



Preterm Birth and Fetal Fibronectin: Assessing Risk Along the Continuum

Jesus Alvarez Perez, MD, FACOG
Board Certified in Maternal Fetal Medicine
Associate Professor of MFM at UMDNJ-NJMS
Director Of Obstetrics and
Director of Maternal Fetal Medicine
HIMA-San Pablo

HOLOGIC



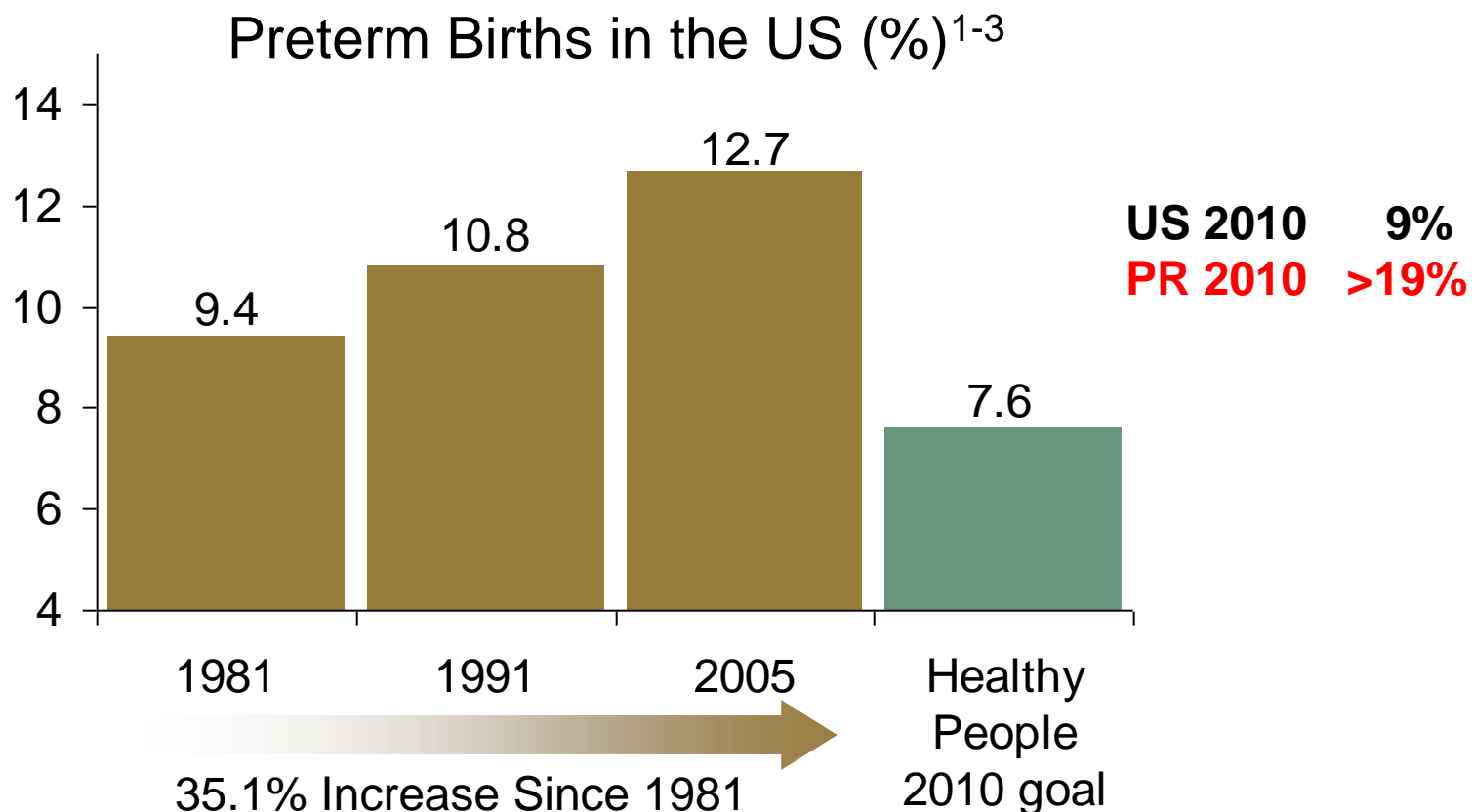
Grupo
HIMA-San Pablo



Learning Objectives for Educational Slides

- At the conclusion of this presentation, the healthcare provider will be able to:
 1. Describe the epidemiology and long-term consequences of preterm birth in the United States
 2. Identify women at risk of spontaneous preterm birth (SPTB)
 1. Symptomatic
 2. Asymptomatic
 3. Understand the role of fetal fibronectin (fFN) testing as an important tool for assessing risk
 4. Describe strategies to benefit women at risk

Preterm Births in the United States: 1 in 8 Infants



1. Martin JA et al. *National Vital Statistics Reports*. 2006;55:1-104.

2. Hamilton BE et al. National Center for Health Statistics. Available at:
<http://www.cdc.gov/nchs/products/pubs/pubd/hestats/prelimbirths05/prelimbirths05.htm>.

3. Healthy People Objectives 2010. Available at: <http://www.healthypeople.gov/document/html/objectives/16-11.htm>.

Preterm Birth: Magnitude of the Problem

- In the PR, preterm birth accounts for:
 - 19% of all births
 - 75% of all neonatal mortality and 50% of long-term neurological impairments in children
 - 33% of all health care spending on infants and 10% of spending for children
- Despite advances in OB care, the preterm birth rate has continued to rise

Prematurity Generates Enormous Health Care Costs

- Average newborn hospital charges: \$4,300 vs. \$58,000 for a preterm baby*
- Total U.S. hospital charges for infant stays due to prematurity/low birth weight: \$11.9 Billion*
- Maternity & related expenses:
 - Often the largest cost to employers' health care plans

* Source: Agency for Healthcare Research and Quality, 2000 Nationwide Inpatient Sample
Prepared by March of Dimes Perinatal Data Center

