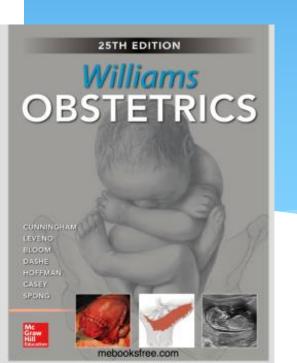
# 安胎病人的照顧及生產時機之選擇



第一版**20200303** 陳宇軒醫師/林啟康醫師

# 課程目標

PGY	UGY
知識: 1.足月生產、早產及流產之定義 2.早期破水 3.子宮頸閉鎖不全 4.安胎藥物之選擇 5.孕期風險及生產時機之選擇 6.生產方式之選擇 7.早產高風險病人之預防	
技能:	

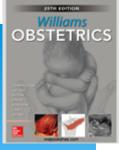
#### 足月生產、早產及流產

流產	Abortion	Before 20 wks	
早產	Preterm	20 0/7-36 6/7	
	Late preterm	34 0/7-36 6/7	
足月產	Early term	37 0/7-38 6/7	
	Term	39 0/7-40 6/7	Fetal motality mobility 最低
過期妊娠	Late term	41 0/7-41 6/7	
	Post term	42 0/7	

#### Preterm labor

- \* Between 20 <sup>0/7</sup> weeks of gestation and 36 <sup>6/7</sup> weeks of gestation
- \* Approximately 12% of all live births occur before term
- \* Clinical criteria of regular uterine contractions accompanied by a change in cervical dilation(2cm), effacement(80%)
- \* Preterm uterine contraction
- \* Threaten preterm delivery

- \* Gestation age: preterm/term/post term
- \* Size:
  - \* Low birthweight 1500-2500g
  - \* very low birthweight 1000-1500g
  - \* extreme low birthweight <1000g
- \* Small for gestation age(<10% for gestation age)

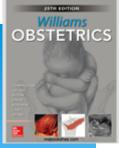


#### Mortality

- Preterm births account for approximately 70% of neonatal deaths
- \* After achieving a birthweight of ≥1000 g or a gestational age of 28 weeks for females, or 30 weeks for males, survival rates reach 95 percent

		Ge	stational Age (wk			)
Outcome	22	23	24	25	26	Total
Liveborn infants (no.)	51	101	144	205	206	707
Survived to 1 year (%)	10	53	67	82	85	70
Percent disabled <sup>a</sup>						
No disability	0	30	34	44	49	42
Mild	40	19	33	29	34	31
Moderate	20	30	21	17	10	16
Severe	40	21	13	10	7	11

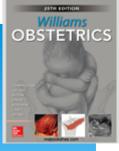
<sup>a</sup>Percentage with disability at 2½ years corrected age. The overall rate of disabilities includes performance on the Bayley III assessments, mental development delay, cerebral palsy, and visual and hearing disabilities.



## Morbidity

\* Newborns born before 37 weeks suffer various morbidities, largely due to organ system immaturity

Organ or System	Short-Term Problems	Long-Term Problems
Pulmonary	Respiratory distress syndrome, air leak, bronchopulmonary dysplasia, apnea of prematurity	Bronchopulmonary dysplasia, reactive airway disease, asthma
Gastrointestinal or nutritional	Hyperbilirubinemia, feeding intolerance, necrotizing enterocolitis, growth failure	Failure to thrive, short-bowel syndrome, cholestasis
Immunological	Hospital-acquired infection, immune deficiency, perinatal infection	Respiratory syncytial virus infection, bronchiolitis
Central nervous system	Intraventricular hemorrhage, periventricular leukomalacia, hydrocephalus	Cerebral palsy, hydrocephalus, cerebral atrophy, neurodevelopmental delay, hearing loss
Ophthalmological	Retinopathy of prematurity	Blindness, retinal detachment, myopia, strabismus
Cardiovascular	Hypotension, patent ductus arteriosus, pulmonary hypertension	Pulmonary hypertension, hypertension in adulthood
Renal	Water and electrolyte imbalance, acid-base disturbances	Hypertension in adulthood
Hematological	latrogenic anemia, need for frequent transfusions, anemia of prematurity	
Endocrinological	Hypoglycemia, transiently low thyroxine levels, cortisol deficiency	Impaired glucose regulation, increased insulin resistance



