Preventing recurrent preterm birth

The North Carolina 17P Project
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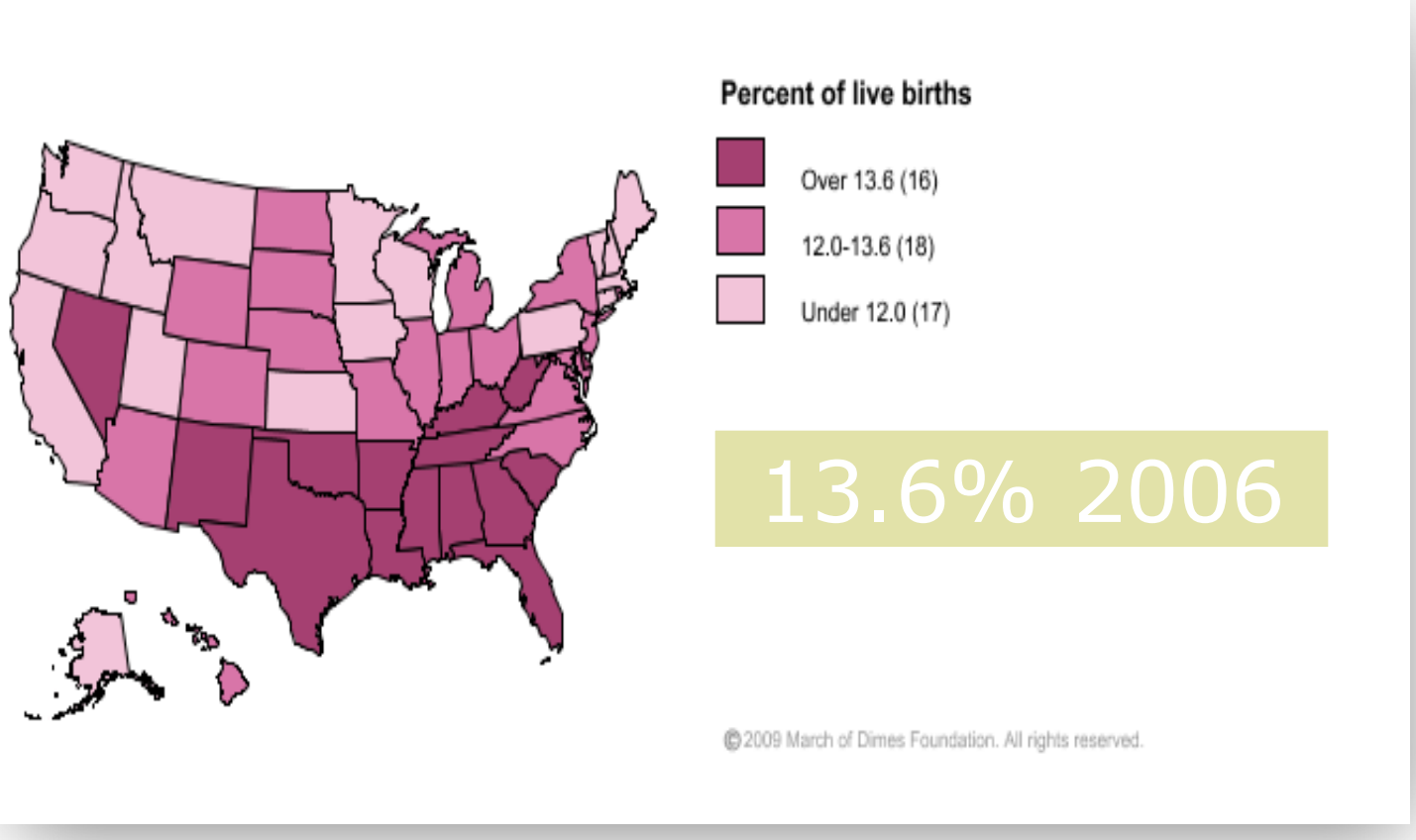
The Problem: Premature Birth

- 1:7 infants in NC is born preterm;1:5 African American infants is born preterm
- Increased 27% since 1982 and continues to grow
- Causes **over 70%** of perinatal morbidity and mortality
- **The most significant known risk factor is a history of preterm birth.** Women with previous PTB are 21% to 45.1% more likely to have a preterm infant than other women.

