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Screening for Neonatal Hyperbilirubinemia: Translating Guidelines into Practice

By Eugene Ng, MD, FRCPC, FAAP

Introduction

Hyperbilirubinemia is a common condition in newborn infants. Although the incidence of severe hyperbilirubinemia is rare,^{1,2} the potential consequence of bilirubin toxicity as a result of severe hyperbilirubinemia can be devastating. In 2004, the American Academy of Pediatrics (AAP) Subcommittee on Hyperbilirubinemia published a clinical practice guideline on the management of hyperbilirubinemia in newborn ≥ 35 weeks' gestation,³ followed by a position statement from the Canadian Paediatric Society (CPS) Fetus and Newborn Committee in 2007.⁴ These guidelines focused on prevention of severe hyperbilirubinemia by early identification of risk factors, universal screening of newborns by a timed total serum bilirubin (TSB) measurement (from here on referred to as "bilirubin screening"), and timely follow-up after the newborn's initial hospital discharge.

Five years after the first publication of these guidelines, emerging data suggest that there is insufficient evidence to support the recommendation of bilirubin screening. In a systematic review of publications in the era after the publication of the AAP guidelines, the authors found no literature evidence that evaluated the impact of bilirubin screening on the incidence of acute or chronic bilirubin encephalopathy.⁵ Such findings have led to the United States Preventive Services Task Force questioning the benefits of bilirubin screening while balancing the harm of treatment by phototherapy and exchange transfusion.⁶ However, the systematic review

also found evidence suggesting that a combination of risk factors assessment and bilirubin screening is effective in predicting significant hyperbilirubinemia, and, in other observational studies, may lead to fewer hospital readmissions for hyperbilirubinemia.⁵ This is further supported by a large retrospective cohort study of 360,000 newborns ≥ 35 weeks' gestation, showing those born in institutions where bilirubin screening was implemented have a significantly lower incidence of severe hyperbilirubinemia.⁷

So, implementing bilirubin screening may still have measurable benefits to at-risk newborn patients. In a commentary, Newman⁸ suggests that the approach to prevention and management of hyperbilirubinemia in the absence of bilirubin screening would have involved steps with many opportunities for errors and omissions, potentially leading to critical failure in the diagnosis of significant hyperbilirubinemia and in instituting timely treatment.

While implementing a bilirubin screening program based on the AAP and CPS guidelines in a community hospital in Canada with over 5,500 newborn deliveries per year, we have encountered many challenges, from developing a clear and concise policy manual, developing tools to educate and enable staff in interpreting results efficiently, to establishing resources for timely post-discharge follow-up of newborn infants at risk. In this review, these particular challenges and their solutions are discussed in the hopes that clinicians and hospital administrators may find our carefully considered approach and our tools helpful while undergoing the same process at their own institutions.

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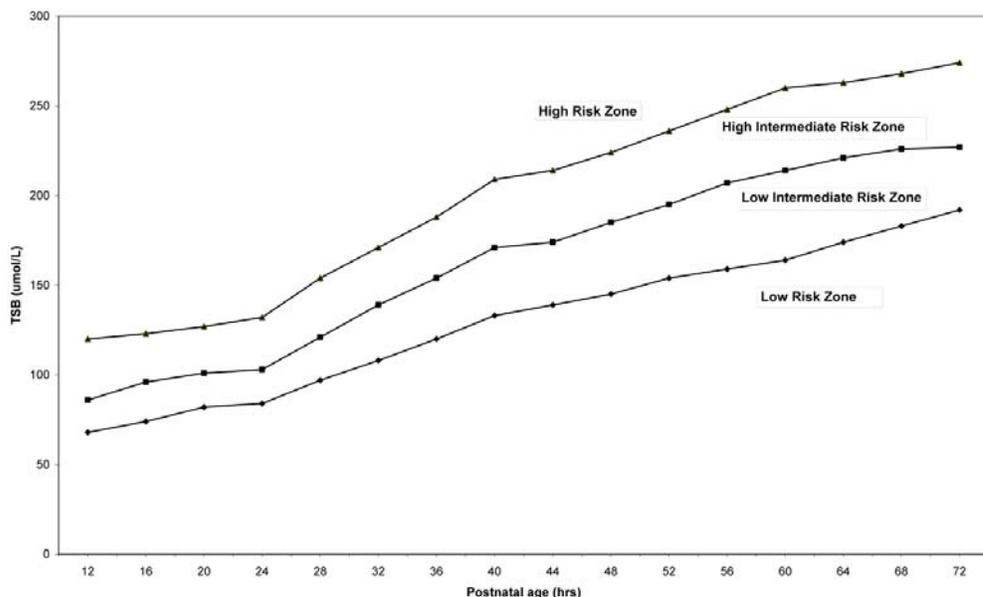


Figure 1: The Bhutani predictive nomogram, re-designed for SI unit of measurement from the original data.¹⁵