Major Complications of Prematurity

- Major determinants of neonatal and infant illness:
 - Neurodevelopmental handicaps (CP, mental retardation)
 - Respiratory Distress Syndrome
 - Chronic pulmonary disease (bronchopulmonary dysplasia)
 - Intraventricular hemorrhage
 - Periventricular Leukomalacia

Continuation

- Patent Ductus Arteriosus
- Jaundice
- Infection
- Retrolental fibroplasia
- Necrotizing enterocolitis
- Neurosensory deficits (hearing, retinopathy of prematurity)



WHAT ARE THE RISK FACTORS FOR PRETERM LABOR

HOLOGIC

Preterm Labor Statistics

Spontaneous PTL

- 60% of all PTL
- Screening tools are only:
 1. Fetal Fibronectin
 2. TV Cervical US

Indicated PTL

- 40% of all PTL
 - 43% Ischemic (IUGR)
 - 37% Placental Disease
- Preeclampsia
- Fetal growth Restriction
- Fetal Distress
- Abruptio

Clinical Risk Factors for Spontaneous Preterm Birth

- Prior history of SPTB^{1, 2}
- Multiple gestation^{1, 2}
- Vaginal bleeding^{1, 2}
- African American or Hispanic^{1, 2}
- Low pre-pregnancy weight^{1, 2}
- Maternal age <17 and >35 years¹
- Low socioeconomic status^{1, 2}
- Maternal stress^{1, 2}
- Cigarette smoking, drug abuse^{1, 2}
- Anemia¹

These risk factors are also the same for Induced PTL!!

1. Iams JD. *Clin Perinatol*. 2003;30:651-664.
2. Goffinet F. *BJOG*. 2005;112(supp1):28-47.

PROBLEM !!!

HOLOGIC

Most Clinical Risk Factors Are Poor Predictors

Risk factors fail in *both* directions

More than **1/2** of women who deliver preterm do **not** have identifiable risk factors and are nulliparous¹

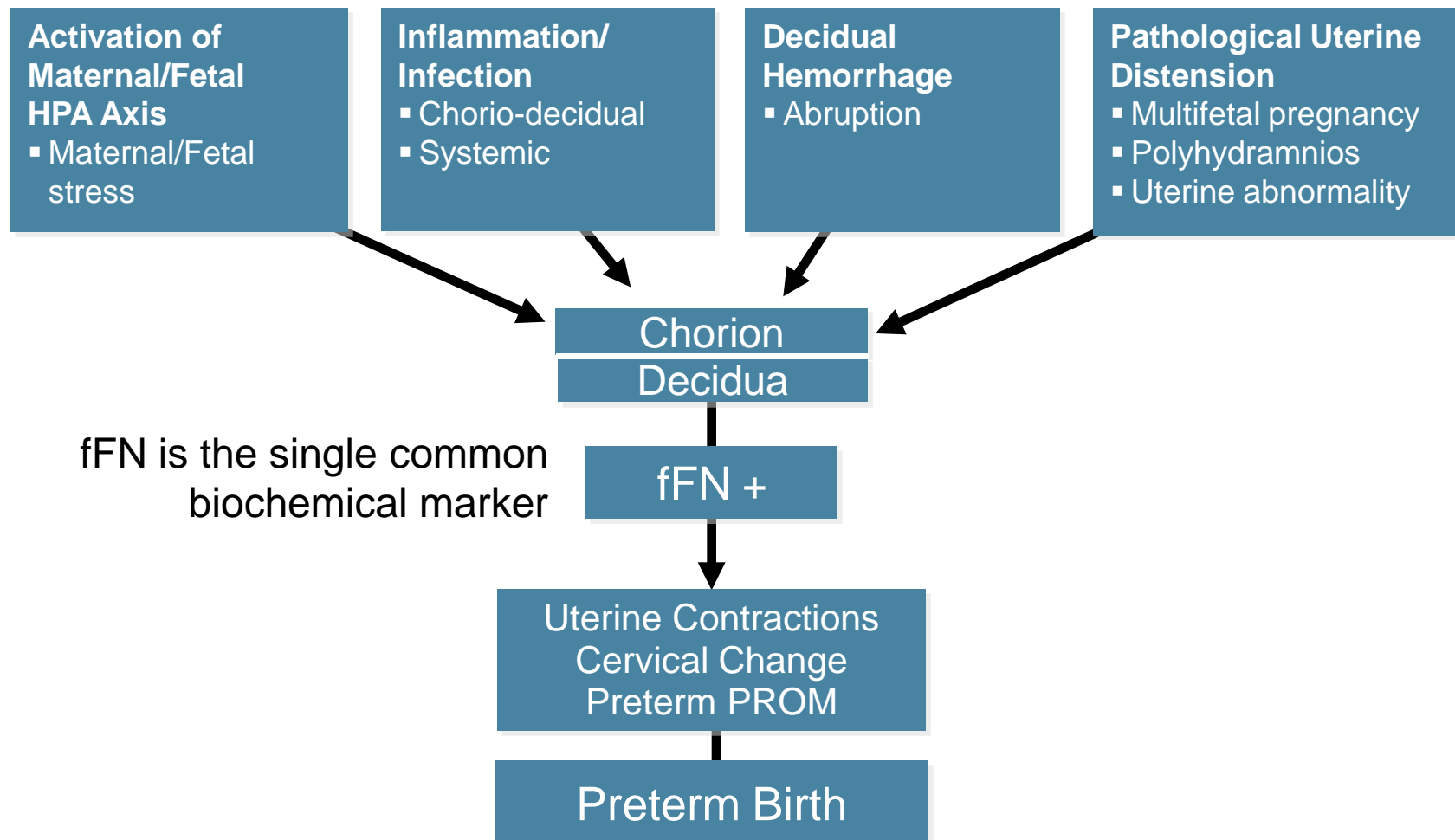
Approximately **2/3** of women with traditional risk factors do **not** go on to deliver preterm²

1. Kramer MS. *Bull World Health Organ.* 1987;65:663-737.
2. Goldenberg RL, et al. *Obstet Gynecol.* 1996;87:643-648.

How Can We Screen for PTL?