The problem – Preterm Birth

In 2006, 17,369 infants were born preterm. 1:7 NC babies are born preterm. 1:5 African American babies are born preterm in NC.



National Center for Health Statistics, retrieved October 15, 2009, from www.marchofdimes.com/peristats.

Risk factors for preterm birth

- Prior PTB ***
- Multiple gestation
- Short cervical length
- Low maternal BMI
- African American
- Maternal age
- Smoking

Interventions to prevent PTB

- Prenatal care
  - Social support
- Lifestyle changes
  - Smoking cessation
  - Improved nutrition
- Cerclage
- Infections
- Tocolytic medications

Trials of acute care of PTL show little benefit in prevention of PTB

How progesterone works – current theories

- Functional prog withdrawal stimulates labor
- Progesterone as anti-inflammatory
- Reduce myometrial gap junctions
  - Decrease conduction of contractions
- Reduces threshold for contractions

Progesterone for prevention of PTB

- Small trials in 1970's and 80's suggested reduction in preterm birth
- Variable dosing - IM vs Vaginal
- Variable populations
- 5 trials in high risk women with 17P vs. placebo

Meta-analysis of 17P in Pregnancy

- 15 published trials of various progesterone compounds in women at high risk
- Pooled analysis of the results of the trials showed no effect on the rates of miscarriages or stillbirths
- 5 trials which treated high risk women with 17P
- Pooled analysis of the results showed:
  - Reduction in rates of preterm birth
    Odds ratio was .50, 95% CI: 0.30-0.85
  - Reduction in rates of low birth weight
    Odds ratio was 0.46, 95% CI: 0.27-0.80

Meis, PJ., Wake Forest University, School of Medicine, May 2008, Progesterone for the Prevention of Preterm Birth Presentation

National Institute of Child Health and Development Maternal Fetal Medicine Unit Network

The NEW ENGLAND JOURNAL of MEDICINE

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Prevention of Recurrent Preterm Delivery by 17 Alpha-Hydroxyprogesterone Caproate

Paul J. Meis, M.D., Mark Klebanoff, M.D., Elizabeth Thom, Ph.D., Mitchell P. Dombrowski, M.D., Baha Sibai, M.D., Atef H. Moawad, M.D., Catherine Y. Spong, M.D., John C. Hauth, M.D., Menachem Miodovnik, M.D., Michael W. Varner, M.D., Kenneth J. Leveno, M.D., Steve N. Caritis, M.D., Jay D. Iams, M.D., Ronald J. Wapner, M.D., Deborah Conway, M.D., Mary J. O'Sullivan, M.D., Marshall Carpenter, M.D., Brian Mercer, M.D., Susan M. Ramin, M.D., John M. Thorp, M.D., and Alan M. Peaceman, M.D., for the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network*

New England Journal of Medicine, 2003; 348 (24)

17P – NICHD Summary

- Works for African-American women as well as for Caucasian women
- Weekly 17P
  - 34% reduction in PTB < 37 weeks
  - 33% reduction in PTB < 35 weeks
  - 42% reduction in PTB < 32 weeks
- Number need to treat
  - 5-6 (95% CI 3.6, 11) for prevention of 1 PTB < 37
  - 12 (95% CI 6.3, 74.6) for PTB < 32

