

NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

Volume 7 / Issue 6

June 2012

IN THIS ISSUE

Antibiotics Therapy in Classic Transient Tachypnea of the Newborn: A Necessary Treatment or Not? A Prospective Study

by Mahmoud Abughalwa, MD; Samer Taha, MD; Nahla Sharaf, MD; Husam Salama, MD
Page 1

DEPARTMENTS

Medical News, Products & Information

Page 9

Global Neonatology Today Monthly Column

Page 11

Upcoming Medical Meetings

(See website for additional meetings)

39th Annual Meeting of Fetal and Neonatal Physiological Society

Jul. 8-11, 2012; Utrecht, The Netherlands
www.FNPS2012.nl

Contemporary Forums - Perinatal Dilemmas

Jul. 15-18, 2012; Jackson Hole, WY USA
www.contemporaryforums.com

Neonatal Nurse Practitioners Symposium: Clinical Update and Review

Oct. 16-20, 2012; Clear Water Beach, FL USA
www.fannp.org/pages/conference.html

Third Port Said Neonatology Conference

Oct. 18-20, 2012; Port Said, Egypt
www.portsaidneogrp.com/index.html

Miami Neonatology 2012 - 36th Annual International Conference

Oct. 31-Nov. 3, 2012; Miami Beach, FL USA
pediatrics.med.miami.edu/neonatology/international-neonatal-conference

NEONATOLOGY TODAY

© 2012 by Neonatology Today
ISSN: 1932-7129 (print); 1932-7137 (online).
Published monthly. All rights reserved.

Corporate Offices:
8100 Leaward Way,
Nehalem, OR 97131 USA

Mailing Address:
PO Box 444
Manzanita, OR 97130 USA

Editorial and Subscription Offices
16 Cove Rd, Ste. 200
Westerly, RI 02891 USA
www.NeonatologyToday.net

Neonatology Today (NT) is a monthly newsletter for Neonatologists and Perinatologists that provides timely news and information regarding the care of newborns and the diagnosis and treatment of prematurity and/or sick infants.

Statements or opinions expressed in Neonatology Today reflect the views of the authors and sponsors, and are not necessarily the views of Neonatology Today.

Antibiotics Therapy in Classic Transient Tachypnea of the Newborn: A Necessary Treatment or Not? A Prospective Study

By Mahmoud Abughalwa, MD; Samer Taha, MD; Nahla Sharaf, MD; Husam Salama, MD

Abbreviation

CPAP: continuous positive air way pressure
CRP: C-reactive protein
HMC: Hamad Medical Corporation, State of Qatar
TTN: transient tachypnea of newborn
WBC: White blood cells

Abstract

Background

Transient tachypnea of the newborn (TTN) is a clinical condition characterized by a self-limiting mild increase in work of breathing for a short period of time, occurring mainly in near- and full-term infants, due to delayed alveolar clearance of the lung fluids immediately after birth. Many infants who have TTN are treated with prophylactic antibiotics for the first 24 to 48 hours until the blood culture results appear to be negative.

Objective

Justification of the routine administration of antibiotics as one line of management of infants presented by classic TTN, based on the rate of positive microbiological blood cultures.

Methods

This was a prospective cohort study that followed up two different treatment approaches in infants aged 37 to 41 weeks' gestation who were admitted with an initial diagnosis of classic TTN at NICU over a ten-month period. The first approach was administering prophylactic antibiotics for 48 hours until the blood culture confirmed negative results, whereas the other approach did not include administering antibiotics. The decision to administer antibiotics was left to the treating physician's clinical evaluation.

Diagnostic criteria of classic TTN were applied in order to exclude neonatal sepsis and other differential diagnoses. Both groups continued to receive routine observation and supportive treatment. All infants had a blood culture, CRP, white blood count, neutrophile count, blood gas and chest X-ray.

“Many infants who have TTN are treated with prophylactic antibiotics for the first 24 to 48 hours until the blood culture results appear to be negative.”

NEONATOLOGY TODAY CALL FOR PAPERS, CASE STUDIES AND RESEARCH RESULTS

Do you have interesting research results, observations, human interest stories, reports of meetings, etc. to share?

Submit your manuscript to: RichardK@Neonate.biz



Introducing
even more support
for a delicate baby's
developing eyes

Similac® preterm infant formulas now have added lutein for the developing eyes

- Lutein is a carotenoid with antioxidant properties and is found in cord blood, colostrum, and human milk¹⁻⁷
- In a clinical study, infants fed Similac preterm formulas with added lutein had significantly greater rod photoreceptor sensitivity, which is highly correlated with retinal maturation*¹

**Choose Similac preterm infant formulas—
added lutein to support eye development**

*A post hoc analysis excluding Retinopathy of Prematurity (ROP); photoreceptor sensitivity assessed by full-field electroretinogram.

References: 1. Rubin LP, et al. *Journal of Perinatology* advance online publication, 14 July 2011; doi:10.1038/jp2011.87. 2. Kanako IN, et al. *Arterioscler Thromb Vasc Biol.* 2007;27:2555-2562. 3. Canfield LM, et al. *Eur J Nutr.* 2003;42:133-141. 4. Schweigert FJ, et al. *Eur J Nutr.* 2004;43:39-44. 5. Patton S, et al. *Lipids.* 1990;25:159-165. 6. Jewell VC, et al. *Proc Nutr Soc.* 2001;60:171-178. 7. Connor SL, et al. *FASEB.* 2008;22:451-454.



