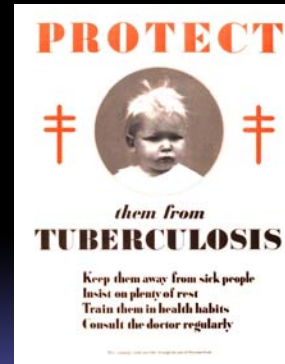


DIAGNOSIS AND MANAGEMENT OF TUBERCULOSIS IN THE PREGNANT PATIENT

Chia-Ling Nhan-Chang, MD, MS
Assistant Clinical Professor
Maternal Fetal Medicine
Department of Obstetrics and Gynecology
Columbia University, College of Physicians and Surgeons



American Lung Association, www.nlm.nih.gov

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Tuberculosis: Global Impact

- Over 900 million women worldwide have TB
- Men more likely to become infected, but women much more likely to progress to active disease
- In reproductive age women (15-44yo), TB contributes to 9% of all deaths
 - HIV/AIDS 3%
 - Heart disease 3%

Tuberculosis: Global Impact

- Worldwide, TB kills more women each year than any other cause of death
- Avoidance of TB or lack of access to medical care may contribute to 1 million deaths/year among TB in women

1 million deaths/year

Tuberculosis: US cases

Tuberculosis cases and deaths per 100,000 population

Year	Tuberculosis Cases			Tuberculosis Deaths				
	Number	Rate	Percent Change	Number ¹	Rate ¹	Percent Change		
1990	25,701	10.3	9.4	82	1,510	0.7	-8.1	-12.5
1991	26,283	10.4	2.3	0.9	1,713	0.7	-5.4	0.0
1992	26,673	10.4	1.5	0.1	1,705	0.7	-0.5	0.0
1993	25,107	9.7	-5.9	-7.1	1,031	0.6	-4.3	-14.3
1994	24,205	9.2	-3.6	-4.8	1,478	0.6	-9.4	0.0
1995	22,727	8.9	-6.1	-7.2	1,336	0.5	-8.6	-16.7
1996	21,210	7.9	-6.7	-7.8	1,202	0.5	-10.0	0.0
1997	19,751	7.2	-6.9	-8.0	1,166	0.4	-3.0	-20.0
1998	18,287	6.6	-7.4	-6.5	1,112	0.4	-4.6	0.0
1999	17,500	6.3	-4.3	-5.4	930	0.3	-16.4	-25.0
2000	16,309	5.9	-6.9	-7.8	776	0.3	-16.6	0.0
2001	15,945	5.6	-2.2	-3.2	764	0.3	-1.6	0.0
2002	15,055	5.2	-5.6	-6.5	784	0.3	2.6	0.0
2003	14,835	5.1	-1.9	-2.3	711	0.2	-10.2	-33.3
2004	14,459	4.9	-2.3	-3.2	682	0.2	-6.9	0.0
2005	14,068	4.8	-3.0	-3.9	648	0.2	-2.1	0.0
2006	13,732	4.6	-2.4	-3.3	644	0.2	-0.6	0.0
2007	13,286	4.4	-3.2	-4.2	554	0.2	-14.0	0.0
2008	12,905	4.2	-2.9	-3.8	560	0.2	6.5	0.0
2009	11,537	3.8	-10.6	-11.3	547	0.2	-6.5	0.0
2010	11,182	3.6	-3.1	-3.8				

Adapted from <http://www.cdc.gov/tb/statistics/reports/2010/pdf/Tables.pdf>

US-born vs Foreign-born

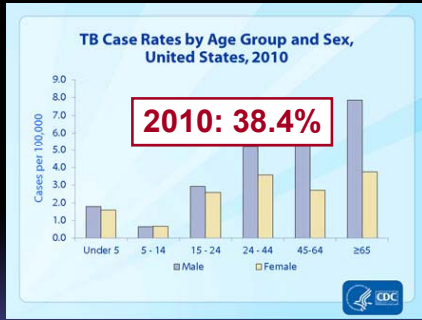
Table 5. Tuberculosis Cases, Percentages, and Case Rates per 100,000 Population by Origin of Birth: United States, 1993–2010

Year	Total Cases	U.S.-born Persons		Foreign-born Persons ¹		Unknown or Missing	
		No.	Rate	No.	Rate	No.	(%)
1993	25107	17438	7.4	7403	34.0	266	(1)
1994	24205	16191	6.9	7750	34.4	204	(1)
1995	22727	14676	6.2	7990	34.9	53	(0)
1996	21210	13398	5.8	7739	31.5	73	(0)
1997	19751	11936	5.0	7742	30.0	74	(0)
1998	18287	10634	4.4	7599	28.9	54	(0)
1999	17500	9898	4.0	7602	29.2	92	(1)
2000	16309	8548	3.5	7619	27.3	42	(0)
2001	15945	7872	3.2	8010	26.9	63	(0)
2002	15055	7282	2.9	7718	25.4	55	(0)
2003	14835	6981	2.7	7929	23.5	45	(0)
2004	14459	6832	2.8	7845	23.2	22	(0)
2005	14068	6309	2.5	7730	22.4	29	(0)
2006	13732	5881	2.3	7815	22.0	36	(0)
2007	13286	5482	2.1	7739	20.7	65	(0)
2008	12905	5254	2.0	7573	20.3	78	(1)
2009	11537	4275	1.7	6927	18.9	35	(0)
2010	11182	4383	1.8	6720	18.1	69	(1)

60%

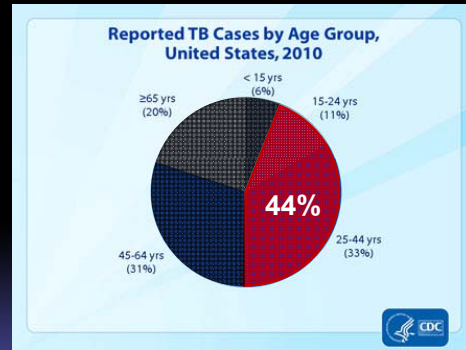
<http://www.cdc.gov/tb/statistics/reports/2010/pdf/report2010.pdf>