#### Threshold of Viability

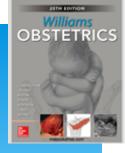
\* The threshold of viability lies between 20 and 26 weeks' destation (William obs 25ed)

	-	Gestational Age (wk)					
Outcome	22	23	24	25	26	Total	
Liveborn infants (no.)	51	101	144	205	206	707	
Survived to 1 year (%)	10	53	67	82	85	70	
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Severe	40	21	13	10	7	11	

<sup>a</sup>Percentage with disability at 2½ years corrected age. The overall rate of disabilities includes performance on the Bayley III assessments, mental development delay, cerebral palsy, and visual and hearing disabilities.

Data from Data

Data from Serenius F, Källén K, Blennow M, et al: Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden, JAMA 2013 May 1;309(17):1810–1820.



# Clinical Management

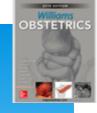
- \* All recommended after 24weeks
- \* Considered 23 0/7- 6/7
- Only antibiotic for PPROM was suggest below 23 0/7

	<22 Weeks	22 Weeks	23 Weeks	24 Weeks+
Neonatal assessment for resuscitation	Not recommended	Consider	Consider	Recommended
Corticosteroid therapy	Not recommended	Not recommended	Consider	Recommended
Magnesium sulfate neuroprotection	Not recommended	Not recommended	Consider	Recommended
Tocolysis	Not recommended	Not recommended	Consider	Recommended
Antimicrobial therapy for PPROM	Consider	Consider	Consider	Recommended
Continuous EFM	Not recommended	Not recommended	Consider	Recommended
GBS prophylaxis	Not recommended	Not recommended	Consider	Recommended
Cesarean delivery for fetal indication	Not recommended	Not recommended	Consider	Recommended
Aggressive resuscitation	Comfort care only	Not recommended unless considered potentially viable	Consider	Recommended

EFM = electronic fetal monitoring; GBS = group B streptococcus; PPROM = preterm premature rupture of membranes. Data from the American College of Obstetricians and Gynecologists, 2017e; Raju, 2014.

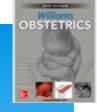
#### Cesarean section or Vagina delivery

- \* In a study of 2906 singletons between 24 0/7 and 31 6/7 weeks, neonatal mortality rates did not differ compared with those associated with planned cesarean delivery(Reddy, 2012).
- \* Analyzed 20,231 newborns delivered at 24 to 34 weeks. Cesarean delivery did not protect against poor outcomes such as neonatal death (Werner and colleagues 2013)
- \* The Obstetric Care Consensus proposes that cesarean delivery be considered for fetal indications at 23 0/7 to 24 6/7 weeks



# Cesarean section or Vagina delivery

\* In our institution( Parkland Hospital), traditional fetal indications for cesarean delivery are practiced in women at 25 0/7 weeks or beyond. Cesarean delivery is not offered for fetal indications before 24 0/7 weeks. At 24 0/7 weeks, cesarean delivery is not offered unless fetal weight is estimated at 750 g or greater. Aggressive obstetrical management is practiced in cases of growth restriction, wherein gestational age is used to guide management rather than fetal size.

