MATERNAL TUBERCULOSIS
Michael Kessler, MD

Tuberculosis is a global menace that has been around since antiquity. It is a bacterial infection caused by Mycobacterium tuberculosis. With the advent of effective medication in the early 1950’s, the number of reported cases decreased by greater than 70%. However, this decline halted in the mid 1980’s secondary to the spread of HIV.

Approximately one third of the world’s population is infected with tuberculosis. The highest mortality rates are in Africa and 33% of total cases are from South East Asia. In the United States there are 10-15 million Americans living with the disease. The rates of tuberculosis in the Hudson Valley in 1994 ranged from 6.6 to 13.9 per 100,000. As of 2005, the rate of new tuberculosis cases fell to an average of 4.7 per 100,000 in the Hudson Valley. Incidentally, Rockland County had the highest rate of new TB cases with Ulster and Putnam having the lowest.

Tuberculosis was once thought to have a sinister impact in pregnancy. This tenet was proven to be false with the advent of modern chemotherapy. In addition there is no risk to the fetus as tubercle bacilli rarely cross the placenta. There have been reported cases of congenital tuberculosis, however, in many of these cases the patients had extrapulmonary tuberculosis and were not treated. There is little if any teratogenic risk from a majority of the current medications used to treat tuberculosis.

In order to eradicate TB we must target latent tuberculosis infection (LTBI). The latter represents a clinical state in which the patient has been exposed to TB but does not have the disease. Continued on page 2

FETAL BREATHING MOVEMENTS: SOME CLINICAL OBSERVATIONS
Frank Manning, MD, Geetha Rajendran, MD, Michael Kessler, MD

Recently here at WMC we have cared for a pregnant patient who had Congenital Central Hypoventilation Syndrome (CCHS), a life-threatening condition characterized by the inability to establish and to maintain automatic breathing. Individuals with this condition will stop breathing when they fall asleep and unless stimulated will die. (This very rare condition was once called Ondine’s curse, named after a German fairy tale nymph who cursed the lover who betrayed her by making him stop breathing whenever he was not thinking of her and subsequently he died when he fell asleep.) CCHS is a genetic disorder caused by an excess number of repeats and is inherited as an autosomal dominant condition with variable gene expression. The genetic disorder present in our patient was found by amniocentesis to also be present in her fetus. This case was the first time that the fetal diagnosis of CCHS had ever been made and created the very unique clinical opportunity to monitor fetal breathing movements in the affected fetus and to extend our understanding of the regulation and control of these movements (1). We were able to determine that fetal breathing movements were normal in this affected fetus conforming to some of the following aspects of this unique fetal physiological event.

Notwithstanding that from antiquity mothers were aware that their unborn children periodically would make rhythmic movements, oft-times reported as hiccoughs and oft-times distinctly visible on the mother’s abdominal wall, until quite recently the prevailing medical science was that fetuses did not make breathing movements in utero but rather the first attempts at breathing occurred at delivery. In the early 1970’s the myth that fetuses did not breath was shattered by experiments that monitored tracheal pressure changes in the sheep and monkey (2, 3) and by direct observation of chest wall and diaphragm movements in the human fetus using real-time ultrasound (4). Thereafter, we have continued to extend our knowledge base regarding the genesis, regulation and clinical significance of fetal breathing (5). It is clear that the signals that initiate fetal breathing movements arise from a collection of respiratory neurons located in the ventral surface of the medulla and that as soon as these neurons appear they begin to function.

As a result, fetal breathing movements are invariably present in the fetus by 16 weeks gestation and can occasionally be seen as early as 10 weeks gestation. Continued on page 3
In 2000, the Center for Disease Control and The American Thoracic Society issued updated guidelines for targeted testing and treatment for LTBI. These recommendations apply to the pregnant population as well. Only patients who fall into a high-risk category should be screened. This group includes patients who have HIV, are recent immigrants to the US within the last five years and are residents of high-risk congregate settings. This group also includes health care providers and patients who use illicit drugs.

