



# Perinatal Gazette



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Westchester Medical Center

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## Prenatal Detection of Congenital Heart Disease



Advances in ultrasound technology and neonatal cardiac surgery in recent years has resulted in an increased number of pregnant women undergoing fetal cardiac ultrasound. In fact, at Children's Hospital of Westchester and our associated outpatient facilities, over 600 fetal echocardiograms were performed in the year 2000!

Generally, fetal echocardiograms are performed at 18-20 weeks EGA with the same technology and application as level 2 obstetrical ultrasounds. Indications for fetal echocardiography are many, and include a suspicion of heart disease by the OB ultrasound, a maternal history of heart disease, or a prior offspring with heart disease. A maternal history of non-cardiac disease may also be an indication. All mothers with Diabetes Mellitus undergo serial fetal echocardiography as there is a well-documented risk of myocardial hypertrophy/cardiomyopathy in those fetuses, thought to be secondary to the abnormal glucose and insulin levels present.

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## Multi-Center Clinical Trial: Early Treatment of Retinopathy Of Prematurity (ROP)

In the United States an estimated 1,300 infants annually develop Retinopathy of Prematurity (ROP) severe enough to require medical treatment. ROP is a leading cause of vision impairment. Clinicians who care for infants with ROP are inclined to treat this disease at an earlier point to affect a better visual outcome. To date there is no study on early treatment for ROP and there is concern that treatment at threshold may be too late for some eyes. The Regional Neonatal Center at Westchester Medical Center is part of a multicenter trial for Early Treatment of ROP. It is hypothesized that treatment of ROP in carefully selected cases at a less-severe stage of ROP than the conventional threshold for treatment will result in improved visual and structural outcome.

The Early Treatment for ROP will enroll approximately 370 infants with ROP at high risk for unfavorable outcomes for a randomized clinical trial. Eligible infants must have a birth weight of 1250 grams or less. At 28 days they are examined by a Pediatric Ophthalmologist, if diagnosed with ROP the parents are asked to sign an informed consent for frequent eye examinations. The infant is enrolled in the randomized trial if prethreshold disease is observed. One eye will be treated by retinal ablation, while the other eye (the control eye) will be managed conventionally. If the control eye reaches threshold ROP it will be treated. The primary outcome measure will be a masked evaluation of visual acuity using the Teller Acuity Card at nine months post-term.

Dr. Mark Horowitz and Dr. Edmund La Gamma are the Principal Investigators at Westchester Medical Center. Dr. Howard Charles is a Pediatric Ophthalmologist who will perform the Laser surgery in the Regional Neonatal Center when necessary. The National Eye Institute of the National Institutes of Health sponsors the Multicenter Trial of Early Treatment of Retinopathy of Prematurity. (The study headquarters is located at the Smith-Kettlewell Eye Institute, San Francisco, California. The Coordinating Center is located at the University of Texas Health Science Center in Houston, Texas).

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## Ranitidine in the NICU and in NICU Graduates

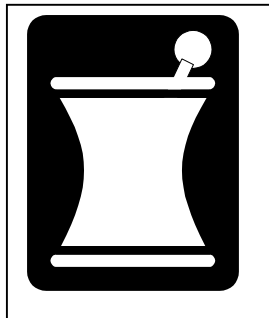
Premature babies receiving neonatal intensive care are occasionally discharged to the care of their pediatrician with the recommendation to receive treatment with ranitidine. The community pediatrician is then faced with the decision whether (and when) to discontinue this medication at some later time. I will briefly review the indications for use of ranitidine in the NICU so those pediatricians will appreciate the indications for originally placing and, later, discharging their patients on this medication.

Ranitidine is a (histamine) H<sub>2</sub>-blocking drug that reduces gastric acidity by inhibiting acid production. It is primarily excreted by the kidneys while about 30% are metabolized in the liver. There are two common indications for its use in the NICU. The first is for prophylaxis (or treatment) of stress ulcers in severely ill neonates. In such cases, treatment has been shown to be effective (*Crit Care Medicine* 1997; 25: 346-351), is started in the first day or two of life and can be discontinued when the baby is stable and feeding. Thus a baby discharged home on ranitidine must have had a different indication for the drug: gastroesophageal reflux (GER).

Unfortunately, the diagnosis and treatment of GER is a somewhat murky topic. Over 40 symptoms and signs have been associated with GER. These may be mild or severe and are characteristically non-specific. Reflux is often found in normal babies and a clinical distinction has to be made between 'functional' GER and 'pathologic' GER (often termed GER disease, GERD). In a study of 285 normal babies with a pH probe, the number of episodes of reflux peaked at 4-6 months of age. At 4 months, these infants refluxed 6 times a day. The frequency (and total duration) of reflux decreased thereafter (*J Am Coll Nutrition* 1998; 17: 308-316). Treatment for reflux may include positioning, change in composition of feeds, and drugs. The decision to initiate treatment is based on symptoms and is often made empirically.