Table 1: Numeric chart of the Bhutani predictive nomogram

| Age (hours) | Low risk (μmol/L)* | Low intermediate risk (μmol/L)* | High Intermediate risk (μmol/L)* | High risk (μmol/L)* |
|-------------|--------------------|---------------------------------|----------------------------------|---------------------|
| 12 | 0-68 | 68-86 | 86-120 | >120 |
| 16 | 0-74 | 74-96 | 96-123 | >123 |
| 20 | 0-82 | 82-101 | 101-127 | >127 |
| 24 | 0-84 | 84-103 | 103-133 | >132 |
| 28 | 0-97 | 97-121 | 121-154 | >154 |
| 32 | 0-108 | 108-139 | 139-171 | >171 |
| 36 | 0-120 | 120-154 | 154-188 | >188 |
| 40 | 0-133 | 133-171 | 171-209 | >209 |
| 44 | 0-139 | 139-174 | 174-214 | >214 |
| 48 | 0-145 | 145-185 | 185-224 | >224 |
| 52 | 0-154 | 154-195 | 195-236 | >236 |
| 56 | 0-159 | 159-207 | 207-248 | >248 |
| 60 | 0-164 | 164-214 | 214-260 | >260 |
| 64 | 0-174 | 174-221 | 221-263 | >263 |
| 68 | 0-183 | 183-226 | 226-268 | >268 |
| 72 | 0-192 | 192-227 | 227-274 | >274 |

* To convert TSB units of measurement from μmol/L to mg/dl, divide by a factor of 17.1

A Paradigm Shift

In the era prior to bilirubin screening, the most common starting point of managing a newborn with hyperbilirubinemia was when jaundice is visible on physical examination. The approach of bilirubin screening in-hospital has systematically shifted the initial assessment of jaundice to an earlier phase for all newborns. This conceptual change from secondary to primary prevention requires hospital staff to acquire new skills in the assessment of risk factors, interpretation of laboratory results, and in arrangement of follow-up for all new-

born patients. To ensure compliance and adherence to the management algorithm in the screening program, much effort has been made in educating staff on the conceptual difference between screening and treatment, in the use of different tools for interpretation, in the trigger points for performing additional tests and the thresholds for notifying newborn healthcare providers. Education resources with formal lectures, seminars, in-services, and executive summaries of the policy manual have been provided at many opportunities within the institution to maximize the consistency of care by newborn healthcare provid-

ers from various disciplines (general pediatricians, neonatologists, family physicians, and midwives).

Challenges in the Development of a Policy Manual

In a busy nursery as ours, operating a universal bilirubin screening program would invariably translate into a higher staff workload. Hence, it is important that the algorithm in the policy manual is clear and easy to follow. The enormous efforts in developing and approving the policy manual and implementation of the bilirubin screening program were shared by nurse educators, manager, and representatives of neonatologists, family physicians, and midwives in a practice council. During the process, we have discovered a number of ambiguous and vague areas in the AAP and CPS guidelines that needed careful interpretation before they can be pragmatically applied to our bilirubin screening program.

Risk Factor Assessment

The AAP and CPS recommend a systematic pre-discharge assessment of risk factors for development of significant hyperbilirubinemia for all newborns. Although factors such as race, sibling with significant jaundice and history of bruising or cephalohematoma are important and are classified as major risk factors,³ they are often difficult to identify or to be included in a policy manual. For practical reasons, we have chosen to use more concrete and validated factors: gestational age at birth, risk of hemolysis, and timed TSB prior to discharge as major predictors in the routine risk assessment.⁹⁻¹² However, that does not preclude the astute clinicians from determining the presence of other risk factors, and to include them in the pre-discharge assessment.

The Direct Antiglobulin Test (DAT)

For mothers with blood group type O, the DAT (or Coombs test) to identify ABO incompatibility is recommended as an optional test, to be performed if the newborn presents with early jaundice, or if the routine TSB falls in the high intermediate or high risk zones in the predictive nomogram by Bhutani et al (Figure 1).^{3,4} At our institution, cord blood samples for all newborns are kept in the blood bank for 7 days, so typing for blood group and DAT can be performed with no additional blood sampling required. The issue with the DAT is technical; it requires a laboratory technician 10-15 minutes of uninterrupted time to complete a test (personal communication), making it extremely challenging for the test to be ordered multiple times during a work day. In addition, if the DAT is ordered only after the screening TSB result is known, waiting for the DAT result will further delay in hospital discharge. In discussion with the laboratory service and the blood bank, it was felt that the most cost-effective strategy would be to perform the DAT routinely on cord blood of