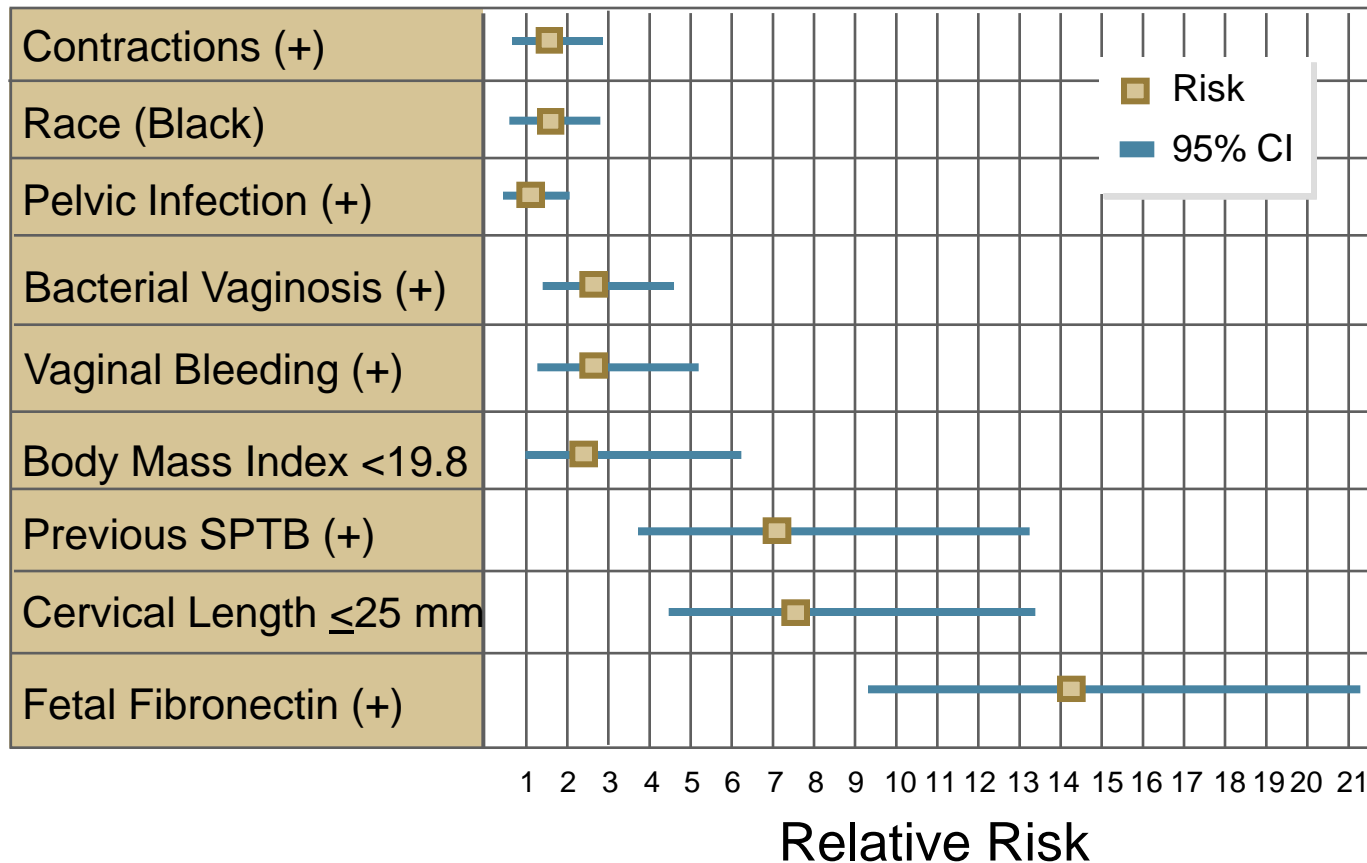
HOLOGIC

Pathophysiologic Mechanisms for Prematurity



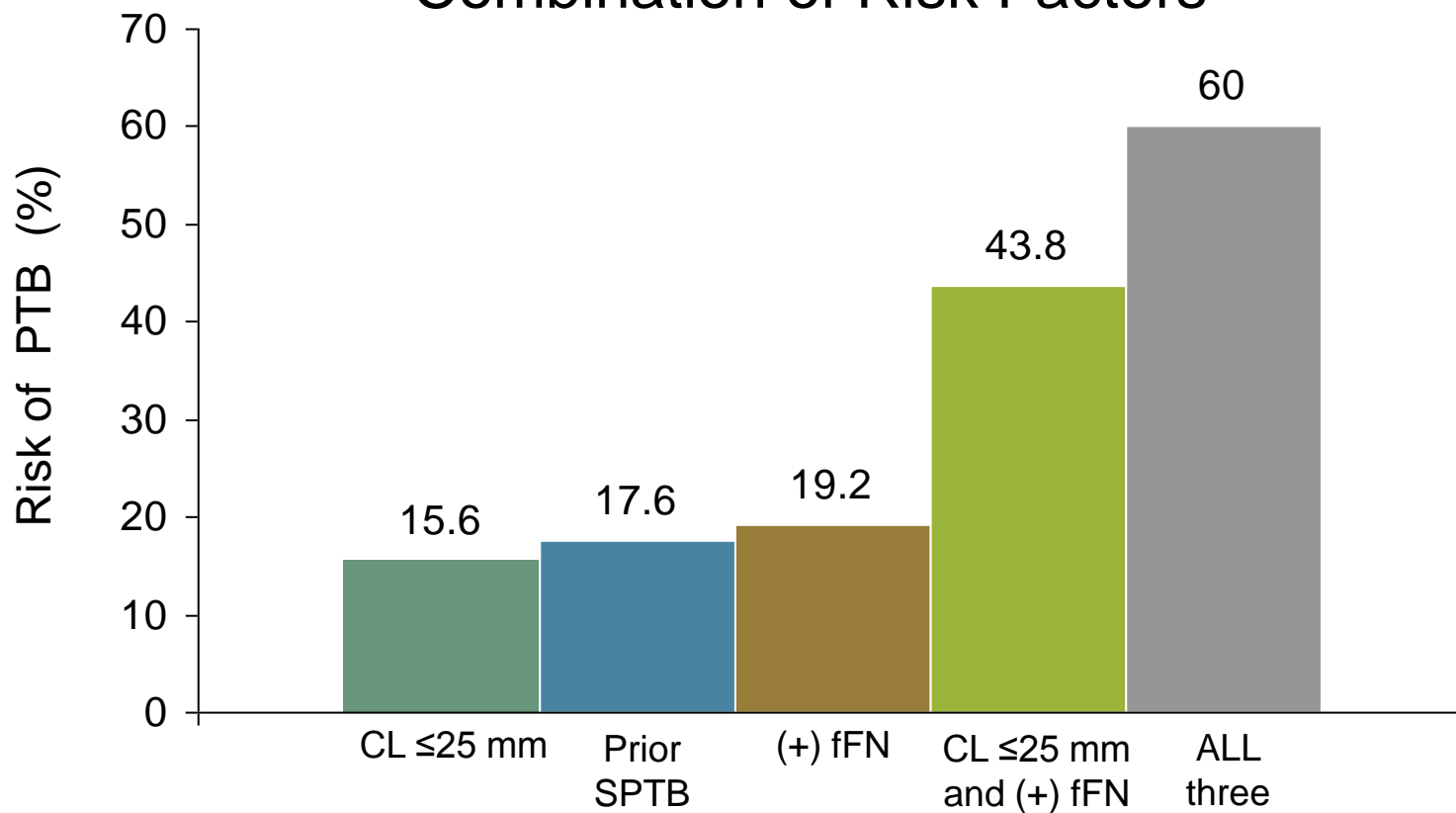
Relative Risk of SPTB <32 Weeks

Risk Factors



Risk (%) for SPTB at <37 Weeks Multiparas Only

Combination of Risk Factors



Biomarkers for Risk Assessment

Biochemical