Meis, 2003, NEJM

17P Safety

- Northern AT, Norman GS, Anderson K et al. Obstet Gynecol 2007;110:856-872.
  - 4 year outcome of exposed children
  - No congenital anomalies
  - Normal neurological development
- Rebarber, 2007, Diabetes Care
  - 17-P associated with 3 x increased risk of GDM (95% CI 2.1,4.1)
    - 12.9% vs. 4.9%

17P is cost effective

- National Savings
  - $3800 per woman treated (if all eligible women treated)
  - $15,900 per infant treated
  - Total - $2 billion annual savings
- North Carolina (2005 data)
  - 4,219 NC women eligible for 17P – 2,023 low income and 1,622 Medicaid
  - Projected cost savings - $1,752,060 for Medicaid – $4,558,384 for all women
  - 313 babies born full term

Bailit JL, Votruba ME. Am J Obstet Gynecol, 2007 & Petrini et al, Obstet Gynecol, 2005.

FDA Approval

- 17P, marketed as Delalutin™, was approved by the FDA in 1956 for prevention of habitual/recurrent abortion, threatened abortion, and postpartum "afterpains." Approval was withdrawn in 2000 when Bristol Myers Squibb stopped manufacturing the product (not as a result of safety concerns).
- Ther-Rx Company is applying for FDA approval for Gestiva™ (17P).
- FDA stipulated an additional randomized trial before approving Gestiva™. This trial is currently underway.

ACOG/SMFM Recommendations

Previous spontaneous preterm birth, currently pregnant with single fetus

- **250 mg IM (1ml) weekly**
- **Start 16-21 weeks EGA**
- **Continue through 36th week**
- **OK to use in diabetes**
- **Continue if hospitalized, including for PTL**
- **Not effective in multiple gestations**

Obstetrics and Gynecology, Vol 112(4), 2008

17P Challenges and Solutions

- Access to treatment
- Lack of available providers in local community who offer 17P
- Fear of taking medication in pregnancy
- Compliance with treatment – up to 21 weekly IM shots

- NC 17P Project provides free drug for uninsured and underinsured via www.mombaby.org
- Medicaid covers 17P in North Carolina but procurement and billing are complicated
- Educational materials (brochures, web site and videos) for patients
- Partnerships with health departments to offer 17P locally
- Partnerships with Baby Love to assist with keeping appts.