Tuberculosis: Global Impact



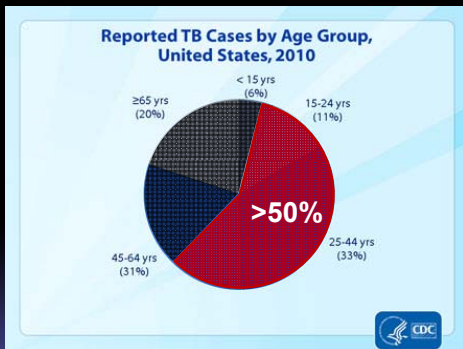
www.cdc.gov/tb/statistics/reports/2010

Tuberculosis: US cases



www.cdc.gov/tb/statistics/reports/2010

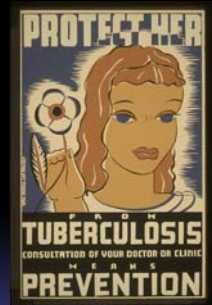
Tuberculosis: US cases



www.cdc.gov/tb/statistics/reports/2010

Tuberculosis in Pregnancy

- Historically, women with tuberculosis were offered termination of pregnancy
- Contemporary studies show that women with pulmonary TB who are treated appropriately do **not** have:
 - Increased rates of maternal complications
 - Neonatal complications



Schaefer G et al. *Obstet Gynecol.* 1975;46:706-715
 Jana N et al. *N Engl J Med.* 1999;341:645-649
<http://memory.loc.gov/ammem/wpaposters/wpahome.html>

Vertical Transmission

- Tuberculosis could be transmitted antepartum:
 - Fetal aspiration of infected amniotic fluid
 - Direct hematogenous spread through the placenta
- Intrapartum
 - Aspiration/ingestion of infected amniotic fluid or genital secretions
- Postpartum
 - Inhalation/ingestion of respiratory droplets

Kaplan C. et al. Am J Obstet Gynecol. 1980;137:858-860
Henderson CE et al. J Natl Med Assoc. 1993;85:685-687
Machin GA et al. Pediatr Pathol. 1992 Sep-Oct;12(5):707-16

Vertical Transmission

- *M. tuberculosis* identified in:
 - Amniotic fluid
 - Placenta (granulomas)
 - Autopsy in neonates
- Identification of TB granulomas in the placenta may reflect only maternal disease and not congenital tuberculosis

Kaplan C. et al. Am J Obstet Gynecol. 1980;137:858-860
Henderson CE et al. J Natl Med Assoc. 1993;85:685-687
Machin GA et al. Pediatr Pathol. 1992 Sep-Oct;12(5):707-16

Vertical Transmission

- There is a higher incidence of congenital TB in women who have extrapulmonary TB
- 15% of neonates sampled in first 3 weeks of life had TB bacilli
 - ? Either vertical or horizontal transmission

Pillay T et al. Clin Infect Dis. 1999;29(2):467-8
Pillay T et al. Lancet Infect Dis. 2004;4(3):155-65
Jones JL et al. Int J Tuberc Lung Dis. 2000 Nov;4(11):1026-31

Vertical Transmission

- TB in HIV+ pregnant women may increase risk of HIV in-utero transmission
 - 19% in-utero infection rate among 42 HIV/TB pregnant women compared to 5-10% in HIV
 - Patients who have access to HAART have perinatal transmission of <1%

Pillay T et al. Lancet Infect Dis. 2004;4(3):155-65
Jones JL et al. Int J Tuberc Lung Dis. 2000 Nov;4(11):1026-31
De Cock et al. JAMA 2000;283:1175-82
European Collaborative Study. Clin Infect Dis. 2005;40(3):458-65

What are the risks?



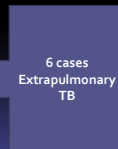
<http://memory.loc.gov/ammem/wpaposters/wpahome.html>

Tuberculosis in Pregnancy

- **Latent TB:**
 - No increased risk to fetus in utero
 - Postpartum risk of developing active TB
- **Active TB:**
 - Complications are controversial

Active TB in pregnancy

- **Higher prevalence than expected in epidemic communities**
 - **New York City 1985-1992**
 - Kings County Hospital and Saint Vincent's Hospital
 - 16 cases of active TB
 - 10 pulmonary TB
 - 2 meningeal TB
 - 1 mediastinal
 - 1 renal
 - 1 gastrointestinal
 - 1 pleural



Margono F et al. *Obstet Gynecol* 1994;83:911-4

Pulmonary Tuberculosis in Pregnancy

Study	Figuroa-Damian et al	Jana N et al	Schaefer G et al	Bejerkedal T et al	Ratner B et al
Number	35	79	68	542	55
Year of study	2001	1994	1975	1975	1951
Origin	Mexico	India	New York	Norway	New York
Prematurity	↑	↑	↔	↔	↑
Low birth weight	↑	↑	↔	↔	N/A
IUGR	↔	↑	N/A	N/A	N/A
Perinatal death	↑	↑	N/A*	↔	N/A*
Fetal distress	N/A	↑	N/A	N/A	N/A
Medical complications	↔	N/A	N/A	↑	N/A

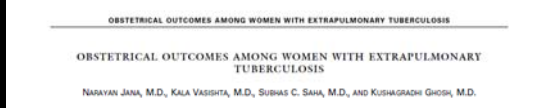
*Cases to be related to prematurity

<10th %ile

Figuroa-Damian R et al. *Archives of Med Research* 2001;32:66-69
 Jana N et al. *Int J Gynaecol Obstet* 1994 Feb;44(2):119-24
 Ratner B et al. *Am J Dis Child* 1951;31:471
 Schaefer G et al. *Obstet Gynecol* 1975;46:706
 Bejerkedal T et al. *Scand J Respir Dis* 1975;56:245

Extrapulmonary TB

- Extrapulmonary TB are associated with adverse maternal and neonatal outcomes



- In a report on the outcomes of 33 women with extrapulmonary TB:
 - 1983-1993
 - 29/33 were treated
 - Majority isoniazid, rifampin, and ethambutol for nine months
 - Compared with 132 healthy pregnant women

Jana N et al. N Engl J Med. 1999;341:645-649

Extrapulmonary TB: Methods of Diagnosis

<2,500gm

Outcome	Lymph-Node TB	Other extra-pulmonary sites	Control	P-value
Mean duration of gestation (weeks)	38.9±1.5	38.6±2.1	38.8±1.7	NS
Mean birth weight (kg)	3.4 (10%)	3.4 (10%)	3.4 (10%)	NS
Apgar score < 7 at 1 minute	0	2 (10%)	2 (2%)	NS
Congenital anomaly	0	2 (10%)	2 (2%)	NS
Perinatal death	0	2 (10%)	2 (2%)	NS

Extrapulmonary tuberculosis that is confined to the lymph nodes has no effect on obstetrical outcomes.