Furthermore, there is a paucity of data to confirm that treatment is effective in relieving clinically relevant outcome measures.

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The most common indication for initiating anti-reflux measures in the NICU is the occurrence of apnea.

The relation between apnea and GER is controversial at best. While some studies have demonstrated a temporal association between GER and apnea, several others have failed to demonstrate such a relationship. Interpretation of these studies is further confounded by the different patient populations studied, by the different types of apnea spells that occasioned investigations (e.g. awake apnea vs. apnea during sleep), and by various other factors. These issues are well reviewed in a recent editorial (*J Pediatr* 2000; 137: 298-300). As a practical matter, neonatologists "screen" for apnea more likely to be related to GER based on various heuristic indicators. These might be apnea occurring frequently in association with feeds, apnea resistant to treatment with methylxanthines, apnea occurring in infants > 36 weeks' post-conceptual age, or apnea occurring in an infant with other signs of GI difficulties.

Antireflux medication is then started. With the withdrawal of cisapride from such use, ranitidine is currently the drug of choice. Therapeutic response is expected within a short period of time. Thus, if apnea were the major indication for treatment, a reasonable expectation would be to note a clinically significant reduction in frequency of apnea in the 3-4 days following treatment when compared to 3-4 days preceding treatment. If there is a therapeutic response, it seems reasonable to continue treatment.

A greater challenge confronts the pediatrician who is taking care of a recent NICU 'graduate' who has been discharged while on ranitidine. The pediatrician does not have the luxury of 24-hr/day monitoring that is available in the NICU and, at the same time, has to contend with concerns of potential aspiration, SIDS and ALTE. It also probably requires greater courage to discontinue a medication started by others. What advice can we provide?

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First, a few words about GER, SIDS and ALTE. The relation between these entities is, as in the case of apnea, controversial (see previous 2 references). There is no epidemiologic evidence to link reflux as a risk factor for SIDS. There is, however, an *animal* study that showed that, in animals made hypoxic, installation of fluid in the pharynx inhibited the process of auto-resuscitation (which presumably follows an ALTE). The data available from human studies also cannot exclude a possible link between GER and ALTE/SIDS (via a common underlying cause, and which need not be temporal). There is, moreover, no evidence suggesting that treatment of GER reduces the risk of ALTE or SIDS. Of note is that the supine sleeping position, currently recommended as reducing the risk of SIDS, is that which is thought to actually promote GER in both symptomatic and asymptomatic infants. This, together with other associated data on sleeping and arousal behavior, has even led to suggestion that reflux may contribute to the increase in arousals noted in the supine position and may therefore be actually protective for SIDS (*Eur J Pediatr* 2000; 159: 726-729). This hypothesis is consistent with the observation that the side sleeping position is intermediate both in its propensity for GER and incidence of SIDS (when compared to the prone and supine positions).

An appropriate approach would thus be empirical while erring on the side of caution. While there is no data to support any particular regimen, a reasonable approach would be to collect data regarding the infant's behavior over the short period following discharge (2 or 3 months, say, although other periods may equally suffice). Particular attention should be directed at symptoms suggestive of significant GER (e.g. during feeding, excessive crying, frequent waking from sleep etc.). If it appears that the infant is relatively free of such symptoms, ranitidine may be discontinued as a therapeutic trial. A follow-up visit shortly thereafter (e.g. 1-2 weeks) might be in order.

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At that time, a careful history should confirm that there has not been a re-occurrence of symptoms of concern. If there are such symptoms, treatment should be renewed (with a further follow-up visit to confirm response). There are various symptom diaries available that parents may use and which aid pediatricians in assessing the need for treatment. Infants with severe or persistent symptoms may benefit from a referral to a specialist since investigations might be warranted (with pH probe or to measure gastric pH response to various doses of ranitidine, etc.). A new drug has recently been used to treat GER in children – the proton pump inhibitor omeprazole. There have not yet been controlled trials in neonates and its pharmacokinetics in infants has yet to be studied thoroughly. Its widespread success in adults and its apparent wide margin of safety suggests that it will soon be tried in younger patients.

As should be clear from this review, there is very little data to back up any particular therapeutic regimen in deciding when to discontinue treatment with ranitidine. I believe that even an observational cohort study with a definite protocol would be a significant contribution in this area. Community pediatricians are best placed to conduct such a study.