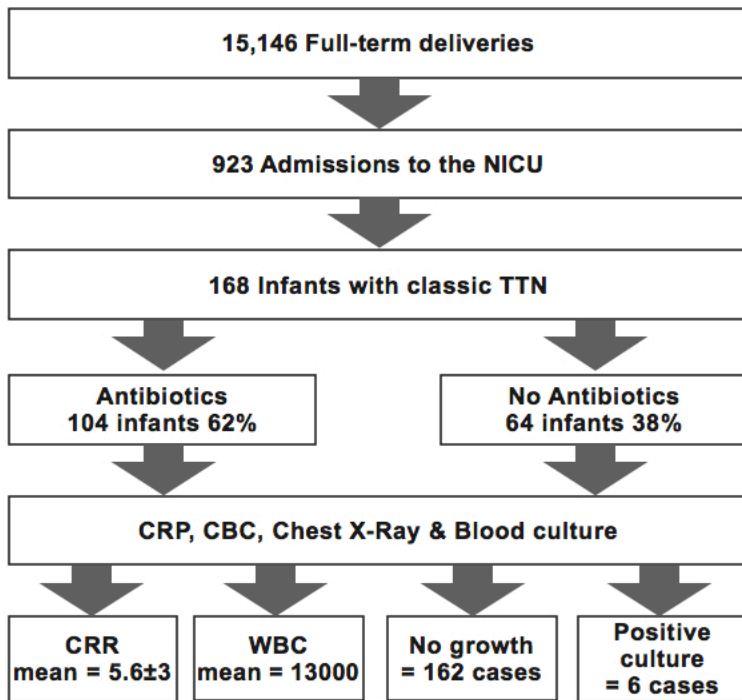


Figure 1. Distribution of infants in the study.

Results

A total of 168 infants fulfilled the recruitment criteria of classic TTN; 106 infants received antibiotics (63%) and 62 infants did not receive antibiotics (37%). There was no difference between both treatment groups regarding CRP, WBC, or neutrophile count. The length of the hospital stay was 72 hours \pm 6 versus 48 hours \pm 3, respectively. The blood culture was positive in 5 out of the 168 cases (2.9%), only two blood cultures proved to be of significance (group B streptococci & staphylococcus aureus), and two cases grew more than one organism, and were described as contaminated. No recorded cases required readmission because of late neonatal sepsis in both groups.

Conclusions

Provided vigilant application of the criteria of classic TTN as defined in the literature, classic TTN cases may not require prophylactic antibiotics while the infant is placed under a close observation inside the NICU until blood culture results are cleared.

Background

Transient tachypnea of the newborn (TTN) is the most common respiratory disorder among the newborn population.¹ It is a clinical condition associated with respiratory distress due to delayed evacuation of the lung fluids, which naturally occurs before, during and immediately after the delivery process. It was first described in 1966 as a major cause of respiratory distress in term and near-term infants.² In 1981, Haliday and McClure described two different clinical entities of TTN: classical and severe.³

The incidence of the condition varies widely among centers. In a review of 29,669 deliveries from 1992 to 1999 from a single center in the United States, TTN occurred in more infants after elective Cesarean than after vaginal delivery (3.1% versus 1.1%).⁴ In another British review of 33,289 term deliveries (37 to 42 weeks), the incidence of TTN was 5.7 per 1000 births.⁵

In a German study that analyzed data from perinatal regional registries of almost 240,000 full-term deliveries from 2001 to 2005, the incidence of TTN was 5.9 cases per 1,000 singleton births.⁶ Elective Cesarean section was the most significant risk factor associated with TTN compared against vaginal deliveries in data from the national German perinatal registry (42% versus 9%). Other risk factors associated with TTN included small for gestational age (16% versus 10%), large for gestational age (14% versus 11%), and male gender (60% versus 51%). Maternal diabetes and asthma are also well-recognized risk factors.⁶

At HMC Women's Hospital, the overall incidence of classic TTN is approximately 1.0% (10 cases per 1000 singleton live birth). The rate of Caesarian section was 21% in 2010. In the same year, the total number of live-born deliveries was 16,550, and the total number of full-term newborn infants admitted to the NICU was 945. The overall rate of positive blood culture among newborn \geq 2500 grams admitted to the NICU was 3.3%, while the incidence of early neonatal sepsis among full-term infants is approximately 3.2%.

Many infants who have TTN are treated with antibiotics for the first 24 to 48 hours until the blood culture is shown to be negative, as sepsis is considered an important differential diagnosis.²

Prescribing intravenous antibiotics in the treatment course of transient tachypnea of the newborn as a standard practice is gradually changing, and is usually left to the clinical judgment of the treating physician. However, long-established textbooks clearly recommend such treatment based on a terror of hidden infection.⁷ However, in several review articles discussing the respiratory outcomes of late

Classic Transient Tachypnea of the Newborn		
Antenatal History	Clinical Signs	Radiological Signs
Absence of: <input type="checkbox"/> PROM <input type="checkbox"/> Chorioamnionitis <input type="checkbox"/> Maternal Infection <input type="checkbox"/> Meconium <input type="checkbox"/> Advanced resuscitation Presence of risk factors: <input type="checkbox"/> Caesarean section <input type="checkbox"/> IMM, bronchial asthma <input type="checkbox"/> Others	<input type="checkbox"/> Tachypnea shortly after birth <input type="checkbox"/> Persist beyond 4 hours of age Rate up to 120 breaths per minute <input type="checkbox"/> Mild increase in work breath <input type="checkbox"/> \pm Grunting <input type="checkbox"/> Need \leq 40% FIO ₂ nasal cannula <input type="checkbox"/> Neurologically normal <input type="checkbox"/> Hemodynamically well <input type="checkbox"/> PCO ₂ is not more than 60 mmHg	<input type="checkbox"/> Normal or increased lung volume <input type="checkbox"/> \pm Mildly cardiomegaly <input type="checkbox"/> Prominent lung markings <input type="checkbox"/> Fluid in the interlobar fissures <input type="checkbox"/> \pm Mild pleural effusions <input type="checkbox"/> Mild pulmonary edema <input type="checkbox"/> No considerations
Normal CBC & CRP		

Figure 2. Clinical diagnosis of TTN.

preterm and term infants, the use of intravenous antibiotics is seldom investigated. Recently, Costa et al. compared TTN against pneumonia in a small sample size retrospective study, the conclusion of which was that both are indistinguishable except in the history of perinatal infection.⁸ Their argument was based on non-microbiological evidence. Considering the importance of increased bacterial resistance to antibiotics used inside the nursery, this study was carried out to justify the use of routine prophylactic intravenous antibiotics and whether it will protect the infants from suspected infection.

Objective

Assess the rate of positive microbiological blood cultures in the course of treatment of classic TTN and whether it mandates empiric use of antibiotics as one line of management in cases of classic TTN.