Fetal fibronectin (fFN)

Biophysical

Cervical length by TVUS

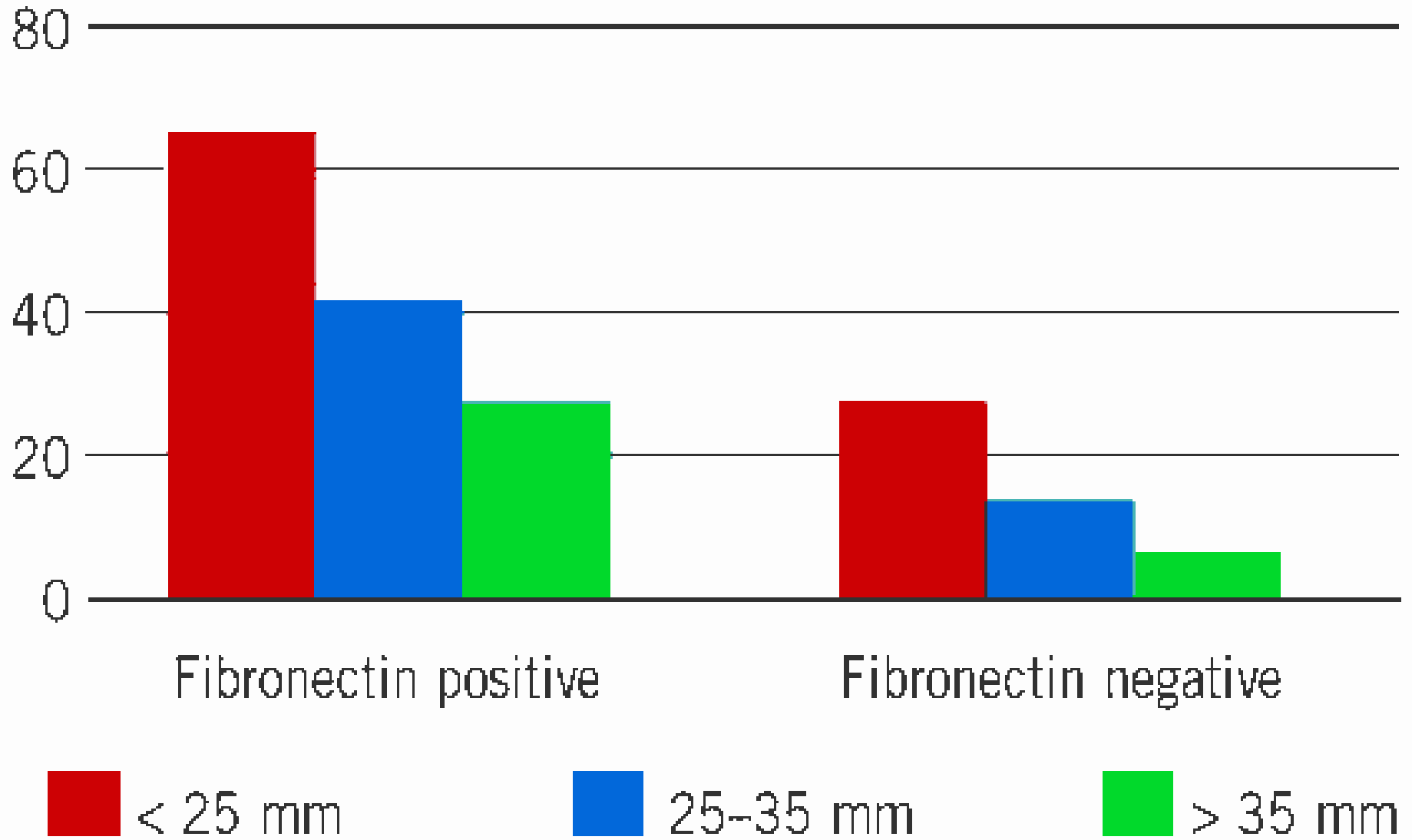
TVUS=transvaginal ultrasound

Allows Physicians to:

- More accurately identify women at risk
- Develop ongoing surveillance programs
- Institute appropriate interventions
- Increase patient education and preparation

