90 sec (intent to tx)
- Room air group: decreased NN mortality RR=0.71 (CI .54-.94)
- No difference in incidence of HIE
- No difference in neuro disability at 24 mos
- Conclusions: insufficient evidence....

### Neonatal Resuscitation Room Air or 100% O<sub>2</sub>?

- Saugstad (2005) meta-analysis (n=881):
- Neonatal mortality favors room air: OR=0.57 (CI .42-.78)
- HR at 90 sec, Apgar score at 5 min, and time to 1<sup>st</sup> breath all significantly better in the room air group
- Hypoxia-reperfusion injury?

### Use and Abuse of the Apgar Score

- Apgar (1953): a scoring system for estimating the probability of newborn survival
- Apgar (1958): use of the scoring system for evaluating the need for newborn resuscitation
- The Apgar score is not intended to be a predictor of neurologic development
- The Apgar score is not intended to be a marker of newborn asphyxia

## Use and Abuse of the Apgar Score

- AAP and ACOG Statements - 1996
- Asphyxia: a combination of hypoxemia and acidemia in the peripartum period resulting in acute neurologic injury.
- Infants should demonstrate:
  - Metabolic or mixed acidemia (pH<7.00)
  - Apgar 0-3 at >5 minutes
  - CNS sx (sz, coma, hypotonia)
  - Multiorgan dysfunction (CV, GI, renal, heme)

## Use and Abuse of the Apgar Score

### Use of Umbilical Cord Gases:

	pH	pCO <sub>2</sub>	BE
• Metabolic acidosis	<7.20	<65	>-12
• Respiratory acidosis	<7.20	>65	<-12
• Mixed acidosis	<7.20	>65	>-12

## Use and Abuse of the Apgar Score

- Correlation of Apgar<7 at 5' and pH<7.20:
- Thorp (1996) (n=1924)
- pH <7.2 in infant w/ Apgar <7 at 5' → 14%
  - most infants w/ low Apgars have good pH
- pH <7.2 in a “depressed” infant → 78%
  - low pH is predictive of true depression
- pH <7.2 in a vigorous infant → 2%
  - there are false positives

## Use and Abuse of the Apgar Score

### Apgar score and later neurologic disability:

- Nelson (1981) (n=49,000)  
n=99 Apgar 0-3 at 10 min studied at 7 y/o:
  - 12% had CP, of whom 11% IQ<50, 6% sz
  - 8% other (non-CP) neuro disability
  - 80% free of major handicap

## Use and Abuse of the Apgar Score

### pH and later neurologic disability:

- Nagel (1995) n=1614:
- 30 had pH<7.0 and studied at 3 y/o:
  - all went to the NICU, 28 survived
  - 10% mild hypotonia
  - 3.5% mild developmental delay

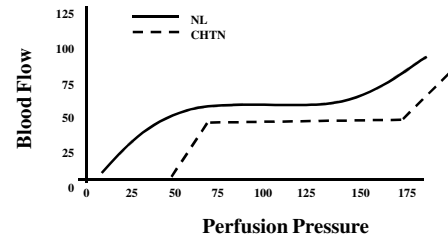
## Use and Abuse of the Apgar Score

### Conclusions:

- Neither Apgar score nor pH predicts future neurologic outcome well
- If you get out of the NICU w/o a major problem you do pretty well
- Pessimism in counseling parents is unwarranted
- Hopefully the lawyers won't be in touch...

## The OB-Peds Interface Got More Issues?

- Maternal medications and breast feeding
- Circumcision (should we be doing it?)
- NSAIDs as tocolytics (NN adverse effects?)
- Hypoglycemia in IDDM (best prevention?)
- Tobacco use: do neonates have withdrawal?
- What else??



JCI 1991; 6: 76