Table 2: Numeric chart of the AAP phototherapy guideline

| Days of Age | Age (hrs) | Low risk (≥ 38 wks and well) | Medium risk (≥ 38 wks + risk factors or 35-37 6/7 wks and well) | High risk (35-37 6/7 wks + risk factors) |
|---|-----------|------------------------------------|---|--|
| Total Bilirubin ($\mu\text{mol/L}$) | | | | |
| | 0 | 116 | 86 | 63 |
| | 4 | 123 | 99 | 72 |
| | 8 | 139 | 116 | 86 |
| | 12 | 154 | 127 | 99 |
| | 16 | 171 | 140 | 109 |
| | 20 | 185 | 154 | 12 |
| 1 | 24 | 197 | 168 | 133 |
| | 28 | 207 | 174 | 140 |
| | 32 | 221 | 188 | 152 |
| | 36 | 227 | 197 | 162 |
| | 40 | 241 | 207 | 171 |
| | 44 | 253 | 214 | 185 |
| 2 | 48 | 258 | 222 | 192 |
| | 52 | 270 | 231 | 200 |
| | 56 | 275 | 241 | 205 |
| | 60 | 280 | 248 | 212 |
| | 64 | 289 | 253 | 219 |
| | 68 | 292 | 257 | 224 |
| 3 | 72 | 303 | 260 | 229 |
| | 76 | 308 | 270 | 236 |
| | 80 | 313 | 275 | 238 |
| | 84 | 323 | 279 | 241 |
| | 88 | 327 | 287 | 243 |
| | 92 | 333 | 291 | 246 |
| 4 | 96 | 339 | 294 | 248 |
| | 100 | 342 | 299 | 251 |
| | 104 | 344 | 306 | 253 |
| | 108 | 347 | 310 | 255 |
| | 112 | 356 | 310 | 255 |
| | 116 | 357 | 310 | 255 |
| 5 | 120 | 359 | 310 | 255 |
| | 124 | 360 | 310 | 255 |
| | 128 | 360 | 310 | 255 |
| | 132 | 360 | 310 | 255 |
| | 136 | 360 | 310 | 255 |
| | 140 | 360 | 310 | 255 |
| 6 | 144 | 360 | 310 | 255 |
| | 148 | 360 | 310 | 255 |
| | 152 | 360 | 310 | 255 |
| | 156 | 360 | 310 | 255 |
| | 160 | 360 | 310 | 255 |
| | 164 | 360 | 310 | 255 |
| 7 | 168 | 360 | 310 | 255 |

* To convert TSB units of measurement from $\mu\text{mol/L}$ to mg/dl, divide by a factor of 17.1

type O mothers whose newborn is either type A or B, and the test will be performed in a batch, once a day. It should also be requested in cases where the mother is screened positive for red cell antibodies, the mother's blood type is unknown at the time of delivery, or when an infant is visibly jaundiced at less than 24 hours of age.

Timed TSB Measurement

The AAP and CPS guidelines recommend a timed TSB measurement on all newborns within 72 hours of age. This screening strategy is based on the predictive nomogram developed by Bhutani et al, in a study of 3,000 racially diverse healthy newborns to estimate risk of developing significant hyperbilirubinemia.¹³ To minimize blood sampling, we have chosen to perform the timed TSB measurement at age 24 hours or 48 hours for those born by vaginal delivery or caesarean section, respectively, corresponding to the timing of the newborn metabolic screening recommended at our institution.

Interpretation of Results

To facilitate the interpretation of the timed TSB results, the age in hours of the newborn must be known. The TSB result should be plotted against the Bhutani predictive nomogram¹³ to determine the risk zone. The nomogram is devised primarily for those using mg/dl as units of TSB measurement. In countries where SI units ($\mu\text{mol/L}$) are used, it is nearly impossible to use the predictive nomogram accurately and conveniently. The adaptation by the CPS⁴ used SI units but lacks clarity and is equally difficult to use. We have used data extracted from the original Bhutani predictive nomogram to re-design the nomogram, including a numeric format that improves accuracy and is more user-friendly (Figure 1 and Table 1). In a busy nursery where quick and accurate interpretation by nursing staff is vital, such adapted tools have become indispensable.

We have also defined two trigger points for more urgent notification of critical results to the newborn's primary healthcare provider or the pediatrician on call. Using the level of TSB to reach the high-intermediate risk zone in the Bhutani predictive nomogram, we have defined thresholds of 100 $\mu\text{mol/L}$ (6mg/dl) and 180 $\mu\text{mol/L}$ (10mg/dl) at 24 and 48 hours as trigger points necessitating urgent notification of results to the newborns' health providers for further investigations and/or for arranging