Materials and Methods

A prospective cohort study was performed to follow up the course of infants aged 37 to 41 weeks' gestation born over a ten-month period, March 2010 to December 2010, at Women's Hospital and admitted to the NICU with an initial and final diagnosis of classic TTN after strict application of the clinical,

laboratory and radiological characteristics of TTN. Women's Hospital is the largest and main tertiary maternity hospital in the state of Qatar. The number of live deliveries exceeded 16400 per year in 2010, where 10% of newborn infants have been admitted to the NICU.

Patient recruitment: Classic TTN was defined in the study according to the following inclusion criteria adopted from the literature^{3, 7, 9, 10} (Figure 2): infants ≥ 37 weeks, with no antenatal/perinatal history to suggest maternal infection who developed tachypnea shortly after birth, and whose condition persisted beyond four hours of age; infants admitted within the first 24 hours of birth with: a mild increase of breathing, namely increased respiratory rate, grunting, mild intercostal and subcostal recession, increased oxygen requirements up to 40% FIO₂ to maintain oxygen saturation $\geq 95\%$, carbon dioxide retention in the blood gas not $>$ than 50 to 60 mmHg, and chest X-ray findings consistent with TTN, which include increased or normal lung volumes, \pm mild cardiomegaly, and prominent vascular markings in a sunburst pattern originating at the hilum, fluid in the interlobar fissures, \pm mild pleural effusions and appear neurologically and hemodynamically normal.^{10,11} The following infants

were excluded from the study: infants with an antenatal history suggestive of chorioamnionitis or maternal infection; infants with a significant congenital malformation, infants with a history of meconium at delivery who required intubation and endotracheal suctioning, a low enough Apgar score to require advanced resuscitation, chest X-ray finding suggestive of pneumonia or significant shadows, which is not consistent with the radiological features of TTN; infants who required mechanical ventilation or CPAP, and those who showed signs of early neonatal septicemia. All infants in the study received an initial blood gas, complete blood count, CRP, blood culture and chest X-ray at four hours of age if the signs persisted. The decision to commence antibiotics was left up to the physician. The infants were cohort in two treatment groups; the first one received intravenous antibiotics (penicillin G & Gentamicin) beside the supportive treatment and the second group received only supportive treatment. Daily follow-up of infants in regard to acuity of their condition, clinical deterioration and recovery progress.

After Discharge Follow-up

After discharge, the infants' medical record number was tracked through the electronic

Table 1: Characteristics of Patients Included in the Study (Number of Infants)

Variables	Antibiotics (106 Infants)				No Antibiotics (62 Infants)		
	GBS	STOUR	STAEPI	Others	GBS	STOUR	STAEPI
Initial diagnosis as TTN	104 infants				64 infants		
Diagnosis of TTN at time of discharge	101 infants				60 infants		
Gestation age (mean)	37.7 \pm 1.9				37.18 \pm 2.1		
Birth weight (mean)	2.9kg \pm 0.7kg				2.9kg \pm 0.8kg		
Apgar score at 5 th min	9.5 \pm 0.8				9.8 \pm 0.4		
Caesarean section	48% (43)				75% (46)		
IDM	10.1%				14.3%		
Bronchial Asthma in the family	0.9%				0.4%		
Positive Maternal culture results*	HVS		Urine		HVS		Urine
	7= Candida		1= Candida		0		0
WBC (mean) in microliter (1x10 ⁻⁶ liters)	13.5 \pm 5.6				13.0 \pm 6		
Neutrophile count (mean) microliter (1x10 ⁻⁶ liters)	7.2 \pm 4.4				6.7 \pm 4.4		
C-reactive protein (mean)	9.3 \pm 1.8				1.6 \pm 5.1		
Positive blood culture	1	1	1	1§	0	1	1
Hospital stay (mean)	72 hours \pm 6 hours				48 hours \pm 3 hours		
Late neonatal sepsis (3-28 days after birth)	0				0		

*HVS= high vaginal swab of mixed bacterial growth. ** Blood culture is positive: STOUR = staphylococcus Aureus 2. STAEPI = Staphylococcus epidermidis 2 cases, and 1 case GBS = Group B strep and 2 growths contaminations. IDM; infant of diabetic mother. § Streptococcus gordonii.

NEONATOLOGY TODAY

News and Information for BC/BE Neonatologists and Perinatologists

About Neonatology Today

Neonatology Today (NT) is the leading monthly publication that is available free to qualified Board Certified (BC) neonatologists and perinatologists. Neonatology Today provides timely news and information to BC neonatologists and perinatologists regarding the care of newborns, and the diagnosis and treatment of premature and/or sick infants. In addition, NT publishes special issues, directories, meeting agendas and meeting dailies around key meetings.

Free Subscription to Neonatologists, Perinatologists and their Teams

Neonatology Today is available in two formats - print or PDF file for those physicians residing in North America, and in a PDF file for those living outside of North America. To receive your free qualified subscription, simply send an email to: SUBS@Neonate.biz. Be sure to include your name, title, organization, mailing address, email, phone and fax.

Submitting Manuscripts to Neonatology Today

Interested in submitting a manuscript? Send it via email to: Articles@Neonate.biz. We are often able to publish accepted manuscripts with 1-3 months of receipt.

Sponsorships and Recruitment Advertising

Interested in receiving information on sponsorship availability or recruitment advertising? Please contact Tony Carlson by phone: +1(301) 279-2005, or by email: TCarlsonmd@gmail.com.

Sponsorships are available in full pages, 1/2, 1/3 pages and horizontal full-color banners. All recruitment advertising includes color and graphics at NO additional charge; the sizes include: 1/3, 1/2, 2/3 and full pages. FREE website banner ad during the month the paid recruitment ad runs. If needed, Neonatology Today will even create the ad for you for free.