On average 50% of close contacts to patients with TB become infected. The lifetime risk of contracting TB after LTBI is 2-10% with the greatest risk being within the first two years. In patients with HIV who are not on Highly Active Anti-retro Viral Therapy, (HAART) the risk is 5-10% per year.

In 1969, Ferebee noted that there was a 68% reduction in tuberculosis activation in patients treated with INH. For those patients who did not receive treatment at the rate of TB activation was 12.8 per 1000 over 10 years. This enthusiasm for widespread LTBI treatment was overshadowed by several population-based trials that found drug-induced hepatitis in 0.15 – 2% of those treated, with death occurring in 0.001%. Unfortunately treatment for LTBI in pregnancy was also discouraged by a retrospective study in 1989 that showed a 2.5-fold increased risk of INH hepatitis and four-fold increased risk of death in pregnancy. Although the study outcomes did not reach statistical significance, the authors urged caution with the use of LTBI treatment in pregnancy. Common medical practice in pregnancy has thus been to delay treatment until the postpartum period.

In 2000, Boggess postulated that antepartum treatment of LTBI would be advantageous. However, this was based on a theoretical cohort of patients. But pregnancy does represent a unique opportunity to provide monitored LTBI treatment. From a public health perspective, an antepartum treatment strategy may result in fewer cases of TB, cost reduction, improved compliance and lessened risk of infant and child exposure. This theory has its merit based on a recent study by Kwara. He noted that patients with LTBI who are young, postpartum, and uninsured are less likely to be compliant with treatment – and this is the population that is at highest risk.

The Department of OB/GYN at the Westchester Medical Center is now evolving its practice in the treatment of LTBI during pregnancy. Toward achieving this goal we will be:

1. Screening pregnant women in the high-risk categories with Quantiferon rather than standard Tuberculin Skin Test (TST). This is to eliminate the potential for interobserver differences in the interpretation of the TST and the boost phenomenon in those patients exposed to BCG. Because Quantiferon is a blood test, there will be no need to have the patient return for a 48-72-hour follow-up.
2. Utilizing the current CDC guidelines set forth to monitor patients both clinically and with laboratory testing.
3. Establishing a registry to follow those patients on therapy and to prospectively study their outcomes.

It is our goal that by implementing these strategies that we can effectively begin to reduce the incidence of new tuberculosis cases in the Hudson Valley.

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References:

PERINATAL OUTREACH COORDINATOR

Westchester Medical Center Perinatal service is seeking a highly motivated Registered Nurse to fill the position of Perinatal Outreach Coordinator.

This position offers an exciting opportunity to join a dynamic, rapidly expanding high-risk obstetrical division offering world-class obstetrical medicine.

Responsibilities include: Maintaining & improving communication between the Regional Perinatal Center (RPC) and its affiliate obstetrical services within our 7 county region; On-site assessment/telephone consultation regarding current standards of obstetrical care; Develop/implement/facilitate outreach education programs on high-risk OB patients for our affiliates; Working collaboratively with L&D personnel and the RPC team relating to maternal transport quality improvement issues; Collection/analysis of WMC maternal statistical data; Participation in RPC quarterly QA Quadrant meetings at affiliate hospitals & the Regional Perinatal Forum.

Qualifications: Masters prepared with at least 5 years recent acute care obstetrical experience; Certification in Inpatient Obstetrical nursing preferred. Preference will be given to candidates with outreach experience.

If interested please contact Melissa Verde at 914-493-7808.

NEW!

Regional Perinatal Center Website
www.worldclassmedicine.com/rpc

What is an RPC? Who is the team? What do we do?
Who are our affiliates? Interested in a mini-grant?

Please visit our website for answers to these questions and for more information about the RPC at Westchester Medical Center.

RPC Mini-Grant Awards

The Regional Perinatal Center at Westchester Medical Center has awarded three mini grants for 2008-09.