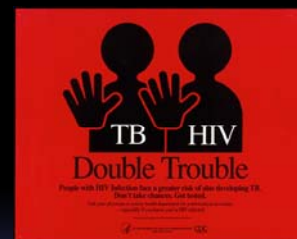
Jana N, et al. N Engl J Med 1999;341:645-9

Low Birth Weight

- Neonatal Complications:
 - Respiratory distress syndrome
 - Intraventricular hemorrhage (IVH)
 - Patent ductus arteriosus
 - Necrotizing enterocolitis
 - Retinopathy of prematurity
- Adult Complications:
 - Hypertension
 - Type 2 (adult-onset) diabetes
 - Heart disease
 - Birth were **10 times** more likely to have metabolic syndrome

March of Dimes

Impact of Concurrent HIV and TB



National Library of Medicine

Impact of Concurrent HIV and TB

- **Maternal outcomes**
 - Increased maternal deaths (Zambia, Durban, Malawi)
 - Secondary to TB, pneumonia, meningitis
 - Lower CD4 counts (compared with TB or HIV alone)
 - Higher antenatal admissions for complications
- **Fetal outcomes**
 - Increased perinatal death
 - Increased prematurity
 - Increased low birthweight
 - Increased SGA
 - Increased TB and HIV transmission to infant



Ahmed Y et al. *Int J Tuberc Lung Dis* 1999;3:675-80
 Khan M et al. *AIDS* 2001;15:1857-63
 Adhikari M et al. *Pediatr Infect Dis J* 1997;16:1108-12
 Wiebanga JE et al. *Malawi Med J* 1992;8:119-23
 Pillay T et al. *Lancet Infect Dis*. 2004;4(5):355-65

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Pregnancy in the US

- 6.4+ million pregnancies in 2005
 - 49-65% are unintended
 - 4.14 million live births
 - 1.21 million induced abortions
 - 1.06 million fetal losses
- Approximately 13% of all pregnant women are uninsured

http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_04.pdf

Pregnancy in the US

- Uninsured pregnant women:
 - Less likely to seek prenatal care in the first trimester
 - Less likely to receive the optimal number of visits during their pregnancy
- 31% higher likelihood of experiencing an adverse health outcome after giving birth
- Universal Prenatal Care Assistance Program (PCAP) is underutilized
 - Patient awareness
 - Undocumented immigrants afraid of deportation

www.acog.org

Prenatal Visits

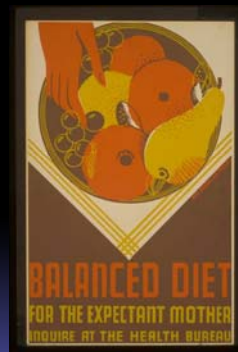
- Visits
 - <28 weeks: q 4 weeks
 - 28–36 weeks: q 2 weeks
 - >36 weeks: q week
- Ultrasound
 - First trimester (genetic screen 11-13 weeks)
 - Second trimester anatomy scan (17-23 weeks)
 - Third trimester scans only if chronic disease or Size ≠ Date

5-14
prenatal
visits

www.acog.org

Prenatal Visits

- Blood pressure
- Weight
- Urine dip
 - Protein
 - Glucose
 - Ketones
- Fundal height
- Fetal heart rate
- Edema



http://memory.loc.gov/janmem/wpaposters/wpahome.html

Monitor Weight Gain



TABLE S-1 New Recommendations for Total and Rate of Weight Gain During Pregnancy, by Prepregnancy BMI

Pregpancy BMI	Total Weight Gain		Rates of Weight Gain* 2nd and 3rd Trimester	
	Range in kg	Range in lbs	Mean (range) in kg/week	Mean (range) in lbs/week
Underweight (< 18.5 kg/m ²)	12.5-18	28-40	0.51 (0.44-0.58)	1 (1-1.3)
Normal weight (18.5-24.9 kg/m ²)	11.5-16	25-35	0.42 (0.35-0.50)	1 (0.8-1)
Overweight (25.0-29.9 kg/m ²)	7-11.5	15-25	0.28 (0.23-0.33)	0.6 (0.5-0.7)
Obese (≥ 30.0 kg/m ²)	5-9	11-20	0.22 (0.17-0.27)	0.5 (0.4-0.6)

KM Rasmussen and AL Yaktine, Editors; Institute of Medicine, 2009

Weight Gain in Pregnancy

TABLE S-1 New Recommendations for Total and Rate of Weight Gain During Pregnancy, by Prepregnancy BMI

Pregpancy BMI	Total Weight Gain		Rates of Weight Gain* 2nd and 3rd Trimester	
	Range in kg	Range in lbs	Mean (range) in kg/week	Mean (range) in lbs/week
Underweight (< 18.5 kg/m ²)	12.5-18	28-40	0.51 (0.44-0.58)	1 (1-1.3)
Normal weight (18.5-24.9 kg/m ²)	11.5-16	25-35	0.42 (0.35-0.50)	1 (0.8-1)
Overweight (25.0-29.9 kg/m ²)	7-11.5	15-25	0.28 (0.23-0.33)	0.6 (0.5-0.7)
Obese (≥ 30.0 kg/m ²)	5-9	11-20	0.22 (0.17-0.27)	0.5 (0.4-0.6)

* Calculations assume a 0.5-2 kg (1.1-4.4 lbs) weight gain in the first trimester (based on Siega-Riz et al., 1994; Abrams et al., 1993; Carmichael et al., 1997).

KM Rasmussen and AL Yaktine, Editors; Institute of Medicine, 2009

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- **Screening guidelines**
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Screening Strategy

- Unique time period in non US-born women
- Many non US-born women first access health care in the US during pregnancy
 - Ideal time period to reach out to the family and community and provide screening and care to immigrant population

Medchill MT. Am J Obstet Gynecol. 1999;180(6 Pt 1):1579-1583

Screening Strategy: CDC and ACOG

- Women with HIV infection
- Close contact with individuals known or suspected to have tuberculosis
- Medical risk factors known to increase risk of disease if infected
 - Lymphoma, diabetes mellitus, chronic renal failure
 - Immuno-suppression/chronic steroid use
 - Low BMI
- Born in country with high tuberculosis prevalence (HBC's)
- Medically underserved, low socioeconomic status
- Alcoholism
- Intravenous drug use
- Residents of long-term care facility
 - Correctional institutions
 - Mental institutions
 - Nursing homes and facilities
- Health care professionals working in congregate settings

CDC
ACOG Committee Health Opinion, Number 452, December 2009

Screening Strategy

- Universal screening programs:
 - Programs in the setting of prenatal care clinics may be more effective than risk based programs
- In a New York City clinic setting with a large immigrant population, universal screening was to be highly effective
 - Resulted in high TST read and treatment compliance
 - Hispanic and US-born women were less likely to be compliant
 - Asian women more likely to be compliant
 - Universal screening strategy also identified LTBI in 11.1% of US-born women
 - TST and chest X-ray compliance was lower when compared with non US-born women