Key Contacts

Tony Carlson - *Founder & President* - TCarlsonmd@gmail.com
Richard Koulibanis - *Group Publisher & Editor-in-Chief* - RichardK@neonate.biz
John W. Moore, MD, MPH, *Medical Editor* - JMoore@RCHSD.org

Publishers of **CONGENITAL CARDIOLOGY TODAY** - www.CongenitalCardiologyToday.com



Table 2: Characteristics of the 5 Positive Culture Cases

	Antibiotics	No Antibiotics
Maternal condition	Temperature $\leq 38\text{ C}^\circ$ No signs of Chorioamnionitis	Temperature $\leq 38\text{ C}^\circ$ No signs of Chorioamnionitis
Maternal blood culture	All Negative	All Negative
Maternal high vaginal/urine swab	Candida	Non
Onset of starting antibiotics	4 \pm 0.8 hours	42 \pm 2 hours
Positive blood cultures	4	2
True GBS in blood culture	1	Non
Staph Aureus in blood culture	1	1
Staphylococcus Epidermidis	1 (1 true growth and one culture is contaminant with mixed growths)	One true infection
Other microorganisms in blood culture	One (Streptococcus gordonii)	Non

pediatric patient data registry, national pediatric emergency registry, inpatient pediatric admission registry, and microbiology registry to identify any re-admissions within 30 days since discharge and their diagnosis.

Results

There were 15146 live births between 37-41 weeks gestation during the study period and of these, 923 full-term infants were admitted to the NICU where 168 infants were admitted with a final diagnosis of classic TTN. The overall rate of TTN was 1.1% or 11 cases per 1000 live birth. The number of cases that received antibiotics was 106 infants, whilst 62 infants did not. The mean CRP was 9.6 \pm 3 in the antibiotic group versus 6.7 \pm 4.4 in the no-antibiotic group. True blood cultures were positive in three infants, whilst two cultures grew more than two non-pathological organisms and were considered contamination. The length of the hospital stay was 24 hours shorter in the no-antibiotic group (72 hours versus 48 hours). No identified cases were re-admitted to pediatric services with a diagnosis of systemic infection or pneumonia among those who did not receive antibiotics (Table 1).

Discussion

It is well known that the excessive use of antibiotics in newborn infants will modify the gastrointestinal micro-flora and increase the risk of antibiotics resistance.^{7, 13, 14} This was the main trigger to conduct this study in an attempt to reduce the use of antibiotics among newborn infants with TTN and dispute the necessity of using empirical antibiotics when the criteria of classic TTN have been adequately applied to affected newborn infants. The results of this study were rather surprising to the authors because even after vigilant efforts

“This study is the first cohort study to challenge the usefulness of prescribing antibiotics as part of the treatment protocol of classic transient tachypnea of the newborn.”

to exclude all risk factors of infection, significant pathological organisms were grown in the blood culture. According to the data presented, the degree of confidence is rather low, even with vigilant and careful application of the diagnostic tools. The rate of positive blood culture results was consistent with the published international figure of early neonatal sepsis, which is 1-3/1000 live births.¹⁶

The World Health Organization (WHO) estimates approximately five million neonatal deaths a year. Almost all deaths occur in developing countries, half of them in the African region.¹⁸ There are no pathognomonic features of neonatal sepsis,¹⁹ and the clinical presentation of neonatal sepsis can vary. In the study conducted in Kenya, difficult feeding, unexplained pallor, cyanosis and unconsciousness were strongly associated with severe sepsis, whereas rapid breathing, nasal flaring, grunting and lethargy were found to be associated with a moderate form of sepsis.²² WHO has established the criteria for the initial diagnosis of neonatal sepsis, but the sensitivity and specificity of the clinical diagnosis can vary considerably.²³ These clinical characteristics can be ef-

fective predictors for positive blood culture, but they have limited specificity and sensitivity.^{25, 26}

The positive rate of neonatal blood cultures has been found to range from 25 to 54%.^{6, 10-12} A blood culture to isolate the offending pathogen remains the gold standard for the definitive diagnosis of septicemia.²⁸ However, the results of a blood culture take hours to days, thus necessitating the initial empirical treatment of suspected cases. In Costa et al.'s study, the risk of perinatal infection was significantly more frequent in patients with pneumonia, and together with Caesarean section, were the only differences between the TTN group and the pneumonia group. They concluded that antibiotics should initially be prescribed until the cultures; biological markers of infection and clinical evolution definitely exclude the presence of infection.⁸

This study is the first cohort study to challenge the usefulness of prescribing antibiotics as part of the treatment protocol of classic transient tachypnea of the newborn. In this study, the authors carefully applied the diagnostic criteria for classic TTN; all patients had a negative blood culture, except for five patients with a significant pathogen. Among the two groups, there was no difference in white blood count, neutrophil count, or CRP, whilst those who were not prescribed antibiotics were discharged 24 hours earlier. To conclude the study, no recorded cases were readmitted to the pediatric service after discharge from the nursery. The present study, contrary to the launched hypothesis, is mandating empirical antibiotics when classic TTN is presented, irrespective of applying vigilant criteria. However, in order to recommend that empiric antibiotics not be used, a larger trial is recommended.

PedHeart

Your solution for patient and staff education

Resource

www.HeartPassport.com



Turn any browser into a multi-level teaching tool for patients and staff

Community Web

www.Congenital.org



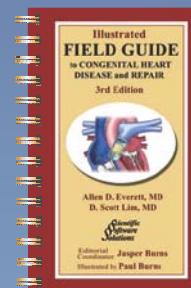
The most complete source of congenital heart information for patients and families - under your institutional banner!

Field Guide

Illustrated Field Guide to Congenital Heart Disease and Repair
NEW 3rd EDITION!

"Every pediatric cardiology attending, fellow, intensive care unit dealing with patients with CHD and every pediatrician should have this manual..."

Ziyad M. Hijazi, MD
Rush University Medical Center



Special Offer!

Try a single-user subscription to the Resource for just \$150!

Get the Field Guide for 20% off!

Use coupon code: NEO2012 at www.PedHeart.com

offer expires 7/1/2012. Applies to single-user subscription for 1 year. Login information may not be shared or transferred.