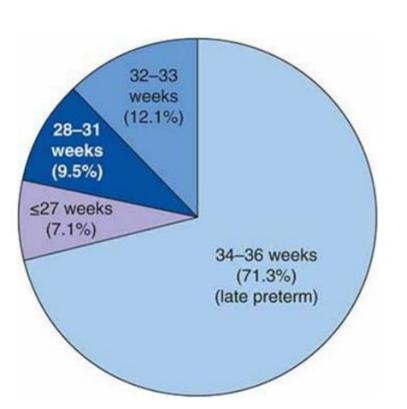


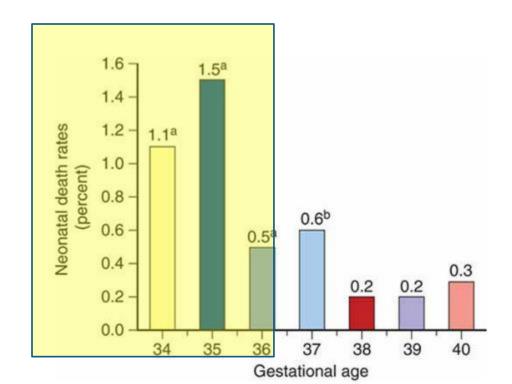
#### cause

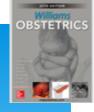
- \* (1) spontaneous unexplained preterm labor with intact membranes (include twins and higher-order multifetal births) 40-45%
- (2) idiopathic preterm premature rupture of membranes (PPROM), 30-35%
- \* (3) delivery for maternal or fetal indications 20%



# Late preterm delivery







# Late preterm delivery

**TABLE 42-5.** Neonatal Morbidity Rates at Parkland Hospital in Live Births Delivered Late Preterm Compared with 39 Weeks

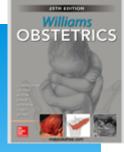
		Preterm Births				
Morbidity <sup>a</sup>	34 Weeks n = 3498	35 Weeks n = 6571	36 Weeks n = 11,702	39 Weeks n = 84,747		
Respiratory distress						
Ventilator	116 (3.3)b	109 (1.7) <sup>b</sup>	89 (0.8) <sup>b</sup>	275 (0.3)		
Transient tachypnea	85 (2.4) <sup>b</sup>	103 (1.6)b	130 (1.1) <sup>b</sup>	34 (0.4)		
Intraventricular hemorrhage						
Grades 1, 2	16 (0.5) <sup>b</sup>	13 (0.2) <sup>b</sup>	7 (0.06) <sup>c</sup>	13 (0.01)		
Grades 3, 4	0	1 (0.02)	1 (0.01)	3 (0.004)		
Sepsis						
Evaluation	1073 (31) <sup>b</sup>	1443 (22) <sup>b</sup>	1792 (15)b	10,588 (12)		
Culture proven	18 (0.5) <sup>b</sup>	23 (0.4) <sup>b</sup>	26 (0.2) <sup>c</sup>	97 (0.1)		
Phototherapy	13 (6.1) <sup>b</sup>	227 (3.5) <sup>b</sup>	36 (2.0) <sup>b</sup>	857 (1)		
Necrotizing enterocolitis	3 (0.09) <sup>b</sup>	1 (0.02) <sup>c</sup>	1 (0.001)	1 (0.001)		
Apgar ≤3 at 5 min	5 (0.1)	12 (0.2) <sup>b</sup>	10 (0.9)	54 (0.06)		
Intubation in delivery room	49 (1.4) <sup>b</sup>	55 (0.8)°	36 (0.6)	477 (0.6)		
One or more of the above	1175 (34) <sup>b</sup>	1565 (24) <sup>b</sup>	1993 (17) <sup>b</sup>	11,513 (14)		

<sup>&</sup>lt;sup>a</sup>Data presented as n (%).

Reproduced with permission from McIntire DD, Leveno KJ: Neonatal mortality and morbidity rates in later preterm births compared with births at term, Obstet Gynecol. 2008 Jan;111(1):35–41.

 $<sup>^{</sup>b}p$  < .001 compared with 39 weeks referent.

 $<sup>^{\</sup>circ}p$  < .05 compared with 39 weeks referent.



# Screening

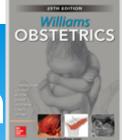
- \* These measures had poor predictive performance as a screening test. In fact, all screening modalities had relative low sensitivity and low positive-predictive values. Based on these findings, routine use of these screening tests in this low-risk population is not recommended
- \* History taking



#### Cervix dilation

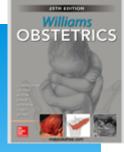
Although women with dilation and effacement in the third trimester are at greater risk for preterm birth, detection does not necessarily improve pregnancy outcome. Buekens and associates (1994) randomly assigned 2719 women to undergo routine cervical examinations at each prenatal visit and compared them with 2721 women in whom serial examinations were not performed. Knowledge of antenatal cervical dilation did not affect any pregnancy outcome related to preterm birth or the frequency of interventions for preterm labor. The investigators also reported that cervical examinations were not related to PPROM. Thus, it seems that prenatal cervical examinations in asymptomatic women are neither beneficial nor harmful.