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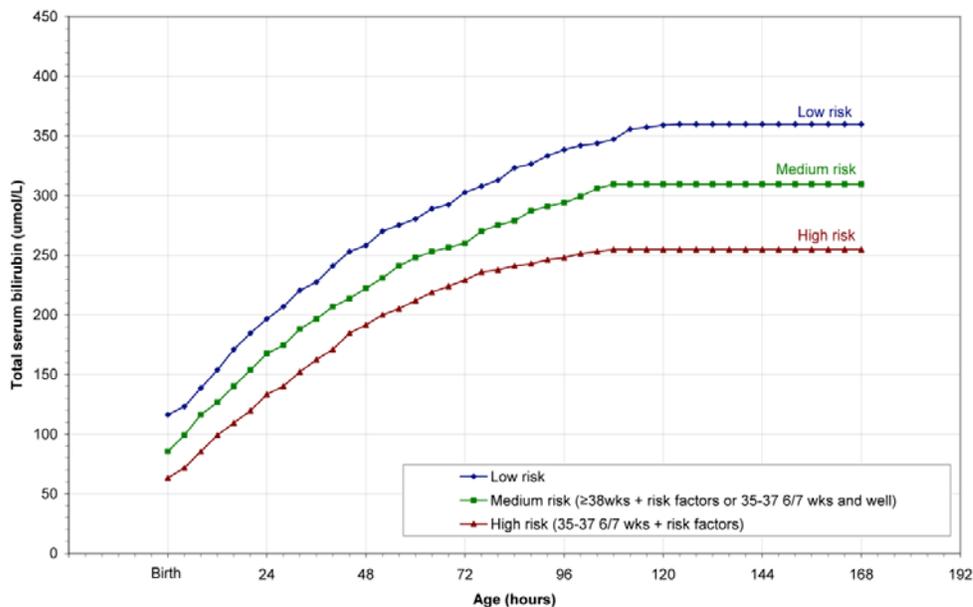


Figure 2: Phototherapy guideline for hospitalized newborn ≥ 35 weeks' gestation from the AAP, re-designed for SI unit of measurement from the original data.³

Risk factors: Isoimmune hemolytic disease (ABO, Rh, and minor blood group incompatibilities), G6PD deficiency or other non-immune hemolytic diseases, asphyxia, suspected or proven sepsis, or documented hypoalbuminemia.

closer follow-up. Having such trigger points has its pros and cons; using values easily remembered threshold values would simplify the task of identifying patients at risk, but over-simplification would run the risk of protocolizing a clinical decision making process that requires some degree of flexibility in its approach.

Having a screening strategy does not replace ongoing clinical assessment of jaundice in newborns. Some newborns might develop jaundice before the time of screening, and some of the TSB values obtained for screening might already be high enough to require treatment. It is therefore important to cross-check the screening TSB value on the phototherapy guide established by the AAP (Figure 2)³, especially if the TSB falls in the high risk zone in the Bhutani predictive nomogram. Similar to the nomogram, we have extracted data from the original graphs published by the AAP and re-designed the phototherapy guide, including a numeric format, to improve accuracy of interpretation and ease of use (Figure 2 and Table 2).

Follow-up of Those at Risk of Developing Jaundice

The objective of the bilirubin screening strategy is to identify infants at risk of developing jaundice, so that closer follow-up may be planned for those at higher risk. Therefore, the primary purpose of determining the timed TSB level pre-discharge would be to plan for appropriate and timely follow-up. The AAP

recommends that all newborns be assessed by a qualified primary health care provider within days of discharge for overall health as well as for jaundice.³ Additional follow-up may be required for those who have demonstrated difficulty with breastfeeding during the birth hospitalization. Poor breastfeeding leading to excessive weight loss and jaundice is a common reason for hospital readmission, especially in those who had shorter length of their birth hospitalization.¹⁴ Timing of follow-up should be based on the likelihood of developing significant hyperbilirubinemia in the presence of risk factors. The CPS guideline suggests a clinical decision-making algorithm based on the timed TSB level, gestational age, and result of the DAT to determine risk of significant jaundice.⁴ This algorithm enables clinicians to quickly decide on the appropriate

follow-up for each infant post-discharge based on their risk of developing jaundice. However, the use of the DAT in the decision making process poses one obvious problem: the DAT is not a universal test and is only recommended for infants at risk of blood group incompatibilities. Therefore, in adapting this algorithm into our discharge planning process, we have decided to use the presence of any risk factors associated with significant jaundice (including a positive DAT) together with gestational age and timed TSB level to determine the appropriate time for post-discharge follow up (Table 3).

Standardizing Newborn Records

Newborn healthcare providers in the community often rely solely on newborn records given to parents during the birth hospitalization to be informed of any perinatal or neonatal complications. Further, the success of a jaundice screening program is completely dependent upon the ability of newborn healthcare providers in the community to continue surveillance and to manage jaundice if it occurs. It is vital, therefore, that information on any investigation and management of jaundice during the birth hospitalization be clearly communicated to the community healthcare providers. While implementing bilirubin screening in our hospital, the newborn records (with a duplicate copy given to parents to be sent to the community healthcare providers) have been significantly revised to include information relevant to jaundice evaluation such as birth time, blood group of mother and baby, birth weight and discharge weight, DAT result, timed TSB result, and recommended follow-up date. We have also decided to include the Bhutani predictive nomogram (Table 1) and the follow-up algorithm (Table 3) in the newborn records so that the rationale for the follow-up plan is transparent to community healthcare providers. It is also important that parents be educated on the signs and symptoms of jaundice and the importance of close follow-up to prevent complications related to severe jaundice.³ We are in the process of drafting a parent information handout that includes the

| RISK ZONE | ≥ 38 weeks' gestation and with no risk factor* | 35-37 ⁶ weeks' gestation or with risk factor(s)* | 35-37 ⁶ weeks' gestation and with risk factor(s)* |
|-------------------|---|---|--|
| High | Further testing+ or treatment required | Further testing+ or treatment required | Phototherapy required |
| High-intermediate | Routine care** | Follow-up within 24-48 hrs | Further testing+ or treatment required |
| Low-intermediate | Routine care** | Routine care** | Further testing+ or treatment required |
| Low | Routine care** | Routine care** | Routine care** |