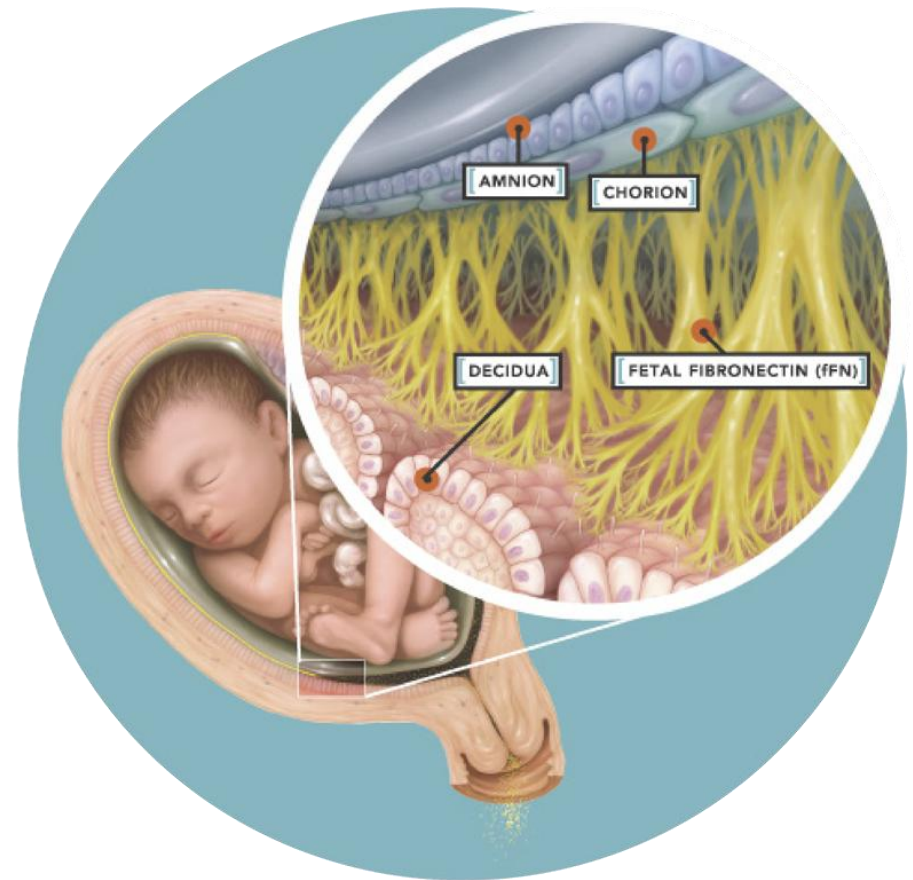
Allows Patients to:

- Avoid unnecessary treatment and expense
- Maintain personal, family, and professional lifestyle

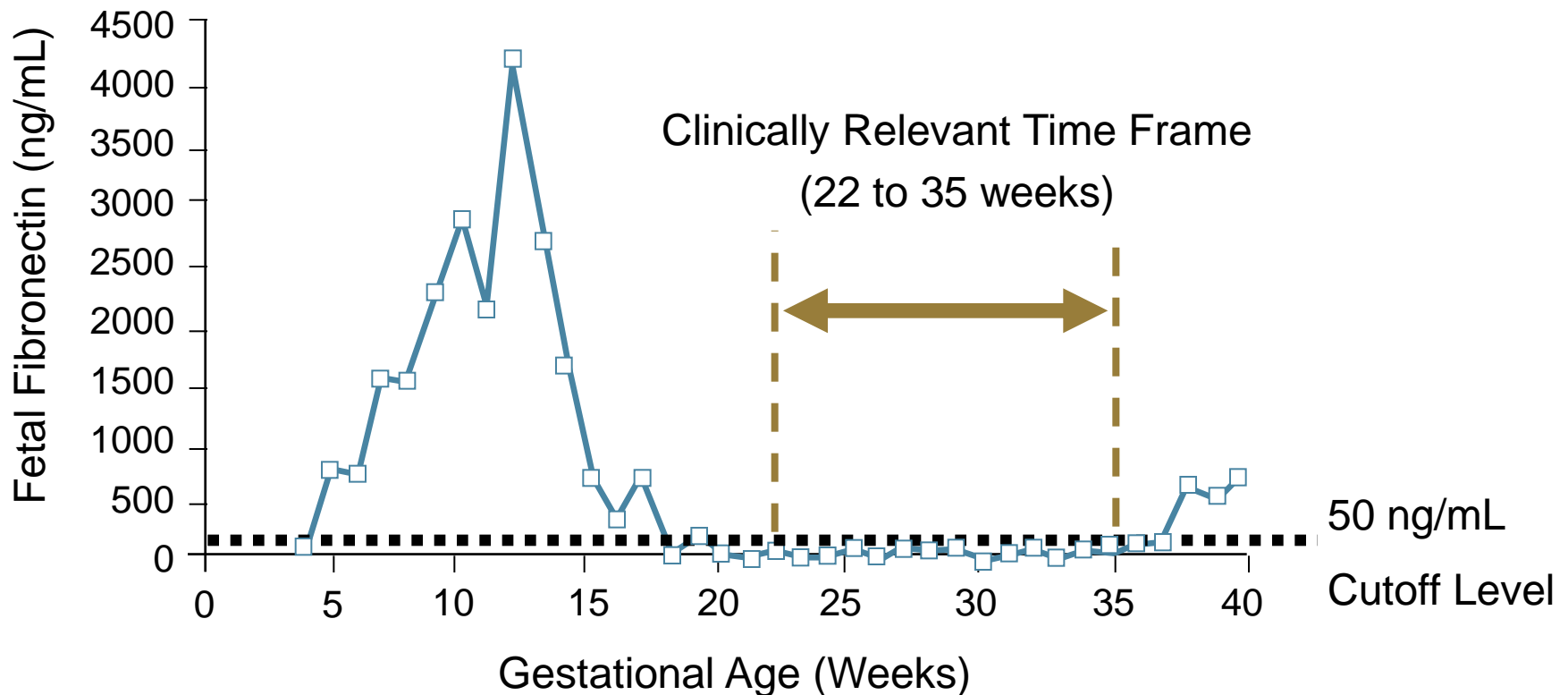


Fetal Fibronectin: Key Biochemical Marker for Risk Assessment

- Adhesive glycoprotein “glue” at the maternal-fetal interface
- Presence in cervicovaginal secretions highly associated with risk of preterm delivery