17P side effects

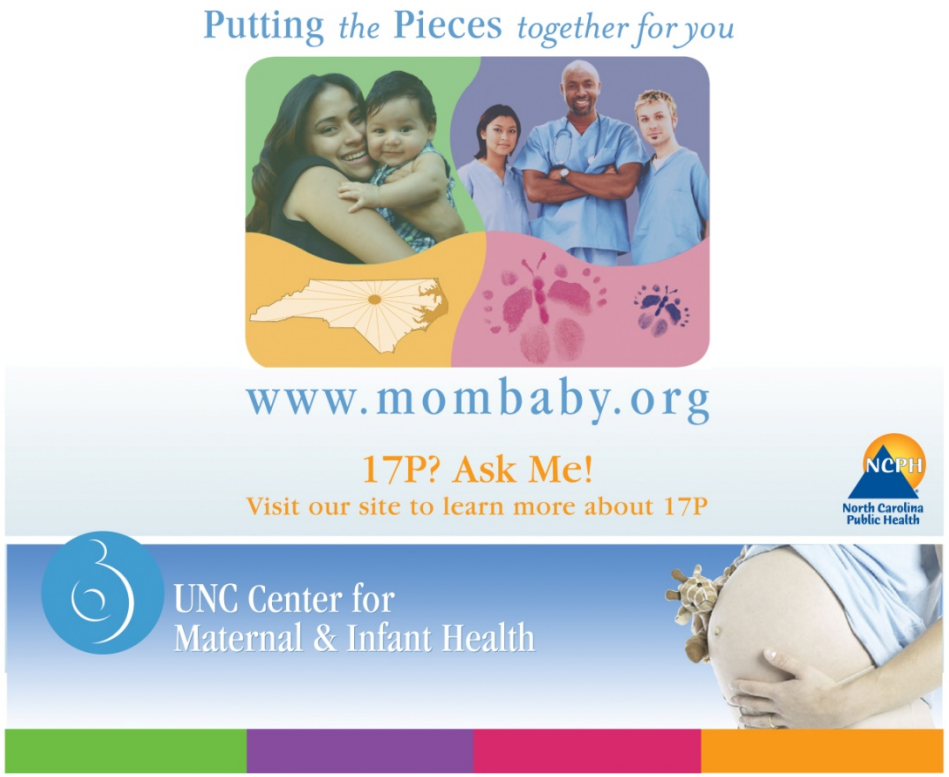
- Meis, 2003 NEJM – injection site s/s

Symptom	%
Soreness	34.2
Swelling	14.1
Itching	11.3
Bruising	6.7

www.mombaby.org

17P order form, new research, emerging issues and ideas for implementation.

Education for women, providers and payers in North Carolina and beyond.



Ordering

- **For uninsured patients**:
  - Use the www.mombaby.org website. Click on the 17P button, the on "order 17P uninsured." The drug arrives in about 4 business days.
- **For Medicaid patients**:
  - Use the www.mombaby.org website. Click on the 17P button, the on "order 17P Medicaid." The drug arrives in about 4 business days.
  - Use a pharmacy listed on the website to place an order for 17P for your privately insured patients.
  - Use another compounding pharmacy* with which your practice has an existing relationship.

*Be sure this pharmacy uses rebatable progesterone.

More ordering information-- Medicaid

- 17P comes in a multi-dose vial, so it is not necessary to order a separate vial for each patient on 17P.
- You can use the same vial for multiple Medicaid patients. When ordering from www.mombaby.org, click "for office use" instead of providing patient information.
- Chart the lot number in the patient's record for each injection as you would with any multidose vial.