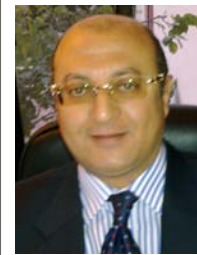
Scientific Software Solutions 434.293.7661
www.PedHeart.com
Support@PedHeart.com

References

1. Kumar A, Bhat B V. Epidemiology of respiratory distress of newborns. *Indian J Pediatr.* 1996; 63:93-8.
2. Avery ME, Gatewood OB, Brumley G. Transient tachypnea of newborn: Possible delayed resorption of fluid at birth. *Am J Dis Child.* 1966 Apr; 111(4):380-5.
3. Haliday HL, McClure G, McC rield M. Transient tachypnea of newborn: two distinct clinical entities? *Arch Dis Child.* 1981, 56,322-25.
4. Levine EM, Ghai V, Barton JJ, Strom CM. Mode of delivery and risk of respiratory diseases in newborns. *Obstet Gynecol* 2001; 97:439.
5. Morrison JJ, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. *Br J Obstet Gynaecol* 1995; 102:101.
6. Tutdibi E, Gries K, Bücheler M, et al. Impact of labor on outcomes in transient tachypnea of the newborn: population-based study. *Pediatrics* 2010; 125:e577.
7. JM Rennie & NR Robertson. Transient tachypnea of newborn. Text book of neonatology. 1999, page 514-516.
8. Costa S, Rocha G, Leitão A, Guimarães H. Transient tachypnea of the newborn and congenital pneumonia: a comparative study. *J Matern Fetal Neonatal Med* 2011 Oct 1.
9. Guglani L, Lakshminrusimha S, Ryan RM. Transient Tachypnea of the Newborn. *Pediatrics in Review* 2008; 29; e59.
10. Hermansend C L, Lorah K N. Respiratory Distress in the Newborn. *Am Fam Physician* 2007; 76:987-94.
11. Imaging in Transient Tachypnea of the Newborn. Margarita A. Updated: May 27, 2011.
12. Sudo N, Sawamura S, Tanaka K, Aiba Y, Kubo C, Koga Y. The requirement of intestinal bacterial flora for the development of an IgE production system fully susceptible to oral tolerance induction. *J Immunol* 1997; 159:1739-45.
13. Bromberger P, Lawrence JM, Braun D, Saunders B, Contreras R, Pettiti DB. The influence of intrapartum antibiotics on the clinical spectrum of early-onset group B streptococcal infection in term infants. *Pediatrics.* 2000; 106:244-250.
14. Bromiker R, Arad I, Peleg O, Preminger A, Engelhard D. Neonatal bacteremia: patterns of antibiotic resistance. *Infect Control Hosp Epidemiol.* 2001; 12:767-770.
15. Anand D. Kantak, MD; John T. McBride, MD. Transient Tachypnea of the Newborn. Neonatal Wet Lung Syndrome. Merck Manual Health Care Professionals. March 2009.
16. Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J. The epidemiology of severe sepsis in children in the United States. *Am J Respir Care Med* 2003;167:695-701.
17. American Academy of Pediatrics. Red Book 2003. 26th ed. 2003;117-123, 237-43, 561-73,584-91.
18. World Health Organization: Essential Newborn Care. In A report of a Technical Working Group WHO Geneva; 1995.
19. Siegel JD, McCracken GH: Sepsis neonatorum. *N Engl J Med* 1981, 304:642-7
20. Yurdakk M: Antibiotic use in neonatal sepsis. *Turk* 1998, 40(1):17-33.
21. French GL. Clinical impact and relevance of antibiotic resistance. *Advanced Drug Delivery Reviews* 2005, 57:1514-1527.
22. English M, Ngama M, Mwalekwa L, Peshu N: Sign and Symptoms of illness in Kenyan Infants aged less than 60 days. *Bulletin of the WHO* 2004, 82:323-329.
23. The WHO Young Infants Study Group: Clinical predilection of serious bacterial infection in young infants in developing countries. *Pediatr Infect Dis J* 1999, 18:s23-31
24. Tumbarello M, Sanguinetti M, Montuori E, Trearichi M E, Posteraro B, Fiori B, Citton R, D'Inzeo T, Fadda G, Cauda R, Spanu T: Predictors of Mortality in Patients with Bloodstream Infections Caused by Extended- Spectrum-Lactamase-Producing Enterobacteriaceae: Importance of Inadequate Initial Antimicrobial Treatment. *Antimicrob Agents Chemother* 2007, 51:1987-1994.
25. Weber MW, Carlin JB, Gatchalian S, Lehmann D, Muhe L, Mulholland EK, WHO Young Infants Study Group: Predictors of neonatal sepsis in developing countries. *Pediatr Infect Dis J* 2003, 22(8):711.
26. M. Jeeva Sankar, Ramesh Agarwal, Ashok K Deorari, Vinod K Paul. AIIMS- NICU protocols Sepsis in the Newborn Division of Neonatology, Department of Pediatrics All India Institute of Medical Sciences Ansari 2008.
27. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza - Tanzania Neema Kayange¹, Erasmus Kamugisha², Damas L Mwizamholya¹, Seni Jeremiah³ and Stephen E Mshana^{*3}.
28. Singh SA, Dutta S, Narang A: Predictive clinical scores for diagnosis of late onset neonatal septicemia. *J Trop Pediatr* 2003, 49(4):235-9.

NT

Corresponding Author



Husam Salama, MD
Department of Pediatrics
Women's Hospital
Hamad Medical Corporation
PO Box 3050
Doha, Qatar
Phone: +974 4393249
Fax: +974 4396142
Hsalama1@hmc.org.qa

Mahmoud Abughalwa, MD
Women's Hospital
Division of Neonatology
Hamad Medical Corporation
Doha, Qatar

Samer Taha, MD
Women's Hospital
Division of Neonatology
Hamad Medical Corporation
Doha, Qatar

Nahla Sharaf MD
Women's Hospital
Division of Neonatology
Hamad Medical Corporation
Doha, Qatar



Help Neonatology Today Go Green!

How: Simply change your subscription from print to PDF, and get it electronically.

Benefits Include: Receiving your issue quicker; an ability to copy text and pictures; hot links to authors, recruitment ads, sponsors and meeting websites, plus, the issue looks exactly the same as the print edition.

Interested? Simply send an email to Subs@Neonate.biz, putting "Go Green" in the subject line, and your name and organization in the body of the email.

Medical News, Products and Information

Prenatal Pollution Exposure Dangerous for Children with Asthma

Newswise - The link between prenatal exposure to air pollution and childhood lung growth and respiratory ailments has been established by several studies in recent years, and now a new study suggests that these prenatal exposures can be especially serious for children with asthma. The study was presented on May 20th, at the *ATS (American Thoracic Society) 2012 International Conference* in San Francisco.