* Risk factors: As in Figure 2
 ** Routine care: routine follow-up with a health provider within 48-72 hours of discharge
 + Further testing: arrange a timely reassessment by measuring TSB; phototherapy may be required depending on TSB level

TSB value, the recommended timing of follow-up, and information on the signs and symptoms of jaundice to be given to all newborn parents prior to discharge.

The Mother and Baby Follow-up Clinic

While newborns are being discharged home any day of the week, prompt follow-up by their health provider in the community is sometimes challenging, particularly if a weekend or holiday must elapse before follow-up can occur. This might be an unacceptable interval between assessments, particular if the risk of developing jaundice is very high. In the early stage of our jaundice screening program, many newborns were brought back to the hospital on weekends and holidays for a follow-up TSB measurement, and the management was left with the pediatricians on duty at the hospital. This informal process is unreliable and cumbersome, and it puts an unnecessary burden on the pediatricians on call who are already multi-tasking and are usually unfamiliar with the newborns.

This had led to several lobbying efforts with the hospital administration, and the result was the establishment of a mother and baby follow-up clinic in June 2009. The clinic is run by staff from the public health unit and by a non-profit organization of visiting nurses. Operating 7 days a week, the objectives of the clinic are to provide ongoing breastfeeding support to mothers and infants, and specifically to follow-up on newborns at high risk of jaundice and those with jaundice where close surveillance and repeat blood sampling for TSB are required before they can be seen by their own community healthcare providers.

Final Thoughts: How Do We Measure Success of the Program?

Upon implementation of such a program, one must identify tangible quality indicators to measure success. Periodic chart audits and critical evaluation of the program must take place to ensure that the objectives are met. Chronic bilirubin encephalopathy and kernicterus are rare events, so success of the bilirubin screening program cannot be realistically measured by a drop in the incidence of these conditions. In moving forward, the program must give proof of its effectiveness and self-worth by: a significant decrease in rate of re-hospitalization for jaundice, a reduction in length of birth hospitalization stay, and secondarily, an improvement in success and duration of breastfeeding.

Acknowledgement

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tal, Toronto, Ontario, in development and implementation of the jaundice screening program. The author would also like to thank Dr. Shaheen Doctor and Dr. Maggie Shu for reviewing this manuscript.

All figures and tables in this article have been packaged into a bilirubin screening tool by the author. To obtain an electronic copy of the tool, please contact the author directly. Please specify the unit of measurement (traditional or SI) preferred. User feedback is welcomed.

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Editor's note: Dr. Ng was the former Medical Director of the NICU at North York General Hospital, Toronto, Ontario, and wrote this paper in that capacity.

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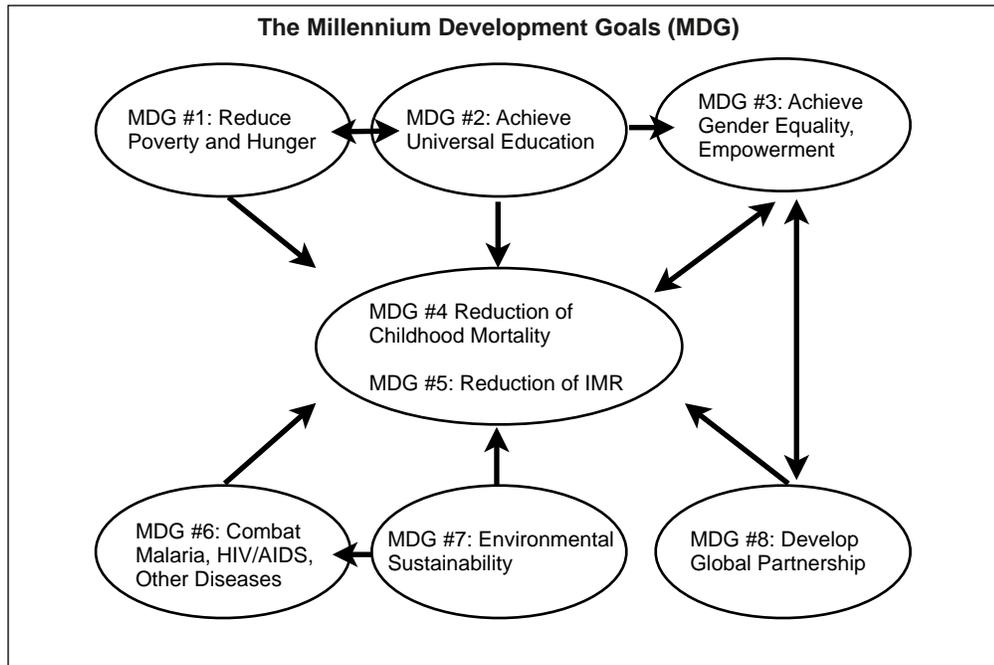
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Global Neonatology Today: A Monthly Column