Cervicovaginal Presence of Fetal Fibronectin from 22 to 35 Weeks Is Abnormal



Guidelines for Performing fFN Test

Obtain Specimen **Prior** to Any Examination or Manipulation of the Cervix:

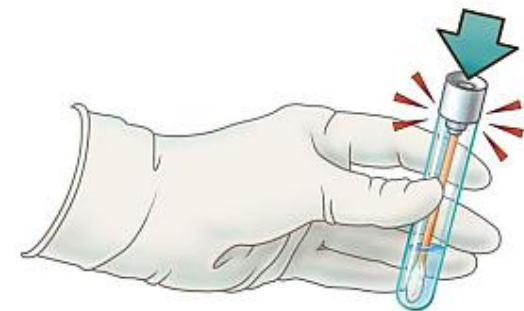
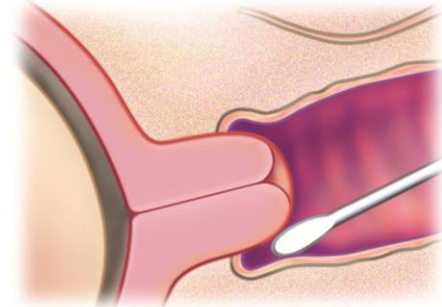
- Digital examination
- Vaginal ultrasound
- Microbiologic culture
- Pap test

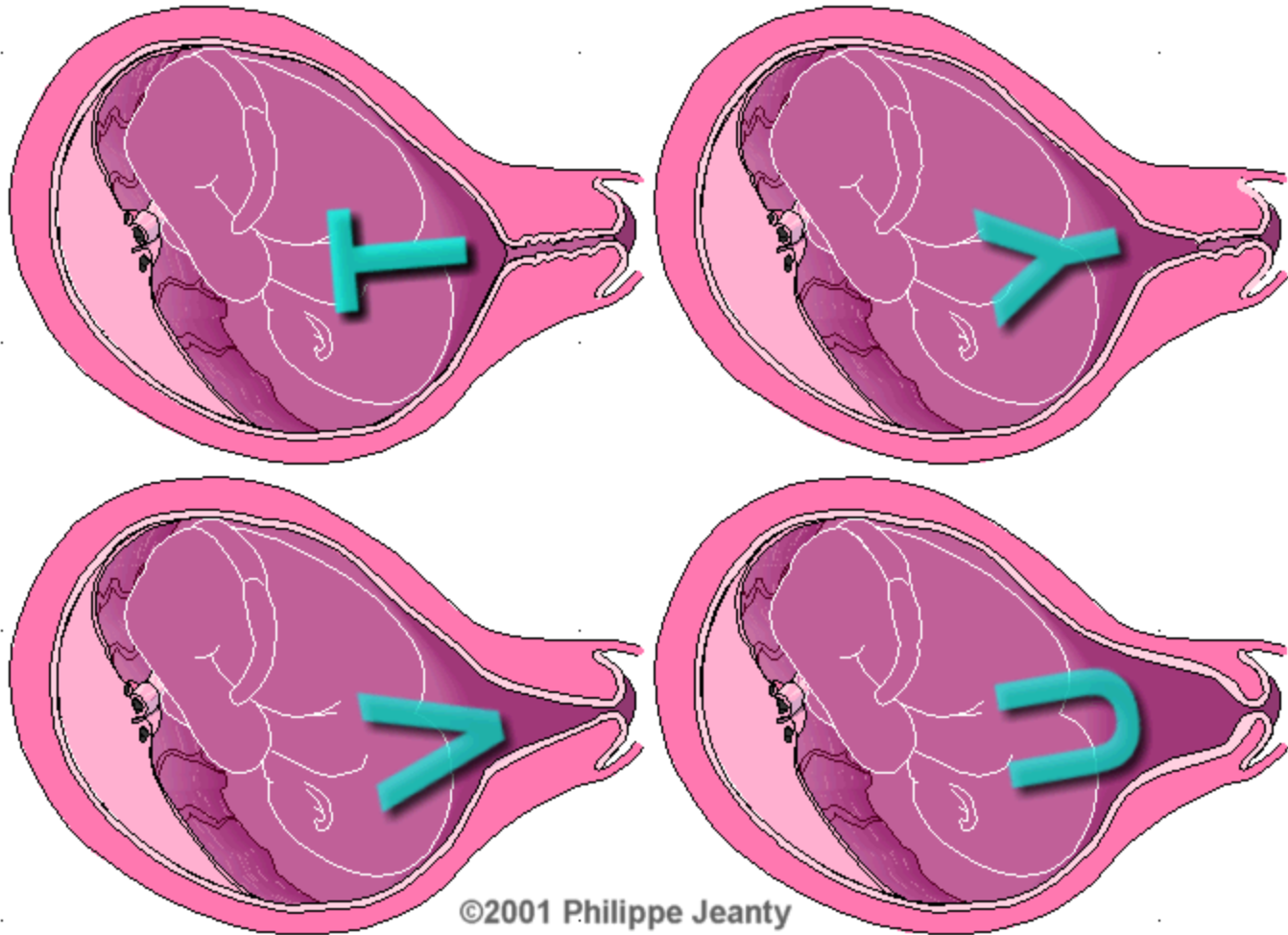
Specimen Should **Not** be Obtained in the Presence of:

- Cervical dilatation ≥ 3 cm
- PPROM
- Soaps, gels, lubricants, or disinfectants
- Cervical cerclage
- Moderate or gross vaginal bleeding
- Sexual intercourse within 24 hours

fFN Specimen Collection Procedure

- During speculum examination, lightly rotate swab across posterior fornix of vagina for 10 seconds to absorb cervicovaginal secretions
- Remove swab and immerse polyester tip in buffer; break shaft at score even with top of tube
- Align the shaft with hole inside the tube cap and push down tightly over shaft, sealing tube; ensure shaft is aligned to avoid leakage





©2001 Philippe Jeanty



©2001 Philippe Jean



©2001 Philippe J



©2001 Philippe Jeanty



©2001 Philippe Jeanty

Cervical length as a screening Test

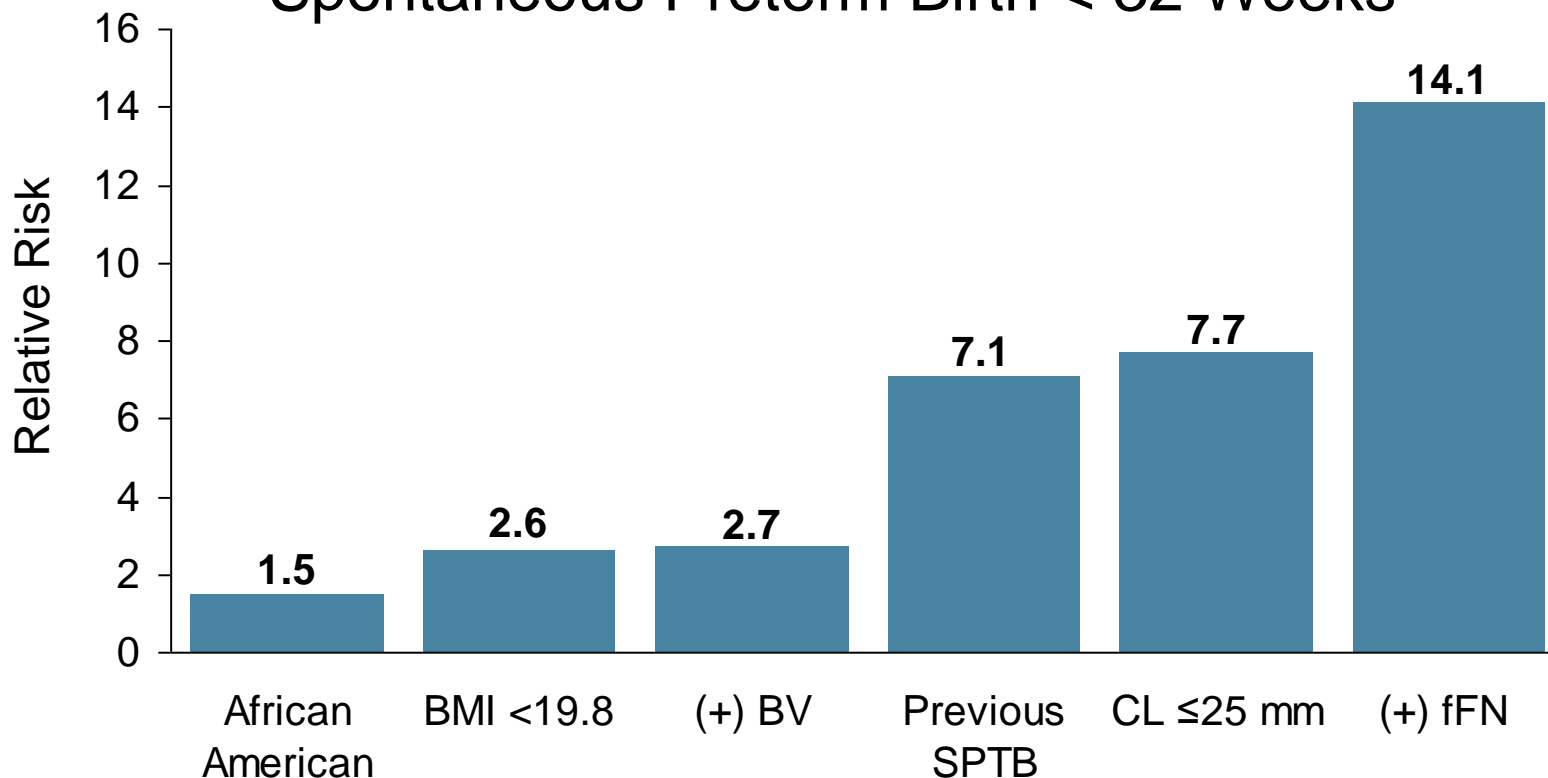
- Have validity
 - Digital vs TVU examinations of CL every 2 wks (GA 14 ~GA 30) predict PTB → TVU superior
 - Sonographic cervical length :11 mm longer than manual estimations.
 - → TVU superior to manual exam for evaluation of Cx & prediction of preterm birth.

Ultrasonography for cervical length

- The association between a short cervix and preterm delivery is significant
- NICHD Maternal-Fetal Medicine Network Trial
 - RR less than 4 cm at 28 weeks: 2.8
 - RR less than 3 cm at 28 weeks: 5.39
 - RR less than 2.2 cm at 28 weeks: 13.88
 - RR less than 1.3 cm at 28 weeks: 24.94

Comparison of Risk Factors(TVUS+FFN)

Spontaneous Preterm Birth < 32 Weeks



Cervical length measurement and fFN testing were performed at 22 to 24 weeks

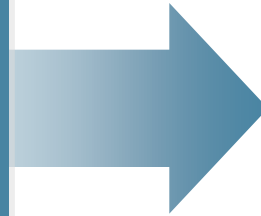
fFN in Symptomatic Patients: High NPV

NPV for delivery within:

7 days = 99.5%

14 days = 99.2%

<37 weeks = 84.5%



Benefits of a Negative Test

- Less intervention
- Avoid hospitalizations
- Physician and patient reassurance

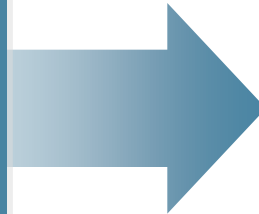
N = 763

Mean gestational age at fFN testing= 30.3±3.0 weeks

Mean gestational age at delivery=38.4±2.6 weeks

fFN in Symptomatic Patients: Helpful PPV

PPV for delivery within:
7 days = 12.7%
14 days = 16.7%
<37 weeks = 44.7%



Benefits of a Positive Test

- Identify group that can be targeted for intervention
- Opportunity for antenatal steroids
- Preparation for optimal neonatal care

N = 763

Mean gestational age at fFN testing = 30.3±3.0 weeks

Mean gestational age at delivery = 38.4±2.6 weeks

1. Peaceman AM et al. *Am J Obstet Gynecol.* 1997;177:13-18.
2. Fetal Fibronectin Enzyme Immunoassay and Rapid fFN for the TLiIQ® System. Information for Health Care Providers. Cytoc Corp., Marlborough, MA.