"In this study, we found that prenatal exposures to airborne particles and the pollutant nitrogen dioxide adversely affect pulmonary function growth among asthmatic children between 6 and 15 years of age," said study lead author Amy Padula, PhD, post-doctoral fellow at the University of California, Berkeley. "This analysis adds to the evidence that maternal exposure to ambient air pollutants can have persistent effects on lung function development in children with asthma."

The study was conducted as part of the Fresno Asthmatic Children's Environment Study (FACES) – Lifetime Exposure initiative, which examines the influence of prenatal exposure to a number of ambient air pollutants on the growth of lung function during childhood and teen years in a high pollution area.

For this analysis, the researchers included repeated evaluations of 162 asthmatic children between the ages of 6 and 15 and their mothers. To determine prenatal exposure levels to pollution, the mothers' residences during pregnancy were geocoded and pollutant concentrations were obtained from the Aerometric Information Retrieval System supported by the US Environmental Protection Agency (EPA). Monthly average pollutant concentrations were assigned from 24-hour averages obtained at a central site monitor and summaries of the entire pregnancy and each trimester were calculated. The researchers looked at several pollutants, including carbon monoxide, nitrogen dioxide, ozone and particulate matter.

To calculate lung function growth, which is determined primarily by changes in lung capacity as a child grows, the researchers used spirometry, a technique which measures the volume and speed of air as it is exhaled from the lungs. For this study, multiple lung function tests were performed and significant changes were noted in four measurements: the FVC, or forced vital capacity, which reflects the volume of air that can be blown out after fully inhaling; the FEV1, or forced expiratory volume in 1 second, which is the volume of air that can forcibly be blown out in one second, after fully inhaling; the FEF, or forced

expiratory flow, which reflects the flow of air coming out of the lungs during the middle portion of a forced exhalation; and the PEF, or peak expiratory flow, which is the maximal flow achieved when air is forcibly exhaled immediately after being inhaled.

Measurement models were performed separately for boys and for girls, and were adjusted for height, age, race and socioeconomic status.

At the conclusion of the study, the researchers found that exposure to nitrogen dioxide during the first and second trimesters was associated with lower pulmonary function growth in both girls and boys in childhood. Among girls, exposure to nitrogen dioxide during the first trimester was associated with lower FEV1 growth and exposure to nitrogen dioxide during the second trimester was associated with lower FEF growth. Among boys, nitrogen dioxide exposure during the first and second trimesters of pregnancy was associated with lower FVC growth. Exposure to particulate matter during the first trimester was associated with lower FEV1 and FVC growth in girls; similar exposures during the third trimester were associated with lower PEF and FEF growth among boys.

Dr. Padula said she and her colleagues hope to conduct future studies on the role of genetic susceptibility to air pollution.

"Currently, our studies are examining the associations between prenatal air pollution and adverse birth outcomes," she noted. "It would be useful to know what makes some people more or less susceptible to the adverse affects of air pollution so we might be able to provide more targeted public health advice."

Background: Previous studies have found associations between prenatal exposure to air pollution and pulmonary function in childhood. Questions still remain about the impact of these exposures during pregnancy, particularly among susceptible groups such as asthmatic children. The Fresno Asthmatic Children's Environment Study (FACES) – Lifetime Exposure examines the influence of prenatal exposure to a number of ambient air pollutants on the growth of lung function in childhood and teen years in a high pollution area.

Methods: Based on maternal self-report, we geocoded all residences during pregnancy with Tele-Atlas. Pollutant concentrations were obtained from the Aerometric Information Retrieval System supported by the U.S. Environmental Protection Agency. Monthly average pollutant concentrations were assigned from 24-hour averages obtained at a central site monitor and

summaries of the entire pregnancy and each trimester were calculated. We used mixed models to estimate the association between air pollutants (carbon monoxide, nitrogen dioxide (NO₂), particulate matter <10 microns per cubic meter (PM10), and ozone) and pulmonary function growth as defined by repeated measures of pulmonary function tests (PFTs) (i.e., FEV1, FVC, PEF, FEF25-75/FVC, FEF25, FEF75) between the ages of 6 and 15. Models were performed separately for girls and boys and the natural log of each PFT was regressed on each pollutant during each exposure period. The models were additionally adjusted for the natural log of height, age, race and socioeconomic status.

Results: Our analysis included 162 children with a total of 1192 observations. NO₂ exposure during the first and second trimesters was associated with lower pulmonary function growth in both girls and boys in childhood. Among girls, NO₂ during the first trimester was associated with lower FEV1 growth and exposure to NO₂ during the second trimester was associated with lower FEF25 growth. Among boys, NO₂ exposure during the first and second trimesters of pregnancy were associated with lower FVC growth. PM10 exposure during the first trimester was associated with lower FEV1 and FVC growth in girls. PM10 exposure during the third trimester was associated with lower PEF and FEF25 growth among boys in childhood.

Discussion: We found that prenatal exposures to NO₂ and PM10 adversely affect pulmonary function growth among asthmatic children between and 6-15 years of age. This analysis adds to the evidence that maternal exposure to ambient air pollutants can have persistent effects on lung function development in children with asthma.

Funded by: American Lung Association and California Air Resources Board.

Immune System Implicated in Prematurity Complication

Despite advances in neonatal care, necrotizing enterocolitis (NEC) – the most common gastrointestinal emergency in premature infants – continues to be a deadly disease.

"We haven't made a lot of progress in identifying babies early who may be at risk for NEC, preventing it or treating it," said Jörn-Hendrik Weitkamp, MD, a neonatologist and assistant professor of Pediatrics at Monroe Carell Jr. Children's Hospital at Vanderbilt.

Now, Weitkamp and his colleagues have discovered that disruptions in immune system regulation — not previously considered to be important in NEC pathophysiology — may play a role in the disease. The findings, reported in the journal *Gut*, suggest a new target for therapeutic interventions for NEC.

NEC is an inflammatory disease that kills intestinal tissue. Premature babies, and particularly those who have early formula feedings (breast milk has protective properties), are at increased risk for developing NEC. About 40% of babies with NEC require surgery to remove dead bowel tissue — and half of these babies do not survive. NEC survivors suffer long-term complications including bowel-related problems and impairments in motor and cognitive function.