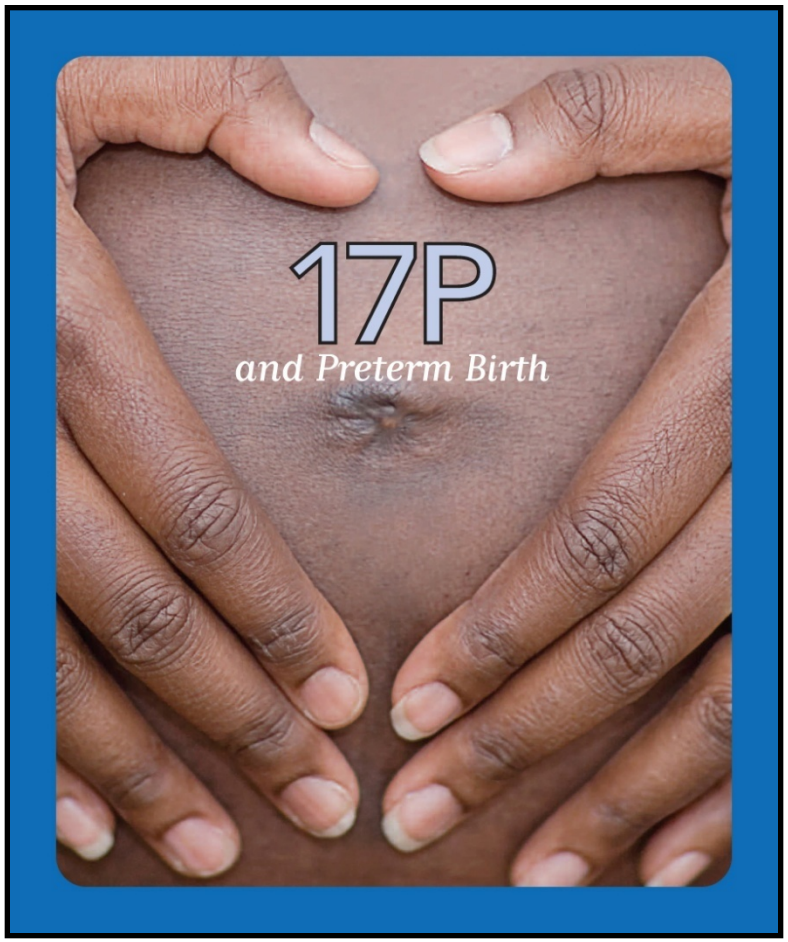
Billing

- Providers who order 17P for Medicaid patients must pay up front for the medication (approximately $90 per10-dose vial, $60 per 5-dose vial, or $15 per single-dose vial). The provider bills Medicaid $20 per dose plus the injection fee. Refer to the 17P 2009 Practice Bulletin for detailed information.
- Uninsured patients can receive 17P free from the NC 17P Project.
- All clinics who serve low-income women may order a free stock vial from www.mombaby.org, to have on hand in case a patient needs to start treatment quickly.
- Providers should submit the 17P invoice directly to private insurers.

More billing information -- Medicaid

- Local health departments must bill for 17P on paper CMS 1500 form, using J3490 code for miscellaneous drug AND the correct NDC code (from the invoice that came with that vial).
- An injection fee can be billed (CPT code 96372) if 17P is given as part of a prenatal visit or if the patient is only seen for the injection.
- 17P can be given as part of a skilled nurse home visit, but then the billing code is for the visit, not the injection code (T1001).
- 17P can be given as part of a nurse visit in clinic (CPT code 99211). You may not bill 99211 and 96372 together.

Resources



- Patient education materials (Eng/Span)
- Provider education materials
- Technical assistance in billing / protocol
- Advisory Council
- QI materials, forms, and project
- Video for mothers

Statewide Quality Improvement Initiative

- Goal to reduce variation in practice, ensure all women in North Carolina have access to 17P.
- 21 sites across the state (health depts, private OB offices, high-risk centers)
- Monthly webinars to identify best practices, troubleshoot challenges
- Data collection to identify systems issues and areas for improvement

17P Statewide Initiative: What are we trying to accomplish?

- Ensure all eligible patients get a recommendation for 17P regardless of where they receive prenatal care, and that patients on treatment get the right doses at the right time.
  - Are all new OB patients screened for 17P eligibility?
  - Do all eligible patients receive a recommendation for 17P treatment?
  - How many patients accept the recommendation, and why do some refuse?
  - Do patients on treatment get all doses according to treatment schedule? Why do some patients miss doses?
- What can we try to do differently to improve care?

Potential areas for improvement

- Provider acceptance of 17P
- Patient identification
- Patient counseling
- Billing for 17P
- Shared care – high risk clinics and local providers
- Compliance with full treatment regimen
  - Provider
  - Patient

Monthly data

	December	January	February	March
# of monthly reports submitted	12	15	15	15
# of new OBs	438	697	674	786
# screened for 17P eligibility	363	688	662	779
# eligible	16	39	41	44
# getting 17P recommendation	10	30	31	29
# accepting 17P	5	15	21	18

Reasons for refusal	Comments
The patient who refused stated that she didn't like shots and worked swing shifts so it would be difficult to keep appts.	one too late to start (28 weeks), one MD reviewed chart and did not recommend (previous PTB @ 36).
Others are **considering** treatment.	One declined; two are too early but will start.
one patient transferred out of county	1 pt undecided re: termination of pregnancy, 1 presented to care at 30 weeks
One declined; two are too early but will start.	2 are **considering** 17P, 3 - nothing was documented.
1 prior pt eligible - offered 17P and refused, she did not want shots.	one patient completed series of injections but hasn't delivered yet
Dr. mentioned 17P to one new OB who delivered twins at 28 wks. However the reason for PTL was twins not a single gestations; therefore not eligible.	1 pt at 7 wks - provider felt too early to offer 17P and prior PTD was at 36 wks
	2 prior pts eligible had a miscarriage in 1st trimester;
	We currently have 2 patients who are receiving 17P and 3 patients who are waiting to begin their injections. The patient who accepted the recommendation this month stated that her acceptance was **pending consult with the father of the baby.**