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

In my previous writings I explored the problems of high NMR/IMR and MMR. It is clear that the scope of the problem is too big to be solved by any single group or a single nation. It takes enormous efforts based on collective wisdom to solve global problems.

In 2000 one hundred ninety two nations and 23 major international organizations under the aegis of The United Nations organization developed "The Millennium Development Goals (MDG)" to address the issues of global poverty, illiteracy and health to be achieved by year 2015. The eight major goals are aimed at reducing global poverty, improving universal education, decreasing maternal and child mortality, and reducing epidemics of infection. Each goal has been given targets with specific measures to be achieved.



The Millennium Development Goals (MDG)

The Millennium Development Goals and their targets are described below. The targets for MDG #4 and #5 in particular are highlighted in italics.

Goal 1: Eradicate extreme poverty and hunger

Goal 2: Achieve universal primary education

Goal 3: Promote gender equality and empower women

Goal 4: Reduce child mortality

- *Target 4A: Between 1990 and 2015, reduce by two-thirds, the under-five mortality rate*
 - *Under-five mortality rate*
 - *Infant (under 1) mortality rate*
 - *Proportion of 1-year-old children immunized against measles*

Goal 5: Improve maternal health

- *Target 5A: Between 1990 and 2015, reduce the maternal mortality ratio by three quarters*

- *Maternal mortality ratio*
- *Proportion of births attended by skilled health personnel*
- *Target 5B: By 2015, achieve universal access to reproductive health*
 - *Contraceptive prevalence rate*
 - *Adolescent birth rate*
 - *Antenatal care coverage (at least one visit and at least four visits)*
 - *Unmet need for family planning*

Goal 6: Combat HIV/AIDS, malaria and other diseases

Goal 7: Ensure environmental sustainability

Goal 8: Develop a global partnership for development

It should be noted that both goals #4 and #5 are closely dependent on achieving other goals and other MDGs as shown in the figure above. Gender equality and empowerment are critical to improving maternal and child health. Improved health is equally dependent improved literacy. Literacy improves earnings (reduction of poverty), thereby, de-

creasing hunger. The figure also shows that MDG goals #4 and #5 cannot be achieved in isolation. The targeted date of MDGs is only 5 years from now (year 2015). How much has been achieved, and how much more is to be achieved will be the subject of my next column.

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Bypass Procedure Used During Infant Heart Surgery Does Not Impair Later Neurological Outcomes

Congenital heart defects (CHD) are the most common birth defects in humans, affecting 8 per 1000 live births with one third of affected children requiring intervention in early infancy. Increasing numbers of survivors combined with developmental expectations for independence, behavioral self-regulation and academic achievement have led to a growing identification of neurobehavioral symptoms in some survivors. A study now suggests that a cooling technique often used in heart operations does not impair neurological outcomes.

Congenital heart disease and its treatment were originally thought to potentially increase neurologic injury in these patients. The technique of deep hypothermic circulatory arrest (DHCA) is used in order to repair these congenital cardiac defects by providing a bloodless surgical field, which may facilitate completion of the best physiologic repair, and decrease the duration of blood exposure to the bypass circuit. However, it involves a period of reduced blood flow in the brain. Cooling is a protective mechanism to reduce metabolism of the brain and other organs during periods of low blood flow.

Stephanie Fuller, MD, a cardiothoracic surgeon at The Children's Hospital of Philadelphia, presented these research findings in the prestigious J. Maxwell Chamberlain Lecture at the annual meeting of the Society of Thoracic Surgeons in Fort Lauderdale, FL. According to the study, DHCA does not impair language skills, attention, and other neurocognitive abilities in school-age children.

Dr. Fuller and colleagues from Children's Hospital and the University of Washington assessed the use of DHCA as a predictor of neurodevelopmental outcomes in children who had cardiac surgery as infants. The infants were enrolled in a prospective study of apolipoprotein-E (APOE) polymorphisms and neurodevelopmental outcome after cardiac surgery and underwent formal neurodevelopmental testing at four years of age.