Weitkamp wanted to explore whether differences in immune system regulation — particularly in the "adaptive" immune response mediated by B cells and T cells — might play a role in NEC. This type of cellular immunity was not considered important in the early neonatal period because it takes time to develop, and because it was not found in mouse models, Weitkamp said. But he knew from other studies that immune responses in newborn mice are not identical to immune responses in newborn humans.

Weitkamp and his colleagues turned to stored human intestinal tissue samples that had been surgically removed from preterm babies diagnosed with NEC or other intestinal diseases. They found high levels of T cells called T regulatory (Treg) cells in the intestine of premature infants, which was surprising given the lack of these cells in the gut of newborn mice. Treg cells suppress the immune response and are critical for keeping the immune system in balance, preventing harmful inflammation.

Because of limitations related to Treg cell detection in stored tissue samples, the investigators collected fresh intestinal tissue samples from babies having surgery for NEC and for non-NEC problems, during or immediately after surgery.

Using multiple cellular "markers" and flow cytometry to identify the Treg cells, they confirmed that premature babies have an abundance of Treg cells in the intestines. Babies with NEC had about 60% fewer Treg cells than babies with non-NEC problems.

The investigators also detected increased expression of inflammatory cytokines (immune system signaling molecules) — particularly those that suppress Treg cell development — in the NEC tissue samples. And in assays of cell function, they found that the Treg cells suppressed cytokine production by and proliferation of T cells.

Follow-up studies on tissue samples from infants who had a second surgery suggest that the reduction in Treg cells is not because of an immune system defect in the babies.

"We believe that the T regulatory cells we've identified are in fact functional Treg cells and that they are down-regulated at the time of NEC," Weitkamp said. "Our studies challenge the dogma that cellular immunity is not important in the immediate neonatal period or in the pathophysiology of NEC."

Now, Weitkamp and his colleagues including neonatology fellow Joann Romano-Keeler, M.D., are studying the intestinal microbiome — the collection of microbes colonizing the gut — in the surgically-removed samples.

"We know that the microbiome and the immune system are important in shaping each other," Weitkamp said.

"We need to understand exactly how that works and which components typically found in human milk — such as certain vitamins, prebiotics and probiotics — are important for healthy microbiome and healthy immune system development."

Such components, he said, might become the basis for interventions to prevent the development of NEC.

Vanderbilt's collaborative environment and the support of colleagues in Pediatric Surgery, Pathology and Neonatology made the collection of fresh surgical tissue samples possible, Weitkamp said.

The studies were supported by grants from the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and Vanderbilt's National Institutes of Health-supported Clinical and Translational Science Award (CTSA) and Digestive Disease Research Center (DDRC).

Other authors include: Tatsuki Koyama, PhD; Michael Rock, PhD; Hernan Correa, MD; Jeremy Goettel, PhD; Pranathi Matta, Kyra Oswald-Richter, PhD; Michael Rosen, MD; Brian Engelhardt, MD; Daniel Moore, MD, PhD; and Brent Polk, MD.

Life-threatening Condition in Premies Linked to Blood Type

Many premature infants suffer a life-threatening destruction of intestinal tissue called necrotizing enterocolitis (NEC). Now a Loyola University Medical Center study has identified a major risk

factor for NEC: Premies with the AB blood type who develop NEC are nearly three times as likely to die from it as premies with other blood types.

The finding suggests that a simple change in blood transfusion practices in neonatal ICUs could significantly reduce the incidence of NEC.

The study is published online ahead of print in the *Journal of Perinatology*. Senior author is Jonathan Muraskas, MD, Co-Medical Director of Loyola's Neonatal ICU. First author is Tricia Thomson, MD, an assistant professor in the Division of Neonatology.

NEC is the most common serious gastrointestinal disorder among preterm newborns. Each year, it affects about 7,000 newborns born at least eight weeks premature or weighing less than 3 pounds, 5 ounces.

NEC occurs when the lining of the intestinal wall dies and tissue falls off. Most cases of NEC are mild to moderate and can be successfully treated with antibiotics. But in severe cases, a hole can develop in the intestine, allowing bacteria to leak into the abdomen and causing a life-threatening infection.

Each year, the number of babies who die from NEC approximates the number of children under age 15 who die of leukemia or meningitis. NEC likely involves several factors, including a decrease in blood flow to the bowel, infection, mechanical injury and abnormal immune response.

Thomson, Muraskas and colleagues examined records of 276 premies in Loyola's neonatal ICU who suffered severe NEC during the last 24 years. AB premies were 2.87 times more likely to die from NEC than babies with other blood types.

Premies often require multiple blood transfusions. Neonatal ICUs typically give Type O, the universal donor type. But this practice may inadvertently cause an enhanced immune reaction. This reaction, in turn, could be a reason why AB babies who develop NEC have a higher mortality.

Researchers suggest it may be prudent to change transfusion practices so that premies receive their specific blood types, rather than the universal donor Type O. "Although this will likely not eradicate NEC, it is an easily modifiable factor that may help to prevent those cases of NEC that develop in relation to the transfusion of blood products," researchers wrote.

Other co-authors include: Omar Habeeb, MD; Phillip DeChristopher, MD, PhD; Loretto Ann Glynn, MD; and Sherri Yong, MD.

Global Neonatology Today Monthly Column - eHealth and Achieving the U.N. Millennium Development Goals (MDGs)

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

The target date for the U.N. MDG's, 2015, is fast approaching. There is lot to be achieved in MDG 4 and 5 (see my previous columns in *Neonatology Today*). Planners are using all available resources to meet the MDGs by 2015. The innovative eHealth technology is one of the newest tools used to accelerate the process, and it seems the strategy is working.

As the World is being connected by mobile phones, so is the health system around the globe. There is increasing interest in using mobile phones to improve health care, particularly in low income countries.

It is reported that the number of mobile phone subscriptions has increased by approximately one billion between the end of 2007 and the end of 2008. At the beginning of 2009, the number surpassed four billion. With this penetration, the use of mobile phones and networks in mobile health has become increasingly popular in low- and middle-income countries.

Now comes MAMA to rescue mothers around the Globe!

Who or What is MAMA ?