Medchill MT. Et al. Am J Obstet Gynecol. 1999;180(6 Pt 1): 1579-1583
Schwartz N et al. Am J Perinatol. 2009;26: 447-451

Screening during Pregnancy: A unique opportunity

Missed Opportunities for Tuberculosis Prevention in New York City, 2003

Meredith E. Slopen, MSW; Fabienne Laraque, MD, MPH; Amy S. Platek, MS; Shama D. Ahuja, PhD, MPH

- 218 patients diagnosed with TB from April to July, 2003
 - Identified using the New York City TB registry
 - 160 (73%) patients had missed opportunities for screening in a community-based setting 1 year or more before TB diagnosis
 - 59 (37%) had 1 screening opportunity
 - 55 (34%) had 2 opportunities
 - 46 (29%) had 3 or more opportunities
 - 58 (27%) patients had no opportunity for prevention or screening

Slopen ME et al. J Public Health Manag Pract. 2011 Sep-Oct;17(5):421-6.

Screening during Pregnancy: A unique opportunity

- Of these 160 patients with missed opportunities
 - Administrative screenings:
 - NYC school (66 patients; 29% of screening opportunities)
 - Employment (40; 18%)
 - Pregnancy (51; 22%)
 - High risk screenings:
 - Drug rehabilitation programs (13 patients; 6% of screening opportunities)
 - Alcohol detoxification programs (9; 4%)
 - Homeless shelters (12; 5%)
 - Jails (24; 11%)
 - Nursing homes (13; 6%)

Slopen ME et al. J Public Health Manag Pract. 2011 Sep-Oct;17(5):421-6.

Screening during Pregnancy: A unique opportunity

- 21 screened patients (29%) were diagnosed with LTBI but not treated:
 - Pregnancy (40%)
 - Nursing home (38%)
 - Job-required examination (33%)

← 25% treated

Slopen ME et al. J Public Health Manag Pract. 2011 Sep-Oct;17(5):421-6.

Screening/Testing Methods



<http://memory.loc.gov/ammem/wpaposters/wpahome.html>

Screening: Tuberculin Skin Test



- The tuberculin skin test (TST) with **Mantoux technique** is the preferred tool to identify patients with LTBI
 - It has been validated for use in pregnant women
- Stimulate a T lymphocyte-mediated delayed type hypersensitivity response
 - Sensitization to mycobacterial antigens
 - Measurable cutaneous irritation 2 to 12 weeks after exposure

CDC, ACOG
Image www.wikipedia.org

Screening: Tuberculin Skin Test

Induration (mm)	Risk factor
≥5	<ul style="list-style-type: none"> •HIV infection •Close contact of active contagious case •Abnormal chest x-ray with radiographic changes consistent with old TB •Immunosuppressed patients: <ul style="list-style-type: none"> TNF-alpha inhibitors, chemotherapy, organ transplantation, glucocorticoid treatment
≥10	<ul style="list-style-type: none"> •Persons with clinical conditions that increase the risk of reactivation: <ul style="list-style-type: none"> Silicosis, chronic renal failure requiring dialysis, diabetes mellitus, Some malignancies (leukemias, lymphomas, carcinoma of the head, neck, or lung) •Underweight (≤9% ideal body weight), malnourished (jejunoileal bypass) •Injection drug users •Children less than 4 y of age •Foreign born from countries with high incidence of TB (HBC's) •Residents and employees in high risk settings, such as prisons, jails, healthcare facilities, mycobacteriology labs, and homeless shelters
≥15	<ul style="list-style-type: none"> •Healthy US born persons with low likelihood of true TB infection

CDC, ACOG

Interferon-Gamma Release Assays



- Interferon-gamma release assays (IGRAs)
 - Detection of cell-mediated immune response in a single sample
- Theoretical compliance is 100% of patients,
 - True screening rate may be as low as 84% owing to phlebotomy failure or clotted specimens
- The US Food and Drug Administration has approved the use of the QuantiFERON®-TB Gold (QFT-GIT) assay
 - Particularly in patients exposed to BCG vaccine
 - Prior infection with nontuberculous mycobacteria
- Supported by the CDC as the primary screening tool for LTBI
 - "May be used in all circumstances for which the Mantoux TST is indicated"

CDC, FDA
www.cellestis.com

Interferon-Gamma Release Assays: In Pregnancy

Kansas Journal of Medicine 2010	Quantiferon-TB Gold Assay
Use of the QuantiFERON®-TB Gold Assay in Pregnant Patients Bassem M. Chehab, M.D. ¹ , K. James Kallail, Ph.D. ² , Riad O. El Fakih, M.D. ³ , Rosalee E. Zackula, M.A. ⁴ , Garold O. Minns, M.D. ²	
¹ University of Kansas School of Medicine-Kansas City Department of Internal Medicine, Division of Cardiovascular Diseases	
² University of Kansas School of Medicine-Wichita Department of Internal Medicine	
³ University of Oklahoma College of Medicine Department of Internal Medicine	
⁴ University of Kansas School of Medicine-Wichita Office of Research	

Chehab BM. *Et al. KJM* 2010; 3(2):24-30

Interferon-Gamma Release Assays

- 152 women between ages 18 and 45
 - HIV negative
 - Concordant results between the tests were shown in 131 subjects (86.2%)
 - Pregnant women (102), 91.2% had concordant results
 - Non-pregnant women (50), 76% had concordant results
 - Significantly more discordant results occurred in non-pregnant women ($p < .022$).
- **Conclusion:**
 - QuantiFERON®-TB Gold assay is accurate to use in pregnant women
 - “The decision to use either test in pregnant women should be based mainly on the compliance of the patient to return to have the TST read”

Chehab BM. *Et al. KJM 2010; 3(2):24-30*

Interferon-Gamma Release Assays

MAJOR ARTICLE

Latent Tuberculosis Detection by Interferon γ Release Assay during Pregnancy Predicts Active Tuberculosis and Mortality in Human Immunodeficiency Virus Type 1-Infected Women and Their Children

Sasi Jonnalagadda,¹ Barbara Lehmann Payne,² Elizabeth Brown,³ Debra Wisniewski,⁴ Elizabeth Maricar-Ordoñez,⁵ Marcel Mujica,⁶ Casey Farquhar,⁷ Phylana Ottens,⁸ Dorothy Mwezi-Nyacha,⁹ and Gene John Staszak¹⁰

¹Department of Epidemiology, ²Neurology, ³Medicine, ⁴Global Health, and ⁵Pathobiology, University of Washington, Seattle, ⁶Treatment of Infections, University of Nairobi, and ⁷Trans-Medical Research Institute, Nairobi, Kenya