Neurodevelopmental testing was completed in 238 out of 307 eligible patients. The surgeons used DHCA in 92 of those infants as deemed necessary to provide better operative expo-

sure with a bloodless and less cluttered surgical field and therefore, a shorter total cardiopulmonary support time. Use of DHCA was not predictive of worse performance for any neurodevelopmental outcome. Significant predictors of worse outcome included lower socioeconomic status, preoperative mechanical ventilation and babies that were younger and smaller at the time of first operation. Neurodevelopmental assessment included cognition, language skills, attention, impulsivity, executive function, social competence, and visual-motor and fine-motor skills.

"Selective use of DHCA during cardiac surgery in infancy may facilitate operative repair and is not associated with impaired neurodevelopmental outcomes," said Dr. Fuller. "Despite added risk factors, the selective use of DHCA during infancy for repair of congenital heart disease without an obstruction in the aorta was not predictive of worse performance at four years of age."

Dr. Fuller added "use of DHCA as a support technique during cardiac surgery in infancy has many advantages; it is not necessary to sacrifice these advantages merely to avoid use of DHCA. Our study adds to the growing literature showing no adverse influence of limited periods of DHCA. New support techniques must be carefully evaluated prior to wide-spread acceptance to confirm they are not inferior to conventional management strategies."

For more information, visit www.chop.edu.

New Smartphone Application Rewards Physicians with CME Credit for Online Medical Research

Newswise — Wolters Kluwer Health, a leading provider of medical information, has launched XtraCredit®, an iPhone® and iPod Touch® application that provides physicians with continuing medical education (CME) credit for clinical research done online. XtraCredit was developed by the Lippincott Continuing Medical Education Institute, a Wolters Kluwer Health subsidiary, in partnership with software developer RSi/Focal Search.

Using XtraCredit, physicians can receive CME credit for online searches of a range of professional sources. Users can download the application at no charge from

<http://xtracredit.com/iphone> or directly from the iTunes AppStore. Following a search, users document their search experience, noting the approved resource and the impact of the search on their work, and pay a small fee to receive CME credit.

"More than 50% of physicians are now using smartphones to support their clinical practice and as first-line reference resources," said Karen Overstreet, Executive Director of Lippincott CME Institute. "We are pleased to offer our readers and customers a simple way to gain the CME credit they need for answering clinical questions to enhance patient care. XtraCredit is a seamless integration of a physician's needs for both credit and clinical information."

The internet point-of-care learning format used by XtraCredit was approved by the AMA in 2006. XtraCredit allows physicians to use text or dictation to earn credit for their online searching, regardless of whether the research is completed on the phone, on a computer, or via an approved evidenced-based clinical decision support system.

Prenatal Phthalate Exposure May Alter Children's Behavior and Cognitive Function

Newswise — A study published January 28 in the peer-reviewed journal *Environmental Health Perspectives* suggests that women with higher exposure to phthalates during their pregnancy report more disruptive and problem behaviors in their children, using standardized measures. The study included 188 children whose mothers enrolled in Mount Sinai School of Medicine's New York Children's Environmental Health Study during their third trimester of pregnancy.

Phthalates are used in numerous consumer items, including cosmetics, fragrances, shampoos, lotions, and housing items like vinyl flooring. Research has indicated phthalates can interfere with reproductive and thyroid hormones. The researchers previously reported that prenatal phthalate exposure was associated with changes in newborn behavior, and their current objective was to assess their potential impact on neurobehavioral development in older children.

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Keynote Speaker: Douglas C. Wallace, PhD, Center for Molecular and Mitochondrial Medicine & Genetics, University of California at Irvine, Irvine, CA

Ten phthalate metabolites were measured in the mothers' urine collected during the third trimester of pregnancy. Mothers were interviewed one to three times while their children were 4-9 years old. Each time, the mothers completed standard questionnaires to assess their children's behavior and cognitive functioning.

The researchers found that prenatal exposure to a group of phthalates commonly found in personal care products was significantly associated with poorer scores for problems with aggression, conduct, and emotional control. Associations did not appear to differ between boys and girls overall, and associations were stronger as levels of exposure increased. However, few children's scores fell within the "at risk" or "clinically significant" range.

This study is the first to evaluate the neurobehavioral development of older children in relation to their phthalate exposure before birth. The data from this study are not sufficient to diagnose clinical conditions such as attention deficit/hyperactivity disorder. However, the results highlight an urgent need to further explore the relationship between phthalates and neurodevelopment.

Authors of the paper were Stephanie M. Engel, Amir Miodovnik, Richard L. Canfield, Chenbo Zhu, Manori J. Silva, Antonia M. Calafat, and Mary S. Wolff. This work was supported by NIEHS/EPA Children's Center grants, the New York Community Trust, and the Agency for Toxic Substances and Disease Registry. Support was also provided by the National Institute of Child Health and Human Development.

The article is available free of charge at <http://ehponline.org/article/info:doi/10.1289/ehp.0901470>.

EHP, an open access journal, is published by the National Institute of Environmental Health Sciences (NIEHS), part of the US Department of Health and Human Services.