\* Thus, it seems that prenatal cervical examinations in asymptomatic women are neither beneficial nor harmful.



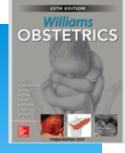
# **Ambulatory Uterine Monitorin**

\* Subsequently, it was proven that the use of this expensive and time-consuming system does not reduce preterm birth rates (Collaborative Home Uterine Monitoring Study Group, 1995; lams, 2002; Urquhart, 2017).



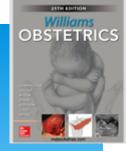
# Cervical length

- \* Transvaginal sonography is safe, highly reproducible, and more sensitive than transabdominal sonographic
- \* After 16 wks
- \* Only indicated with a history of prior spontaneous preterm birth, the Society for Maternal-Fetal Medicine (2016b) recommends transvaginal cervical length screening



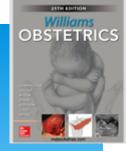
## Fetal Fibronectin(fFN)

- \* Present in high concentrations in maternal blood and amnionic fluid, fFN is thought to function in intercellular adhesion during implantation and in maintenance of placental adherence to uterine decidua (Leeson, 1996).
- \* Values exceeding 50 ng/mL are considered positive
- \* The American College of Obstetricians and Gynecologists (2016c) does not recommend screening with fFN tests. Its use in conjunction with cervical length measurement is discussed next.



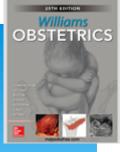
#### Conclusion for screening

\* These measures had poor predictive performance as a screening test. In fact, all screening modalities had relative low sensitivity and low positive-predictive values. Based on these findings, routine use of these screening tests in this low-risk population is not recommended



#### Prevention

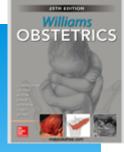
- \* Cervical Cerclage
- \* Progesterone



## Cervical Cerclage

#### Three indication

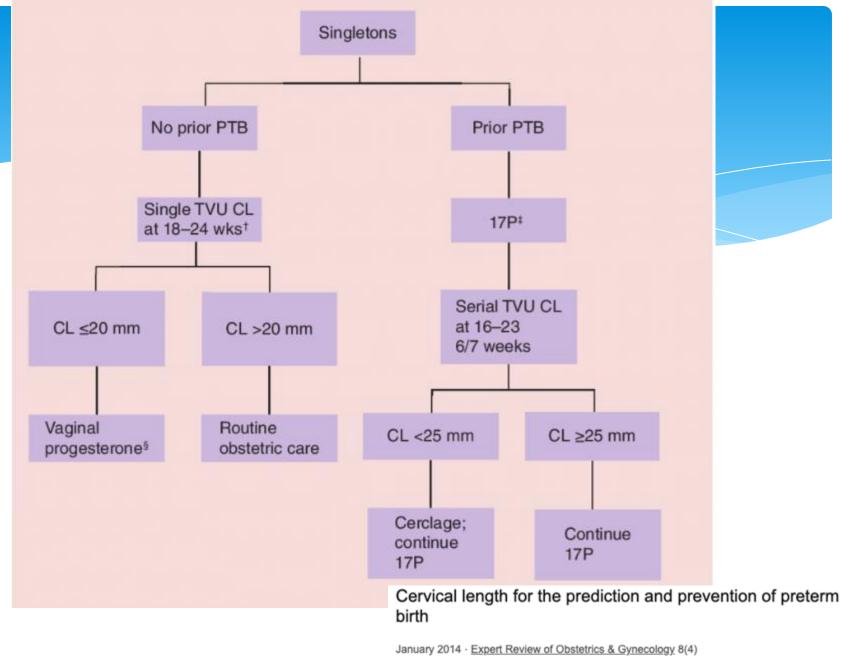
- Recurrent midtrimester losses and who are diagnosed with cervical insufficiency
- \* "Rescue" cerclage, done emergently when cervical incompetence is recognized in women with threatened preterm labor
- \* American College of Obstetricians and Gynecologists (2016c) concluded that in women with a singleton pregnancy, prior spontaneous preterm birth before 34 weeks, cervical length <25 mm, and gestational age <24 weeks, cerclage placement may be considered.