- 333 women tested (cryopreserved blood)
 - 52 (15.6%) had indeterminate IGRA results
 - 281 women with interpretable results

Jonnalagadda S *et al. J Infect Dis. 2010 Dec 15;202(12):1826-35.*

Interferon-Gamma Release Assays

- 120 (42.7%) Positive
 - Associated with a 4.5-fold increased risk of active tuberculosis (aHR 4.5; 95% CI, 1.1-18.0)
 - In patients with CD4 cell count, <250 cells/ μ L, positive IGRA results were associated with increased:
 - Maternal mortality (aHR 3.5; 95% CI, 1.02-12.1)
 - Maternal active TB or mortality (aHR 5.2; 95% CI, 1.7-15.6)
 - Infant active TB or mortality (aHR 3.0; 95% CI, 1.0-8.9)
- **CONCLUSION:**
 - “Positive IGRA results for HIV-1-infected pregnant women were associated with postpartum active tuberculosis and mortality among mothers and their infants.”

Jonnalagadda S *et al. J Infect Dis. 2010 Dec 15;202(12):1826-35.*

After a Positive Screening Test



- Chest X-Ray
- Reassess for evidence of active TB
- Encourage family to be screened

Diagnostic Imaging in Pregnancy



- American College of radiology and American Congress of Obstetricians and Gynecologists
 - "No single diagnostic x-ray results in radiation exposure to a degree that threatens the developing preembryo, embryo, or fetus."

ACOG Committee Opinion. Number 299, September 2004
Brent RL. Semin Oncol. 1989;16:347-68

Diagnostic Imaging in Pregnancy

- 1-2 rad = 1.5-2.0 fold increase the risk of leukemia
 - 1 in 2,000 of leukemia exposed to ionizing radiation
 - 1 in 3,000 background rate
- 100 rad = 40% risk of mental retardation
- 150 rad = 60% risk of mental retardation

20-40 rad

Brent RL. Semin Oncol 1989;16:347-68.
Hall E.J. Radiographics 1991;11:509-18.

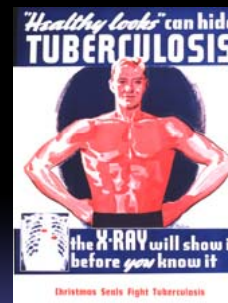
Diagnostic Imaging in Pregnancy

Procedure	Fetal exposure
Chest X-ray (2 views)	0.02-0.02 mrad
Abdominal film (single view)	100 mrad
Hip film (single view)	200 mrad
Mammography	7-20 mrad
Intravenous pyelography	≥ 1 rad
Barium enema or small bowel series	2-4 rad
CT scan of head or chest	<1 rad
CT scan of abdomen and lumbar spine	3.5 rad
CT pelvimetry (low exposure technique)	250 mrad

Cunningham FG et al. Williams Obstetrics 21st ed. NY; McGraw-Hill; 2001.

X-Ray in Pregnancy

- Informed consent
- Double lead shielding of abdomen
- After 15 weeks
- "Thick" slice protocol



<http://www.nlm.nih.gov/exhibition/visualculture/tuberculosis.html>

Testing in Pregnancy: Cultures

- **Culture**
 - The gold standard for the diagnosis of pulmonary TB
 - Take 2 to 10 weeks
- **Method:**
 - Three sputum specimens
 - Sputum induction with inhalation of hypertonic saline or bronchoscopy (those who are unable to provide sputum)
 - An acid-fast bacillus stain (AFB) on a smear immediately

Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med. 2000;161(4 Pt 1): 1376–1395.

Testing in Pregnancy: Cultures

- **Other sources for culture:**
 - Early morning gastric aspirate
 - Pleural fluid
 - Blood or the body fluid
 - Tissue biopsy from the organ of clinical suspicion
 - Amniotic cavity

Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med. 2000;161(4 Pt 1): 1376–1395.

Testing in Pregnancy: Cultures

Extrapulmonary Site	Method of Diagnosis
Lymph nodes	Fine-needle or surgical biopsy
Intestines	Laparotomy or fine-needle or endoscopic biopsy
Skeleton	Radiography of bones and joints
Kidney	Urinalysis and intravenous pyelography
Meninges	Cerebrospinal fluid analysis
Endometrium	Placental biopsy or amniotic fluid

Jana N, et al. N Engl J Med 1999;341:645-9

Testing in Pregnancy

- **Rapid Assay**
 - 2 to 7 hour turnaround time
 - Nucleic acid amplification technology (NAAT)
 - RNA based
 - Gen-Probe MTD: Gen-Probe Incorporated, San Diego, CA
 - DNA PCR based
 - Amplicor Mycobacterium tuberculosis test: Roche Diagnostic Systems, Inc., Branchburg, NJ
 - Anyplex MDR TB test: detect the mutations of drug-resistant genes to rifampicin, (INH), and inhA promoter: (Seegene, Korea)
 - The sensitivity and specificity of the rapid assays have mixed reviews; therefore, these tests support but do not replace the standard culture
 - NAAT results may remain positive for months after treatment due to the presence of dead mycobacterium

Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med. 2000;161(4 Pt 1): 1376–1395.

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- **Signs and symptoms of TB in pregnancy**
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Signs & Symptoms



“Great Masquerader”

<http://danceofthemasks.blogspot.com/2010/10/la-traviata-by-giuseppe-verdi.html>

Signs

- The clinical presentation of TB in pregnancy is similar to that of non pregnant women
 - **Fever**
 - Cough
 - Night sweats
 - Anorexia
 - Weight loss
 - General malaise & weakness
- May have fewer of the typical TB symptoms
- 20-67% of pregnant patients with pulmonary TB unaware of their disease and without significant symptoms
 - Pulmonary signs and symptoms are present in only one-third of the patients

Extrapulmonary TB: Common Sites

- Lymph glands
- Pleura
- Genito-urinary tract:
 - Uterus and fallopian tubes
 - Kidney and bladder
- Skeletal (both bones and joints)
- Meninges
- Bowel and/or peritoneum
- Pericardium
- Skin

↑HIV

Extrapulmonary TB: Presenting symptoms

- Of note, extrapulmonary TB has presented during pregnancy as:

- Perineal abscesses
- Degenerating leiomyomata
- Ascites
- Nausea and vomiting
- Back pain
- Neurologic deficits
- Paraplegia