Patient tracking – Sample

Initiated	# of shots	Delivered	Comments
18 weeks	18	38.0	SVE 2cm at 29 weeks; 1 missed appt
18 weeks	20	39.1	
17 weeks	18	35.6	Last shot at 34 weeks
15.6 weeks	21	40.2	Last shot at 35.2 weeks
26 weeks	10	35.3	
16 weeks	20	36.2	Week 24 given in hospital
21 weeks	15	40	
16 weeks		22.4	Private pt. injected at home (sister)
16 weeks	16	37.3	
17 weeks	16	38.3	Missed dose during Christmas week

Patient tracking – sample

Initiated	# of shots	Delivered	Comments
		35.4	IUFD; private pt. injected at home
17 weeks	14	37.1	Shared care – high risk clinic/LHD
21 weeks	8	35.1	Noncompliance
18 weeks	4	22.0	
16 weeks		37.1	Private pt. injected at home; elective IOL!
16 weeks	18	37.0	Patient refused at weeks 34, 35
24 weeks	12	37.1	
16 weeks	19	34.6	
18 weeks	12	31.4	Accreta with vaginal bleeding
21 weeks	16	37.0	

Reasons for refusal	Other comments
One patient **wanted to discuss with father of baby**; 1 patient was referred to high-risk clinic.	Currently have 2 patients on 17P, one just starting, one has been receiving for several months. The other patient on 17P transferred out of county but was 35 weeks gestation at time of transfer.
Preferred just not to get 17P, was given all of information.	Providers at this facility feel intake at 5-6 weeks is too early to offer 17P.
All <16 weeks - plan to start.	4 patients waiting for MD evaluation.
One **pt has not decided** - not yet 16 weeks.	2 pts - MD felt too early to discuss 17P @ 5 weeks gestation. 1 pt entered care @ >24 weeks gestation, so not eligible per protocol.
It isn't necessary." "**Considering**." (pt is 6 weeks)	3 patients are "pending"
One patient eligible but no documentation regarding offering of 17P and wasn't screened.	Couldn't locate 2 charts to determine screening or eligibility.
Two are too early to order. One refused with past pregnancy (has a history of PTB at 34 weeks), went to 36.4.	Pt did not start 17P here because she was transferred to another clinic.

Advice from the field

- Use the www.mombaby.org website!
- Network with other programs that have had success in billing for 17P.
- Put everything into place (policy, billing, MD order, pt education, medication log) so you can screen patients and be ready for an eligible candidate
- Develop a consent/declination form
- Use the 17P materials from the NC 17P Project

Other Considerations

- 17P does not guarantee a full term pregnancy.
- Patients should be counseled at every visit about recognizing the signs of preterm labor.
- The benefits of partial therapy outweigh the risk of no therapy.
- Patients should continue to receive 17P during any antepartum hospitalizations, including for preterm labor.

Don't Forget – Primary Prevention Strategies

- Promote lifestyle modifications
  - Good nutrition
  - Cessation of use of tobacco, alcohol and drugs
  - Increase rest, lower stress
- Manage chronic conditions like diabetes or hypertension
- Screen for sexually transmitted infections
- Encourage routine dental exams
- Combat the effects of poverty, racism, and domestic violence

Questions?

- For questions about the NC 17P Project or to obtain a password to order 17P from www.mombaby.org, contact Kate Berrien, RN, BSN, MS, 919-843-9336, kberrien@unch.unc.edu.
- Learn more about the NC 17P Project and the NC Perinatal outreach program on www.mombaby.org: click on 17P and NC Initiatives.