## Progesterone

- Progesterone withdraw in most animal
- Progesterone receptor activity decrease in human
- 17-alpha-hydroxyprogesterone caporate(Progeston depot 250mg im) for prior history of preterm birth
- micronized progesteron(Utrogestan 200mg vag)
   for cervical length <15mm without history of preter birth</li>
- \* The OPPTIMUM Study

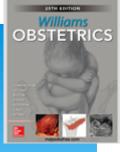
Investigator	Women Randomized	Cervical Length®	Progestogen Compound	Progestogen vs Placebo
Fonseca (2007)	n = 250; 5% nulliparous, 10% twins, 15% prior PTB; 8 hospitals. UK, Greece, Brazil, Chile	<15 mm	Progesterone, 200-mg vaginal capsules daily	Delivery <34 weeks: 19% vs 34%, p = .02
Flassan (2011)	n = 465; singletens only; 55% nulliparous; 13% prior PTB; 44 hospitals in 10 countries	10-20 mm	Progesterone, 90-mg vaginal gel daily	Delivery <33 weeks: 9% vs 16%, p = .02
Grobman (2012)	n = 657; singletons only; nulliparous only; 14 centers across US	<30 mm	17-OHP-C, 250 mg IM weekly	Delivery <37 weeks: 25% vs 24%, p = NS



DOI: 10.1586/17474108.2013.811932

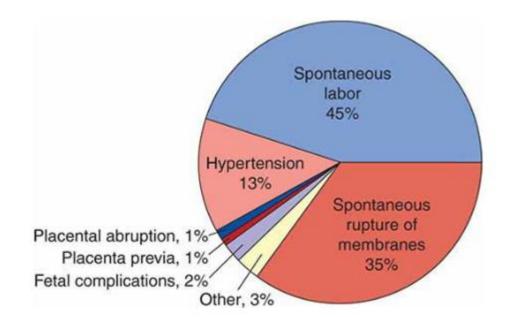
Mariarosaria Di Tommaso ⋅ 
 Vincenzo Berghella

# Management



#### **PPROM**

Preterm premature rupture of membrane(PPROM)



# Williams OBSTETRICS

#### Induction or Expectant managemer

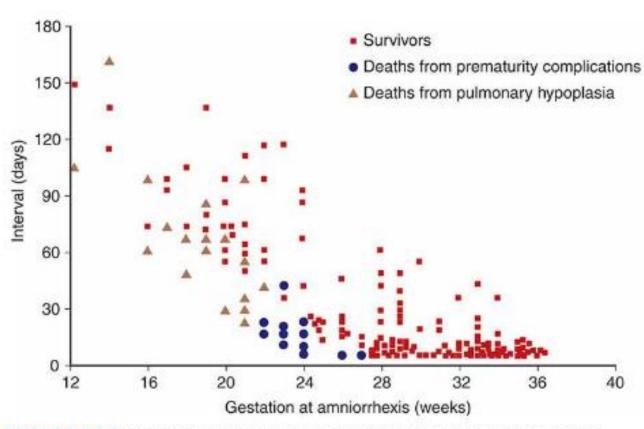
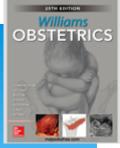


FIGURE 42-9 Relationship of time between preterm membrane rupture and delivery in 172 singleton pregnancies. (Reproduced with permission from Carroll SG, Blott M, Nicolaides KH: Preterm prelabor amniorrhexis: Outcome of live births, Obstet Gynecol 1995 Jul;86(1):18–25.)