Genital, Urinary and
Peritoneal TB

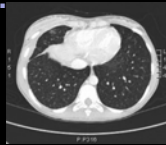
Meningeal and Spinal TB

Extrapulmonary TB: Case Report

- Recent case report
- 24-year-old African native woman arrived in Italy at 23 weeks
 - C/o frequency, urgency, dysuria and macroscopic hematuria. Treated with oral cephalosporin for a presumed UTI.
 - A few days later, represented c/o fever, low back pain, suprapubic heaviness and headache
 - Admitted for treatment of presumed pyelonephritis and developed vaginal bleeding and uterine contractions.
 - During hospitalization, developed a non productive cough
 - Developed progressive anemia, leukocytosis

Pasticci MB et al. New Microbiol. 2011 Jul;34(3):327-30

Extrapulmonary TB: Case Report

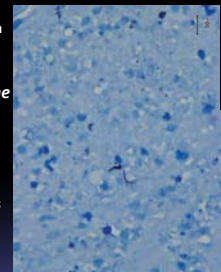


- Recent case report
 - Tested positive for influenza A/H1N1v on naso-pharyngeal secretions
 - Chest radiograph demonstrated right lower lobe infiltrate with pleural effusion
 - Treated with: Ceftriaxone, azithromycin, oseltamivir
 - Developed uterine contractions and vaginal bleeding persisted. Given betamethasone for fetal lung maturity and atosiban for tocolysis
 - HIV, syphilis, hepatitis, toxoplasmosis, leishmaniasis, malaria, and Herpes 2 tests were negative.
 - IgG for Cytomegalovirus, Herpes1 and Rubella were positive
 - Negative blood, urine, cervical, urethral and vaginal bacterial cultures

Pasticci MB et al. New Microbiol. 2011 Jul;34(3):327-30

Extrapulmonary TB: Case Report

- Amniocentesis was performed and acid-fast bacilli were identified
 - M. tuberculosis confirmed with DNA amplification
- Anti-TB therapy (isoniazid, rifampin and ethambutol) was started and labor induced
- Pansusceptible *M. tuberculosis* grew from the amniotic fluid while blood, respiratory and urine cultures were negative
- Delivered premature infant at 23 3/7 weeks
 - RDS, chronic lung disease, intraventricular hemorrhage, retinopathy of prematurity, hyperbilirubinemia and neonatal tuberculosis (pulmonary)
- Final diagnosis:
 - acute miliary tuberculosis complicated by deciduitis, sub-chorionitis



Pasticci MB et al. New Microbiol. 2011 Jul;34(3):327-30

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- **Treatment guidelines**
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

LTBI in Pregnancy

- Post-partum treatment
- Exceptions:
 - Women with HIV
 - Women with close recent contact with a patient with active TB
 - Women who have had a skin test conversion within the last 2 years

Treatment for LTBI in Pregnancy: Why wait?

- Unfounded fear of teratogenicity and toxicity to the fetus
- Low risk of LTBI to mother and fetus during the pregnancy

Bogges KA et al. *Obstet Gynecol.* 2000;96(5 Pt 1):757-762
Cruz CA et al. *Am J Obstet Gynecol.*2005;192:1455-1457

Treatment of LTBI in Pregnancy: Why wait?

- The postponement of treatment to the postpartum period may result in delay and loss of follow-up for a large number of patients

Bogges KA et al. *Obstet Gynecol.* 2000;96(5 Pt 1):757-762
Cruz CA et al. *Am J Obstet Gynecol.*2005;192:1455-1457

Post-partum compliance

- Compliance with post-partum treatment:
 - In a San Francisco clinic population
 - 42% compliance** with a follow-up visit in their TB clinic
 - 18% overall treatment completion rate**
 - Reasons for non-compliance:
 - Lack of treatment referral (31%)
 - Failure to keep referral appointment (18%)
 - Non-adherence with prescribed treatment (35%)

Cruz CA et al. Am J Obstet Gynecol.2005;192:1455-1457

Important Strategy:

- Current approach strategy for LTBI:
 - Referral for treatment
 - Aggressive follow-up on the part of the prenatal care provider
 - Involvement of cultural case managers
 - Directly observed preventive therapy programs

Boggess KA et al. Obstet Gynecol. 2000;96(5 Pt 1):757-762
Cruz CA et al. Am J Obstet Gynecol.2005;192:1455-1457

Why wait? "It's too expensive"

- Cost-Effectiveness:
 - Markov decision-analysis model comparing antenatal to postpartum INH treatment strategies
 - Assumptions:
 - INH started at 20 weeks gestation for 6 months
 - 67% completion rate
 - 0.1% serious hepatitis
 - 0 fetal deaths from hepatitis
 - Showed an overall marginal **increase in life expectancy** despite an increased risk of side effects in the antenatal treatment group

Boggess KA et al. Obstet Gynecol. 2000;96(5 Pt 1):757-762

Cost-Analysis

Table 2. Predicted Cases of Tuberculosis Within the Cohort, Cases Secondary to Horizontal Transmission, Cases of Fatal and Nonfatal Hepatitis, and Discounted and Undiscounted Total Costs and Life Expectancy

Assumption and Strategy	Cases of TB per 100,000 within the cohort	Additional cases secondary to horizontal transmission	Total TB cases presented vs. no treatment	TB deaths	Cases of TB-related hepatitis	Hepatitis deaths	Undiscounted total cost (\$)	Discounted life expectancy (y)	Total costs discounted at 5% annually (\$)	Life expectancy discounted at 5% annually (y)	Incremental cost/life-year saved (discounted) (\$)
Case-fatality rate 0%											
age 20-34											
Antepartum	1403	1744	4098	4	200	2	33.9 million	37.1	22.4 million	26.7	...
Postpartum	1790	2147	3539	0	90	0	30.1 million	37.1	24.8 million	26.7	Dominated
No treatment	3316	3979	...	0	0	0	75.1 million	37.1	64.2 million	26.7	Dominated
Case-fatality rate 0.1%											
age 20-34											
Antepartum	1403	1744	4098	0.9	200	2	28.1 million	37.2	19.4 million	26.7	...
Postpartum	1790	2147	3539	1.2	90	0.9	40.3 million	37.2	30.4 million	26.7	476,988
No treatment	3316	3979	...	2.3	0	0	57.2 million	37.2	37.3 million	26.7	1,324 million



- Antepartum treatment was the least expensive.
- At 1% rate of case-fatality:
 - Antepartum treatment resulted in a marginal increase in life expectancy
- At 0.1% rate of case-fatality:
 - Antepartum treatment become the least advantageous strategy

Boggess KA et al. Obstet Gynecol. 2000;96(5 Pt 1):757-762

Active TB in Pregnancy



- **Treat! Treat! Treat!**
- **Maternal and fetal benefits outweigh any potential harm to fetus**
 - **Beware of organogenesis in early first trimester**