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**Kids Fair 2001:**



Neonatal nurses participated in the Kid's Fair this past month. Pictured helping out in the "NICU booth" are Mary Kay Wayne, Patty Simon, Anama John and two special helpers. We met a number of NICU graduates and their families!

## First Breaths:



## A Kinder, Gentler Neonatal Ventilation

The ultimate goal in neonatology is to assist each baby to reach her or his optimal potential in life. Often, the rate-limiting component of survival is the ability to make the transition from a placental circulation to an air-breathing environment. The respiratory management of the newborn infant, particularly an extremely low birth weight infant, has undergone a number of innovations within the past forty years. The ventilators have become more sophisticated—patient-assisted ventilation, high frequency ventilation, pressure-regulated volume control and volume-assured pressure support. Devices to assess the effectiveness of ventilation have made parallel advances—pulse oximetry, blood gas measurements from microsamples of blood, and display of real-time respiratory graphics during ventilation.

A few key concepts are emerging from this rapid explosion in technology. First, the *in utero* environment is critically important to the outcome of the premature infant. Our perinatal colleagues—Tejani, Verma, et al—have demonstrated that when elevated proinflammatory mediators are present in the amniotic fluid of mothers in premature labor, there are increases in the incidence of respiratory distress syndrome, the progression to chronic lung disease, the susceptibility to intraventricular hemorrhage, and the presence of periventricular leukomalacia. My laboratory has detected elevations of these same pro-inflammatory mediators in tracheal aspirates obtained from premature infants as early as the first day of life, in those who progress to chronic lung disease. Thus, maternal management is critically important when premature delivery is threatened. The use of maternal steroids has been shown to result in dramatic improvements in respiratory and neurologic outcomes. Additional understanding of the factors that precipitate and sustain pro-inflammatory mediators *in utero*, along with specific therapies directed at counteracting their effects will be important to further limit their effects, both on premature labor, and on the developing fetus.

Second, neonatal respiratory management has undergone a revolution. The survival of smaller and more immature infants is constantly improving, but the percentage of infants progressing to chronic lung disease has *not* dramatically increased. While some of this can be attributed to maternal steroid administration, additional credit is likely due to neonatal respiratory advances in providing a “Kinder and Gentler” ventilation. This “Kinder and Gentler” ventilation

starts in the delivery room. Not only has overdilatation from high pressures (barotrauma) and high volumes (volutrauma) been associated with a breakdown in the capillary-alveolar barrier with a resultant “leakage” of serous fluid into the alveolus, but underdistention has also been associated with respiratory damage, particularly in the surfactant-deficient premature infant. The introduction of surfactant has ameliorated some of the respiratory compromise in the extremely low birth weight infant by stabilizing the ventilated airways.

If the lung in the premature infant is thought of as a collection of interconnected Mickey Mouse balloons, high pressures or high volumes tend to distend the “face” of the balloon rather than the “ears.” The goal for ventilation would be to uniformly distend the airways so that each of the “ears” or alveoli has the capacity to “open” or ventilate. While surfactant helps by distributing surface-active fluid throughout the alveoli, positive end-expiratory pressure (PEEP) also helps by recruiting underventilated regions of the lung. Thus, in the presence of surfactant nasal continuous positive airway pressure (NCPAP) has become a standard modality for stabilizing ventilation in the premature infant.

Additional newer ventilator modalities include patient-triggered ones. Previously, the ventilators were not sensitive or rapid enough to respond to the rapid respiratory rate and high demands of the premature infant. Now, assist controlled ventilation (AC), in which the patient triggers all of his or her own breaths, or synchronized intermittent mechanical ventilation (SIMV), in which only a specified number of respirations per minute are assisted by the ventilator (often in a weaning strategy) are becoming more popular than setting an arbitrary rate (IMV) that the patient must attempt to vary the “rate of rise” of the inspiration, and to wean the ventilator support based on the patient’s demand.

By utilizing the new respiratory graphics information, ventilator strategies are being adapted to focus on achieving the optimal Functional Residual Capacity (FRC) (LaGamma and Mishra). Optimal FRC includes interactions between PEEP, PIP, airway compliance, airway resistance and analysis of pressure-volume loops. Stay tuned for more information about this strategy.