# By gestational age

Gestational Age	Management	
34 weeks or more	Plan delivery: labor induction unless contraindicated	
	Group B streptococcal prophylaxis <sup>2</sup>	
	Single corticosteroid course may be considered up to 36 <sup>5/7</sup> weeks <sup>b</sup>	
32 weeks to 33 completed weeks	Expectant management	
	Group B streptococcal prophylaxis*	
	Single corticosteroid course <sup>c</sup>	
	Antimicrobials to prolong latency	
24 weeks to 31 completed weeks	Expectant management	
	Group B streptococcal prophylaxis*	
	Single corticosteroid course <sup>c</sup>	
	Tocolytics: no consensus	
	Antimicrobials to prolong latency	
	Magnesium sulfate for neuroprotection may be considered	
<24 weeks	Expectant management or induction of labor <sup>e</sup>	
	Group B streptococcal prophylaxis is not recommended	
	Single corticosteroid course may be considered <sup>e/</sup>	
	Tocolytics: no consensus <sup>ed</sup>	
	Antimicrobials: may be considered <sup>eg</sup>	

<sup>\*</sup>Figure 64-7 (p. 1222) outlines group B streptococcal prophylaxis for preterm gestations.

Data from American College of Obstetricians and Gynecologists 2016a, d, 2017a, e.

<sup>&</sup>lt;sup>5</sup>May be considered between 34<sup>97</sup> and 36<sup>97</sup> weeks in those who have not received a previous course of antenatal corticosteroids,

Repeat, or rescue, course of corticosteroids with preterm rupture of membranes is controversial.

Magnesium sulfate for neuroprotection in accordance with one of the larger studies.

<sup>&</sup>quot;See Periviable Neonatal Survival (p. 806) to aid patient counseling and decision making.

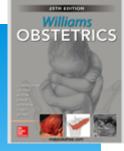
Intervention not recommended before viability but may be considered as early as 23°7 weeks of gestation.

<sup>&</sup>lt;sup>9</sup>May be considered as early as 20<sup>07</sup> weeks of gestation.

# Williams OBSTETRICS

#### **PPROM**

- Use speculum examination, avoid digital examination
- \* Tocolysis: no consensus
  - \* Prophylactic: no benefit, increase rate of chorioamnionitis
  - \* Therapeutic: no significant benefit to perinatal outcome
- \* Antimicrobial therapy:recommend
  - \* longer latency, fewer chorioamnionitis and sepsis
  - Duration: 3day=7day> prolong antimicrobial therapy
  - \* Ampicillin + Erythromycin
- Antenatal corticosteroid
- \* Antenatal magnesium sulfate

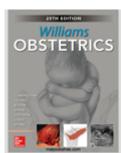


#### Complication

- \* Oligohydramnios:
  - \* less rate to delivery in third trimester
  - \* Limb compression deformity
- \* Chorioamnionitis:
  - \* Higher incidence of mobidity
  - \* Fever
  - \* Fetal tachtcardia

# Management of preterm labor

- \* Antenatal corticosteroid for fetal lung maturation
- \* Antenatal magnesium sulfate for neuroprotection
- \* Antimicrobials
- \* Bedrest



# Williams OBSTETRICS

#### Antenatal corticosteroid

- For fetal lung maturation
  - \* 24 0/7 34 0/7 wks: recommend
  - \* 34 0/7 36 6/7 wks: considered (ACOG 2017, SMFM 2016), only 3% less morbidity, not use in Parkland hospital
- Single course
  - \* Betamethasone 12mg + 12mg IM, 24hours apart
  - Dexamethasone 6mg \*4 dose, 12hours apart
- \* Repeated course
  - \* Reduce respiratory morbidity
  - not recommend byACOG and Parkland hospital
- Rescue therapy
  - \* Lower respiratory morbidity, similar mortality
  - Considered by ACOG, not in Parkland hospital

#### Antenatal magnesium sulfate

- For neuroprotection(IVH, CP)
  - \* no consensus so far
  - \* 24 0/7- 31 6/7 by
  - \* 24 0/7 27 6/7 in Parkland hospital
- \* Dose:6g bolus in 30min, 2g per hour

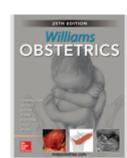
TABLE 42-10. Magnesium Sulfate for the Prevention of Cerebral Palsya