Treatment -1st Line Agents

Medication	Dose	Maternal Effects	Pregnancy
 Isoniazid	Latent TB* : 300 mg per day for 9 months Active TB* : 15 mg/kg per day After 2 mo: 15 mg/kg, twice a week * Take with 25mg Pyridoxine per day	Hepatic dysfunction Hepatitis Gastrointestinal upset Peripheral neuropathy Skin reactions Anemia, thrombocytopenia CNS symptoms	Pregnancy risk factor – C Breastfeeding – Probably safe Crosses placenta Embryocidal in rat and rabbit studies No teratogenic effect in humans identified
 Rifampin	Latent TB : 10 mg/kg (maximum 600 mg) per day in patients who are not taking Isoniazid Active TB : 10 mg/kg (maximum 600 mg) per day Or 15 mg/kg 3 times a week	Hepatic dysfunction Hepatitis Skin reactions Gastrointestinal upset Anemia, thrombocytopenia Fever Flu-like symptoms	Pregnancy risk factor – C Breastfeeding – Compatible Crosses placenta Teratogenic in rat and mice studies in high doses No teratogenic effect in humans identified Associated with neonatal hemolytic anemia. Recommend vitamin K to neonate at birth

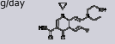
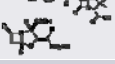
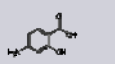
CDC, Micromedex
GG Briggs et al. *Drugs in pregnancy and lactation: Eighth Ed. Lippincott Williams & Wilkins*

Treatment -1st Line Agents

Medication	Dose	Maternal Effects	Pregnancy
 Ethambutol	Latent TB with HIV : 15 mg/kg per day Active TB : 15 mg/kg per day, 30 mg/kg per day for meningeal TB 30-50 mg/kg 2-3 times a week (extended for 12 months)	Optic neuritis Decreased color discrimination Skin reactions Gastrointestinal upset	Pregnancy risk factor – C Breastfeeding – Compatible Crosses placenta Teratogenic in animal studies in high doses No teratogenic effect in humans identified
 Pyrazinamide	Active TB : 25 mg/kg (maximum 2gm) per day Or 50 mg/kg 3 times a week	Hepatic dysfunction Hepatitis Gastrointestinal upset Arthralgia, Myalgia, Malaise Gout	Pregnancy risk factor – ??? Breastfeeding – Probably safe Limited data Not used in US No animal studies No teratogenic effect in humans reported

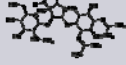
CDC, Micromedex
GG Briggs et al. *Drugs in pregnancy and lactation: Eighth Ed. Lippincott Williams & Wilkins*

Second Line Agents (MDR-TB, XDR-TB)

Medication	Maternal Effects	Pregnancy
 Fluoroquinolones Ciprofloxacin 500mg twice daily or ofloxacin 400 mg/day	1% to 10%: dizziness, insomnia, nervousness, somnolence, fever, headache Rash, Nausea, diarrhea, elevation of liver enzymes	Pregnancy risk factor – C Breastfeeding - Manufacturer: not recommended, American Academy of Pediatrics: compatible in low doses Cipro crosses placenta Animal studies -> damage articular cartilage and juvenile arthritis Human exposure during the first trimester -> no musculoskeletal but a trend for higher rate of medical abortion
 Amoxicillin-clavulanic acid	>10%: Gastrointestinal effects 2% to 10%: Rash, urticaria, nausea, vomiting, vaginitis	Pregnancy risk factor – B Breastfeeding - Enters breast milk/use with caution There are no data on the use of clavulanic acid in early pregnancy In the second and third trimester, this has been used as antibacterial prophylaxis in preventing infection following premature rupture of membranes with an increased incidence of neonatal enterocolitis
 Paraaminosalicylic acid	10-30% Gastrointestinal effects 5-10% hypersensitivity rash Rare: pericarditis, vasculitis, Encephalopathy, fever, goiter, agranulocytosis, anemia, leukopenia, thrombocytopenia, Hepatitis, jaundice	Pregnancy risk factor – C Breastfeeding - Enters breast milk/not recommended Collaborative Perinatal Project identified 43 women who had been exposed to the drug in the first trimester with 5 babies showing various malformations. A subsequent study identified an inconsistent association with limb and ear abnormalities

CDC, Micromedex
GG Briggs et al. *Drugs in pregnancy and lactation: Eighth Ed. Lippincott Williams & Wilkins*

Medications Not Used

Medication	Pregnancy
Streptomycin 	Pregnancy risk factor – D 1 in 6 risk of hearing impairment and irreversible congenital deafness in offspring of women who were treated with streptomycin in pregnancy (any trimester)

Robinson GC et al. *N Engl J Med* 1964; 271: 949-51
 Varpela E, et al. *Scand J Respir Dis* 1969; 50: 101-9
 Scheinhorn DJ et al. *West J Med.* 1977 Sep;127(3):195-8
 Snider DE Jr et al. *Rev Respir Dis* 1980; 122: 65-79

Monitoring in Pregnancy

Medication	Monitoring	Special Consideration
Isoniazid	Liver function testing Complete blood count	Antacids reduce absorption Take with Pyridoxine
Rifampin	Liver function testing Complete blood count	Turns secretions orange Take on an empty stomach
Ethambutol	Check color vision and acuity	Unilateral ophthalmology exam
Pyrazinamide	Liver function testing Uric Acid	

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- **Postpartum care and breastfeeding**
- Family planning strategies
- Deficits in research

Breastfeeding



- **Breastfeeding is the preferred method of feeding for newborns and infants**
- **The ACOG recommends that exclusive breastfeeding be continued until the infant is 6 months old**

ACOG Committee Opinion, Number 361 • February 2007

Breastfeeding

- Breast milk does not contain tuberculosis bacilli
- TB is a respiratory disease transmitted by aerosol droplets
 - Concern for horizontal transmission

Breastfeeding

- Latent TB:
 - No contraindication to breastfeeding
- Active TB:
 - Highest risk periods for transmission from mother to baby
 - Close respiratory proximity to the baby
 - A mother with newly diagnosed untreated active disease should be separated from her infant to prevent respiratory exposure/transmission, regardless of mode of infant feeding
 - Resume her breast-feeding after anti-TB medications have begun and negative sputum cultures are documented

Breastfeeding



- Contact insurance
 - Low or no-cost equipment
 - Hospital grade rentals

www.medela.com, www.aetna.com

Breastfeeding: Exceptions

- Exceptions are women:
 - Who take street drugs or do not control alcohol use
 - Have an infant with galactosemia
 - Infected with human immunodeficiency virus (HIV) or human T-cell lymphotropic virus type I or type II
 - Active untreated tuberculosis
 - Active varicella
 - Active herpes simplex virus with breast lesions