CONGRATULATIONS to the following recipients

Hudson Valley Hospital Center – Traveling Health Fair
Lower Hudson Valley Perinatal Network – Community Health Education Day, Breastfeeding
Planned Parenthood Hudson Peconic, Inc. – Increasing Access to Prenatal Care in Westchester County for Underserved, Low Income & Spanish Speaking Women
In the fetus the frequency of discharge of the respiratory neurons is modulated by a host of normal and abnormal physiological variables and by exogenous variables introduced from the maternal environment. Variation in fetal sleep-wake cycles are the most significant modulating variable in the normal fetal state. In quiet sleep, characterized by high voltage low frequency EEG activity and absence of rapid eye movements, the input from higher centers to the respiratory neurons is diminished and as a result the fetus will exhibit long periods of apnea (up to 40 minutes duration) and breathing movements, when present tend to be brief and breaths are typically slow in rate and deep in excursion. In contrast during active (REM) sleep, breathing movements are present for the most of the time and tend to be vigorous and rapid, and may sometimes demonstrate a crescendo pattern in rate and excursion. During fetal wakefulness, breathing movements tend to be regular and mimic the patterns seen in the awake but quiet newborn. In our patients with CCHS (the affected mother and subsequently her newborn) this pattern of periodic fetal breathing, with active breathing during wakefulness and apnea during sleep persisted. Thus, what is a normal phenomenon in the fetus with no pathophysiological consequences can result in death from respiratory failure in the newborn. In normal pregnancy the placenta regulates fetal gas exchange and as a result fetal oxygen and carbon dioxide values, while different from maternal values, are generally constant with very little variation. However when the fetus is exposed to an increase in carbon dioxide levels (hypercapnia) it will respond as the newborn does, with an increase in respiratory rate. In addition with hypercapnea the proportion of time the fetus spends breathing increases (diminished periodicity). Similarly fetal hyperglycemia (always a result of maternal hyperglycemia) will induce fetal breathing and sometimes can induce continuous fetal breathing and striking tachypnea. If left untreated these fetuses may often die in utero (6). The effect of lowering the blood oxygen (hypoxemia) on breathing movements is diametrically opposed between the fetus and the newborn. In postnatal life hypoxemia is a powerful stimulant to breathing. In contrast, in the fetus hypoxemia, even when very minimal, induces fetal apnea. This fetal response forms the basis for why fetal breathing movements are included as an intrical part of fetal biophysical profile scoring (7). Since making breathing movements requires an expenditure of energy for the fetus yet is not required for exchange of gases, the benefit of activity to the fetus requires some consideration. At least two major advantages to the fetus can be identified. First, as in all aspects of fetal development there is a reciprocal relationship between structure and function. If the developing fetal lung is not subjected to the distorting forces of chest wall and diaphragm movements or if these torsion forces are damped by compression in the presence of oligohydramnios normal development will not occur and pulmonary hypoplasia may ensue. It must also be true that if the muscles that propel respiration are not regularly exercised then function at birth would be compromised. Thus it seems likely that prenatal practice is essential for postnatal survival. Secondly, fluid is continuously produced in the periphery of the fetal lung and by a mechanism of lateral crowding flows up the airways to the pharynx to be then either swallowed or expelled through the nodes and mouth. Fetal breathing movements are generally not of sufficient force to move the fluid column in the airways. However, periodically the fetus makes what appear to be a sighing-type respiratory effort, characterized by a short rapid inspiratory phase and then a slow prolonged expiratory effort. These occasional movements, independent of fetal sleep state, result in a visible gush of fluid out of the mouth and nose. It is probable that this type of breathing movement functions to clear the upper airways of amniotic fluid debris.

Thus fetal breathing movements are essential to maintain airway toilet. In fetuses with sustained pathologic apnea the airways are usually filled with debris and subsequently at birth, air exchange may be compromised. Sometimes a fetus may make large amplitude slow breathing inspiratory breathing movements. These movements usually occur against a closed glottis and therefore aspiration of amniotic fluid does not occur. However, occasionally the larynx does not close with inspiration and as a result aspiration of amniotic fluid and its contents (vernix, meconium) can occur. This abnormal fetal breathing pattern is the most likely explanation for meconium aspiration in utero (9).