Considering the great urgency to reduce maternal and infant mortality, an innovative program Mobile Alliance for Maternal Action (MAMA) was launched by the US Government. appropriately on Mother's Day last year by Secretary of State, Hillary Clinton. MAMA is aimed at reducing pregnancy-related morbidity and mortality in developing countries by using mobile technology. The program was launched across 22 countries, from Afghanistan to Zambia. MAMA is a partnership between the USAID (The United States Agency for International Development), Johnson & Johnson (J&J), the United Nations Foundation and BabyCenter.

"Today we celebrate the one-year anniversary of the Mobile Alliance for Maternal Action, an innovative alliance that harnesses the power of mobile technology to deliver critical health information directly into the hands of pregnant women and new mothers, empowering them to make healthy decisions for themselves and their families," said USAID Administrator Dr. Rajiv Shah recently.

More than one billion women in low- and middle-income countries own mobile phones. Mobile health messages are developed and sent on mobile phones to inform, dispel myths, highlight warning signs, and connect pregnant women and new moms with local health services.

"More than anything else, mothers and mothers-to-be hope for the health and survival of their babies. MAMA is dedicated to providing timely health information to women in even the most remote areas, where and when it is needed," said Sharon D'Agostino of J&J.

There are other non-profit organizations involved in using eHealth technology to improve global health. The study "Socio-Economic Impact of mHealth," commissioned by Telenor Group and carried out by The Boston Consulting Group conducted a comprehensive survey of the impact that mHealth initiatives can have in 12 countries, including the US, Norway, Thailand, and India. The investigators noted that the necessary infrastructure - "the mobile phone" and its network capacity is sufficient both on simple feature phones and on smart devices, and they are already in everyone's hands!

According to Mobile Technology for Community Health (MOTEC): 1.6 billion users are under the age of 30; 79% are in the developing world; there is a widespread use in both urban and rural areas; and the highest rate of mobile phone growth is in developing countries. Worldwide, 200,000 text messages are sent every second.

It is projected that there will be 7.4 billion mobile subscriptions by 2015. Currently, there are more than 500 mobile health projects around the World. Using mobile phones for health purposes will lead to:

1. Cost reduction by 25% in elderly.
2. Maternal and perinatal mortality reduction by 30%.
3. Doubling the number of rural patients that will be able to access a doctor.
4. Improvement in Tuberculosis treatment compliance by 30-70%.

Let the mobile phone ring loud and clear, and save the mothers and babies around the world!

The Clock is Ticking !!!

NT

Dharmapuri Vidyasagar, MD, FAAP, FCCM
University of Illinois at Chicago
Professor Emeritus Pediatrics
Division of Neonatology
Phone: +312.996.4185
Fax: 312.413.7901
dvsagarmd@yahoo.com

NEONATOLOGY TODAY

© 2012 by Neonatology Today
ISSN: 1932-7129 (print); 1932-7137 (online).
Published monthly. All rights reserved.
www.NeonatologyToday.net

Publishing Management:

- Tony Carlson, Founder, President & Senior Editor - TCarlsonmd@gmail.com
- Richard Koulbanis, Group Publisher & Editor-in-Chief - RichardK@CCT.bz
- John W. Moore, MD, MPH, Medical Editor - JMoore@RCHSD.org
- Virginia Dematatis, Assistant Editor
- Caryl Cornell, Assistant Editor
- Loraine Watts, Assistant Editor
- Chris Carlson, Web Manager
- William Flanagan, Strategic Analyst
- Rob Hudgins, Designer/Special Projects

Editorial Board: Dilip R. Bhatt, MD; Barry D. Chandler, MD; Anthony C. Chang, MD; K. K. Diwakar, MD; Willa H. Drummond, MD, MS (Informatics); Philippe S. Friedlich, MD; Lucky Jain, MD; Patrick McNamara, MD; David A. Munson, MD; Michael A. Posencheg, MD; DeWayne Pursley, MD, MPH; Joseph Schulman, MD, MS; Alan R. Spitzer, MD; Dharmapuri Vidyasagar, MD; Leonard E. Weisman, MD; Stephen Welty, MD; Robert White, MD; T.F. Yeh, MD

FREE Subscription - Qualified Professionals

Neonatology Today is available free to qualified medical professionals worldwide in neonatology and perinatology. International editions available in electronic PDF file only; North American edition available in print. Send an email to: SUBS@Neonate.biz. Include your name, title(s), organization, address, phone, fax and email.

Sponsorships and Recruitment Advertising

For information on sponsorships or recruitment advertising call Tony Carlson at 301.279.2005 or send an email to TCarlsonmd@gmail.com



Sign up for a free membership at 99nicu, the Internet community for professionals in neonatal medicine. Discussion Forums, Image Library, Virtual NICU, and more...!

www.99nicu.org



NICU Innovation— strengthened by the power of protein

Innovation inspired by experts. Convenience designed for you.



Enfamil® Human Milk Fortifier Acidified Liquid

- 4 g protein/100 Cal when mixed with preterm human breast milk (25 mL)
- Commercially sterile, single-dose packaging meets Academy of Nutrition and Dietetics and CDC infant feeding preparation guidelines^{1,2*}



Enfamil® Premature 30 Cal

- Customized nutrition to help meet the needs of the smallest infants
- One-step mixing with Enfamil® Premature High Protein 24 Cal for adjustment of caloric density and protein levels



Enfamil® Premature High Protein 24 Cal

- 3.5 g protein/100 Cal—to help meet the needs of rapidly growing VLBW and ELBW infants who may require high protein formula



Trust the Enfamil® portfolio of NICU products to meet the nutritional needs of your patients

meadjohnsonprofessional.com

CDC = Centers for Disease Control and Prevention

VLBW = very low birth weight

ELBW = extremely low birth weight

*No endorsement of this product by the Academy of Nutrition and Dietetics or CDC is intended or implied.

References: 1. Steele C, et al. Microbiology and Infection Control. In: Robbins ST, et al eds. *Infant Feedings: Guidelines for Preparation of Human Milk and Formula in Health Care Facilities*. 2011;108-121. 2. Baker RD. *Pediatrics*. 2002;110:833-835.



HOSPITAL FEEDING SYSTEMS

Mead Johnson Nutrition... dedicated to pediatric nutrition