ACOG Committee Opinion, Number 361 • February 2007

Postpartum Period

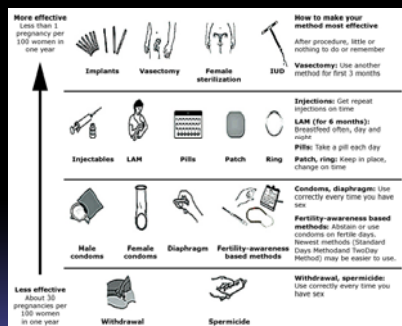
- Family planning strategies should be initiated during prenatal care
 - Give information about methods and services that will help them meet their reproductive goals

ACOG Committee Opinion, Number 361 • February 2007

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
 - Prenatal care in the United States
 - Screening guidelines
 - Signs and symptoms of TB in pregnancy
 - Treatment guidelines
 - Postpartum care and breastfeeding
 - Family planning strategies
 - Deficits in research

Contraception



Surgical Contraception

- Bilateral Tubal ligation
 - Post-partum mini-laparotomy
 - During cesarean delivery
 - Laparoscopic tubal ligation
- Bilateral Tubal occlusion
 - Essure® method

Blocking the tubes

Essure is a procedure where a doctor inserts spring-like coils, called micro-inserts, through the vagina, cervix and uterus and into the fallopian tubes. The procedure is performed. It is an outpatient operation that requires no incisions or anesthesia.

Using a hysteroscope, a doctor places a micro-insert into the fallopian tube. The micro-insert expands, filling the tube. Doctor removes scope, leaving micro-insert in place.

During the next three months, scar tissue grows around the micro-insert, creating a blockage that sperm can't penetrate.

After three months, a test is repeated in the uterus, and a special type of x-ray confirms that the tubes are blocked.

Source: www.essure.com

Hormonal Contraception

- **Pills**
 - Typical use: 92 %
 - Not contra-indicated with breast-feeding
- **Progestin-only "mini" pill**
 - Typical use: 92 %
 - Preferred method with breast-feeding
- **Transdermal Patch**
 - Ethinyl estradiol and norelgestromin
 - Typical use: 92 %
- **Vaginal contraceptive ring "Nuvaring"**
 - Ethinyl estradiol and etonogestrel
 - Typical use: 92 %

Hormonal Contraception

- ~~**Pills**~~
 - Typical use: 92 %
 - ~~Not contra-indicated with breast-feeding~~
- ~~**Progestin-only "mini" pill**~~
 - Typical use: 92 %
 - Preferred method with breast-feeding
- ~~**Transdermal Patch**~~
 - Ethinyl estradiol and norelgestromin
 - Typical use: 92 %
- ~~**Vaginal contraceptive ring "Nuvaring"**~~
 - Ethinyl estradiol and etonogestrel
 - Typical use: 92 %

Rifampin:
Back-up method recommended

Hormonal Contraception

- **Implants:**
 - **Implanon (subcutaneous)**
 - Typical use: 99%
 - Single-rod progestin implant
 - Contraception is provided for 3years
 - Protection from pregnancy occurs within 24 hours
 - Fertility returns rapidly after removal of the rod
 - Pregnancies have been reported post-marketing
 - Manufacturer: 0.38 pregnancies/100 women-years of use
 - **Mirena (intrauterine)**
 - Typical use: 99%
 - Intrauterine Levonorgestrel device
 - Approved for 5 years of use
 - Benefit of decreased menstrual flow or amenorrhea

Hormonal Contraception

- **Implants:**
 - **Implanon (subcutaneous)**
 - Typical use: 99%
 - Single-rod progestin implant
 - Contraception is provided for 3 years
 - Progestin only
 - Fertile
 - Pregnancy: 0.36 pregnancies/100 women-years of use
 - **Mirena (intrauterine)**
 - Typical use: 99%
 - Intrauterine Levonorgestrel device
 - Approved for 5 years of use
 - Benefit of decreased menstrual flow or amenorrhea

Rifampin:
Back-up method recommended

Other forms of Contraception

- **Condoms**
 - Male
 - Typical use: 85%
 - Female
 - Typical use: 79%
- **Copper IUD**
 - Approved for 10 years of use
 - Typical use: 97-99%
- **Cervical Cap**
 - Typical use: 84%
- **Spermicides**
 - Typical use: 78-90%
- **Withdrawal method**
 - Not reliable: 73-80%
- **Amenorrhea method**
 - The woman is less than six months postpartum
 - She is breastfeeding exclusively (ie, not providing food or other liquid to the infant)
 - She is amenorrheic
 - Typical use: 95%
- **Vasectomy**
 - Typical use: 99%

Infertility

- **1% and 10% of women with infertility have genital TB**
- **Genitourinary TB is usually caused by reactivation:**
 - ≤ 2 years following the primary infection by *M. tuberculosis*
 - Hematogenous or gastrointestinal spread

Nezar M et al. Arch Gynecol Obstet. 2009;280:787-791
Das P et al. Indian J Urol. 2008 Jul;24(3):356-61

Infertility

- **Women (cohort of 420 women) undergoing diagnostic laparoscopy for infertility:**
 - PCR of peritoneal fluid and biopsy specimens identified evidence of TB in 5.7%
- **Women with nongenital tuberculosis and genital tuberculosis frequently have menstrual disorders:**
 - Amenorrhea
 - Oligomenorrhea

Nezar M et al. Arch Gynecol Obstet. 2009;280:787-791.

Infertility

- Lead to salpingitis & impairment of cilia
 - Overcome with artificial reproductive technology (ART)
- May be of concern in the future if undiagnosed
 - -Presentation when immuno-compromised

Tuberculosis in Pregnancy

- Tuberculosis in Reproductive Aged Women
- Prenatal care in the United States
- Screening guidelines
- Signs and symptoms of TB in pregnancy
- Treatment guidelines
- Postpartum care and breastfeeding
- Family planning strategies
- Deficits in research

Research

- Evaluation of drug safety and pharmacokinetics in pregnancy
 - PZA
- Assessment of drug resistance
 - Emerging drug resistance during pregnancy or the postpartum period

Research

- Cost-Analysis
 - Antepartum versus postpartum treatment
 - HIV-1 infected women
- Use of QuantiFERON®-TB rapid testing
 - Large scale for compliance
 - Non cryo-preserved blood
 - At delivery to late presenting women
 - Similar to Rapid HIV

Thank You



www.sciencemuseum.org.uk
<http://protomag.com/assets/public-health-posters-gallery>