	Treatment				
Perinatal Outcome®	Magnesium Sulfate No. (%)	Placebo No. (%)	Relative Risk (95% CI)		
Infants with 2-year follow-up	1041 (100)	1095 (100)	_		
Fetal or infant death	99 (9.5)	93 (8.5)	1.12 (0.85-1.47)		
Moderate or severe cerebral palsy:					
Overall	20/1041 (1.9)	3/1095 (3.4)	0.55 (0.32-0.95)		
<28-31 weeks <sup>b</sup>	12/442 (2.7)	30/496 (6)	0.45 (0.23-0.87)		
≥24-27 weeks <sup>b</sup>	8/599 (1.3)	8/599 (1.3)	1.00 (0.38-2.65)		

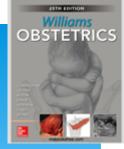
<sup>\*</sup>Selected results from the Beneficial Effects of Antenatal Magnesium Sulfate (BEAM) Study.

CI = confidence index.

Data from Rouse, 2008.



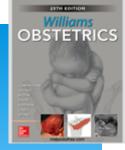
bWeeks' gestation at randomization.



#### Antibiotic

- \* For pt' with intact membranes, only GBS prophylaxis have benefit
  - => Check cervix culture at admission

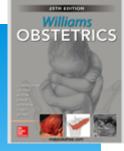
with intact membranes did not reduce preterm birth rates or affect other clinically important short-term outcomes (Flenady, 2013). However, rates of short- and longer-term harm were higher for children of mothers exposed to antibiotics. Kenyon (2001) reported the ORACLE Collaborative Group study of 6295 women with spontaneous preterm labor and intact membranes, but without evidence of infection. Women were randomly assigned to receive antimicrobial or placebo therapy. The primary outcomes of neonatal death, chronic lung disease, and major cerebral abnormality were similar in both groups. In a follow-up of the ORACLE II trial, fetal exposure to antimicrobials in this clinical setting was associated with an increased cerebral palsy rate at age 7 years compared with that in children without fetal exposure (Kenyon, 2008b). Importantly, antimicrobial use described here is distinct from that given for group B streptococcal prophylaxis (Chap. 64, p. 1222).



#### Bedrest?

#### Bed Rest

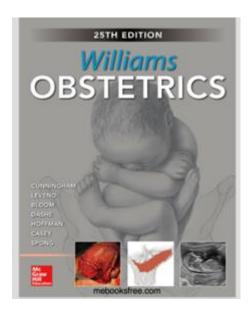
This is one of the most often prescribed interventions during pregnancy, yet one of the least studied. One systematic review concluded that evidence neither supported nor refuted bed rest for prevention of preterm birth (Sosa, 2004). Goulet and coworkers (2001) randomly assigned 250 Canadian women to either home care or hospitalization after treatment of an acute episode of preterm labor and found no benefits. There have, however, been reports of possible harm. Kovacevich and associates (2000) reported that bed rest for 3 days or more increased thromboembolic complications to 16 per 1000 women compared with only 1 per 1000 with normal ambulation. Promislow and colleagues (2004) observed significant bone loss in pregnant women prescribed outpatient bed rest. More recently, Grobman and associates (2013) noted that women with activity restriction were nearly 2.5 times more likely to have a preterm birth before 34 weeks. This finding, however, may reflect ascertainment bias. That is, women with restricted activity may have been assigned to bed rest because they were viewed to be at more imminent risk of preterm delivery. McCall and coworkers (2013) summarized the literature on bed rest, and they found insufficient evidence to support its use. The American College of Obstetricians and Gynecologists (2017d) suggests that, although frequently prescribed, bed rest is only rarely indicated, and ambulation should be considered in most cases.



#### Tocolysis

- Do not prolong gestation
- Delay delivery for up to 48 hours, antenatal corticosteroid and magnesium sulfate, transfer patient to center
- \* Medication:
  - \* Nifedipine(Nedipin) Calcium channel blocker
  - \* Ritodrine(Yutopar)-B-adrenergic receptor agonist
  - \* Indomethacin(Tenton)-PGE inhibitor
  - Magnesium sulfate

#### Refferences



#### Cervical length for the prediction and prevention of preterm birth

January 2014 · Expert Review of Obstetrics & Gynecology 8(4)

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