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Cool Cap Exclusion Criteria:
- Infants > 6 hours of age
- Imperforate anus
- Evidence of head trauma or skull fracture causing major intracranial hemorrhage
- Birth weight < 1,800grams

If there is a possible brain insult at birth, provide basic cardiorespiratory support and maintain rectal temperature between 34-35 °C by turning off the radiant warmer, and applying ice packs (in plastic bags) to the sides of the head and the chest wall. Call the Westchester Medical Center Transfer Center as soon as possible at 866-468-6962. Discuss selective head cooling with the family, but make no promises regarding the use of cooling and the outcome of the baby. These are often the sickest infants, with multi-system involvement. Most importantly, initiation of selective head cooling must begin within 6 hours following hypoxia-ischemia, which may have started in utero. This requires prompt notification whenever hypoxia-ischemia is suspected, whether or not full manifestations are present, and even when this scenario is expected prior to delivery. The sooner the call is made, the quicker transport can be arranged.

For further information please contact Dr. Lance Parton at lanceparton@nymc.edu or Dr. Caroline Chua at carolineoehua@yahoo.com.
Selective Head Cooling for Acute Hypoxic Ischemic Encephalopathy - Cool Cap®

Perinatal asphyxia occurs in approximately 2-3/1000 births and may account for up to 30% of cases of cerebral palsy. Currently, there is no specific treatment for acute perinatal hypoxic–ischemic encephalopathy except for supportive care and pharmacological treatment of seizures. A new treatment modality has recently been approved by the FDA for babies at risk for developing this condition-selective head cooling with the Cool Cap®.

The Cool Cap® covers the scalp and contains tubing connected to a refrigerated cooler which circulates cold fluid of about 100-110˚C (50-51.8˚F). While the head is being selectively cooled, the core body temperature is carefully maintained between 34-35˚C (93.2-95˚F). Randomized controlled trials in full-term newborns suggest that treatment with mild hypothermia is effective and safe and may improve survival without disabilities up to 18 months of age, especially in newborns suffering from moderate encephalopathy.

The goal of selective head cooling is to preserve cerebral energy metabolism, reduce cerebral tissue injury and improve neurological function. A cascade of reactions follows hypoxia-ischemia. There may be primary energy failure of the brain, which could be so severe that permanent brain injury results. Alternatively, resuscitation may be successful so that limited or no injury results. Finally, limited primary energy failure may be followed by a latent phase, during which oxidative metabolism has normalized, but in which there is hyperactivity of the glutaminergic receptors (excitotoxicity), and the intracytoplasmic components of the apoptotic cascade are activated resulting in the initiation of a secondary inflammatory reaction. This may be followed by subsequent deterioration, which leads to delayed neuronal death after 72 hours. Animal studies have shown that there is a potential therapeutic window of 6 hours to initiate head cooling following hypoxia-ischemia, after which little therapeutic gains are realized. The head cooling is continued for 72 hours, with the goal of decreasing secondary deterioration and limiting the subsequent neuronal cell death.

ELIGIBILITY FOR TREATMENT AT MARIA FARERI CHILDREN’S HOSPITAL (MFCH)

Three criteria need to be satisfied (A, B and C) to qualify for head cooling:

A. Infants > 36 weeks gestation and at least one of the following:
   - Apgar score ≤ 5 at 10 min
   - Continued need for resuscitation, including endotracheal or mask ventilation, at 10 min after birth
   - Acidosis defined as either umbilical cord pH or any arterial pH <7.00 within 60 min of birth
   - Base deficit ≥ 16 mmol/L in umbilical cord blood sample or any blood sample within 60 min of birth (arterial or venous blood)

B. Moderate to severe encephalopathy, consisting of altered state of consciousness (lethargy, stupor or coma) and at least one of the following
   - Hypotonia
   - Abnormal reflexes including oculomotor or pupillary abnormalities
   - Absent or weak suck
   - Clinical seizures

C. Infant has an amplitude-integrated encephalogram/cerebral function monitor (aEEG/CFM) recording of at least 20 minutes duration that shows either moderately/severely abnormal aEEG background activity or seizure

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