NICHD Preterm Prediction Study: Asymptomatic Patients

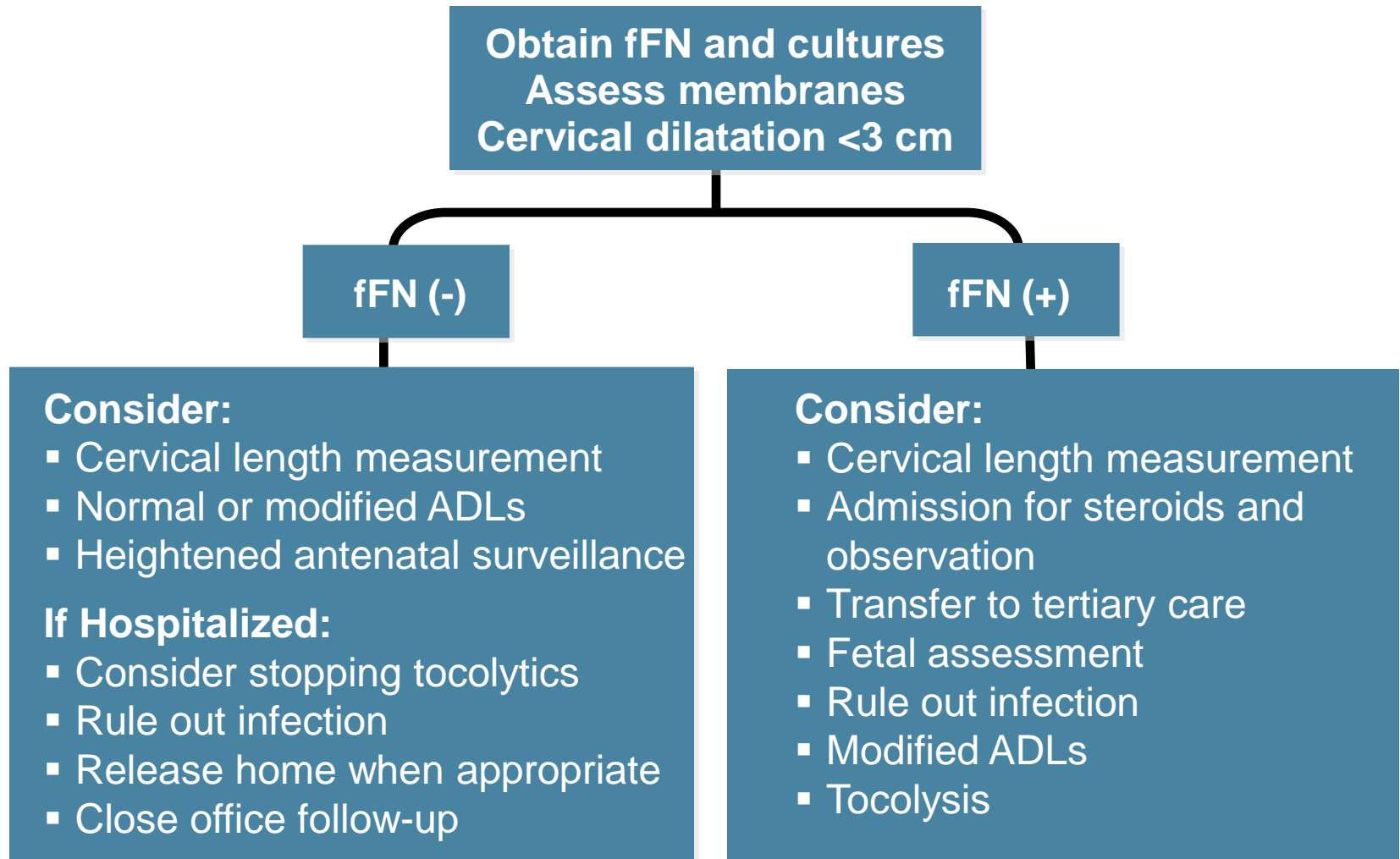
If fFN positive at 22 to 24 weeks:

Delivery	Sensitivity	Relative Risk
<28 weeks	63	59.2
<30 weeks	54	39.9
<32 weeks	38	21.2
≤34 weeks	21	8.9

N=2929. Single testing at 22 to 24 weeks.

NICHD=National Institute of Child Health and Human Development.

Potential Interventions for Symptomatic Patients Based on fFN Results



Potential Interventions for Asymptomatic Women at Risk Based on fFN Results

fFN (-)

Consider:

- Routine follow-up
- Biweekly fFN testing
- Cervical length measurement

fFN (+)

Consider:

- Increase intensity of prenatal observation
- Educate on signs and symptoms
- Examine for other risk factors
- Cervical length measurement
- Rule out infection
- Antenatal Steroids
- Serial fFN testing

Summary

- Preterm birth remains a serious problem
- Women at risk need to be identified early for evaluation and intervention
- fFN is a powerful, actionable predictor of SPTB
 - A negative test can avoid unnecessary interventions and provide reassurance
 - A positive test can be used to target interventions in women most likely to benefit
 - Cervical length can further improve prediction

Conclusions

fFN determination has an essential place in management of women at increased risk of spontaneous preterm birth