The RNICU recently participated in a multicenter trial that tested High Frequency Oscillatory Ventilation (HFOV) against SIMV. The results were just announced at the Society for Pediatric Research. The infants (600-1200 grams) were randomized to either ventilator by 4 hours of life. An aggressive weaning strategy was in place for both modes of ventilation. The results *continues next page*

**Continued from page 1- Prenatal Detection of Congenital Heart Disease**

In fact, infants of diabetic mothers are also at increase risk of having structural heart defects. Mothers with connective tissue disorders demonstrate an increased risk of having a fetus with congenital heart block. Another common indication for fetal echocardiography is the presence of a suspected heart rate abnormality or arrhythmia, as estimated by fetal heart rate monitoring,

Benefits to having the diagnosis of congenital heart disease include the ability to triage the timing and location of delivery, as well as optimizing communication. Mothers whose fetuses have high risk heart defects likely to make the neonate sick early after birth, often arrange for delivery at a tertiary care facility where the pediatric cardiac and neonatal staff are on-hand, have a good understanding of the abnormal cardiac physiology, and are ready to support the newborn as necessary. This can include anything from continuous prostaglandin infusion to bedside atrial septostomy to CPR for cardiac arrest. Another very important component to prenatal diagnosis is the education and time afforded to the family. Obviously, it can be very traumatizing and anxiety provoking to learn that your new unborn child has heart disease. Early detection allows the family to “digest” the information, self-educate, and seek advice or other opinions as deemed necessary.

Treatment for almost every form of congenital heart disease is now available. High risk or complex heart defects may need continuous cardiac infusions for stability, until cardiac surgery can be performed. The majority of heart defects requiring surgery will be corrective in nature, whereas a smaller but still significant number of patients will need a “palliative” or staged procedure. Very rarely is heart transplantation the recommended treatment option, as cardiac surgical procedures today demonstrate very good outcomes, and availability of neonatal heart donors is extremely limited.

Health care professionals or individuals who may have questions regarding fetal echocardiography or congenital heart disease are encouraged to call the division of pediatric cardiology at (914) 594-4370.

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**Continued from page 2- A Kinder, Gentler Neonatal Ventilation**

demonstrated an earlier extubation in the HFOV group. Importantly, there were no differences in IVH< PVL, or mortality between the two groups of ventilation.

Additional recognition that “Kinder and Gentler” ventilatory strategies are being adapted includes the concept of permissive hypercapnea. Permissive hypercapnea has become an accepted modality, as long as the pH remains above approximately 7.25. A decrease in pH below this level has been associated with an increase in intracranial pressure, an increase in mean pulmonary arterial pressure, a decrease in arterial oxygen saturation, and an increase in physiologic shunting.

But we still have further to travel along this “Kinder and Gentler” pathway. Some of the future strategies may include: the use of inhaled nitric oxide in premature infants (we are participating in a nationwide trial to address this potential); the use of intratracheal ventilation (a cannula is placed at the tip of the endotracheal tube and decreases the dead space, as well as the pressures needed for ventilation-this technique requires testing in the premature infant); the use of liquid ventilation (early trials have not been as positive as anticipated); and, the development of “newer” surfactants, or surfactant-enabling medications, that have improved surface-lowering capabilities, specifically for the premature infant, while being resistant to inactivation. This is truly an exciting time to be associated with the care of premature infants!

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*For a copy of our newsletter or to be placed on our mailing list contact us by phone or e-mail.  
(See Above)*

**New Children's Hospital Faculty:**

**Dr. David Harter** has been named the new Director of Pediatric Neurosurgery at Children's Hospital at Westchester Medical Center. Dr. Harter, a native of Westchester County, New York, attended Medical school at Georgetown University School of Medicine, and completed his residency in neurosurgery at the University of Maryland. Dr. Harter completed his pediatric neurosurgery fellowship at Children's Memorial Hospital in Chicago. His clinical interests include pediatric neuro-oncology, hydrocephalus, cranial endoscopy, epilepsy, spasticity and spina bifida. His research interests are Medulloblastoma, Ependymoma and Cavernous malformations.

**Dr. Praveen Ballabh** is joining the Division of Neonatology and will be based in the Neonatal ICU at Sound Shore Medical Center in New Rochelle. Dr. Ballabh completed his pediatric residency at Christ Hospital and Medical Center at the University of Illinois College of Medicine in Chicago. He recently completed his fellowship in neonatology at New York Presbyterian Hospital / Cornell Medical Center, Weill Medical College of Cornell.

**Dr. Catherine Ekwa-Ekoko** is joining the Division of Neonatology and will be based in the Neonatal ICU at Hudson Valley Hospital Center in Cortlandt Manor. Dr. Ekoko completed her pediatric residency at New York Medical College in Valhalla. She recently completed her fellowship in neonatology at Mount Sinai Medical Center New York

Children's Hospital at Westchester Medical Center

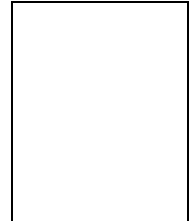
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