Study Finds Higher Risk of Stillbirth in Women With Fibroids

In a study presented in February at the Society for Maternal-Fetal Medicine's (SMFM) annual meeting, The Pregnancy Meeting™, in Chicago, researchers unveiled findings that show that there is an increased risk of intrauterine fetal death (IUFD), commonly known as stillbirth, in women who have fibroids.

IUFD, or still birth, is rare and affects only six to seven out of every thousand births.

The study, conducted by researchers at Washington University in St. Louis, MO, identified women who had fibroids detected during their routine second trimester ultrasound for anatomic survey at 16-22 weeks.

"Fibroids are very common," said Dr. Molly J. Stout, one of the study's authors. "We think they occur in 5% to 20% of all women, but most women are asymptomatic and don't even know they have them."

The study was a retrospective cohort study of 64,047 women. Data were extracted on maternal sociodemographics, medical history, and obstetric outcomes. Pregnancies with any fetal anomalies were excluded. Women with at least one fibroid detected at the time of fetal anatomic survey were compared to women without fibroids. The primary outcome was IUFD after 20 weeks gestation. Univariate and multiple logistic regression analyses were used to estimate the risk of IUFD in women with fibroids. Subgroup analysis was conducted by presence or absence of fetal growth restriction (IUGR).

The study found that of 64,047 women, the incidence of fibroids was 3.2% (n=2,058). The incidence of IUFD was significantly higher in the fibroid group than in the no-fibroid group (1.6% v. 0.7%, aOR 1.8, 95%CI 1.3-2.7) even after adjusting for factors including black race, tobacco exposure, chronic hypertension, and pregestational diabetes. In subgroup analysis, the risk relationship between fibroids and IUFD only persisted within the IUGR subgroup.

"Our results showed that women with a combination of fibroids and fetal growth restriction were at two-and-a-half times the risk of having a stillbirth, though the absolute risk remained rare," said Dr. Alison G. Cahill, another of the study's authors. "This may lead to a future recommendation for serial growth scans to monitor fetal growth in women with fibroids."

For more information, visit www.smfm.org.

Mussel-inspired 'Glue' for Fetal Membrane Repair

Sealant shown to be biocompatible and effective in repairing defects in human tissue

A sealant inspired by mussels' ability to stick to surfaces under wet conditions has shown



NEONATOLOGIST NEEDED

NEONATOLOGISTS - Florida - The Department of Pediatrics at the University of Florida College of Medicine-Jacksonville is inviting applicants for a Neonatologist position in the Division of Neonatology at the non-tenure accruing level of Assistant Professor/Associate Professor (# 00024373). Our citywide neonatology program serves both area level III and three level I-II centers, and receives neonatal-perinatal referrals from Northeast Florida and Southwestern Georgia. Major responsibilities for these positions are patient care and teaching with opportunities to participate in clinical research and administrative duties. Experience with initiation and management of ECMO in the treatment of neonates with medical and/or surgical disease is desirable but not necessary.

Applicants should possess a MD/DO degree and be Board Eligible/Board Certified in neonatal/perinatal medicine. Applications will continue to be received until the position is filled. Salary is negotiable.

Forward letter of intent, curriculum vitae, and the names and addresses of three references to:

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 Professor and Associate Chair, Search Committee Chair
 Department of Pediatrics
 University of Florida
 College of Medicine-Jacksonville
 653-1 West Eighth Street
 Jacksonville, FL 32209
 904-244-3050, and/or fax 904-244-3028, and/or e-mail:
ufpeds.recruitment@jax.ufl.edu.

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NEONATOLOGIST/MEDICAL DIRECTOR WANTED

FLORIDA - The Department of Pediatrics at the University of Florida College of Medicine - Jacksonville, is inviting applicants for a new Neonatologist position in the Division of Neonatology at the non-tenure accruing level of Assistant / Associate Professor (# 00022978). The primary role of this faculty will be to serve as the Medical Director of a new regional level II NICU that will open in late summer/early fall of 2010. In-house clinical coverage will be provided by neonatologist(s) and physician extenders (neonatal ARNPs or physician assistants). An opportunity to provide clinical care at other NICUs in our regional neonatology program that currently serves two level III and three level I-II centers is negotiable.

Applicants should possess a MD/DO degree and be Board Eligible/Board Certified in neonatal/perinatal medicine. Salary is negotiable. Anticipated start date is Fall 2010.

Forward letter of intent, CV and the names and addresses of three references to:

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Professor and Associate Chairman and
Search Committee Chair
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promise in the repair of defects in human fetal membranes, according to a recent Northwestern University study.

During pregnancy, defects -- ruptures or holes -- in the fetal membrane can lead to the leakage of amniotic fluid, resulting in premature labor or termination of the pregnancy. Although some defects do repair themselves naturally,

no method currently exists to effectively repair those that don't. One idea is to find a biocompatible material to seal off the opening.

"We tested our mussel-inspired sealant on living fetal tissue and found it was both biocompatible and effective at sealing the tiny holes -- two features essential in such a material," said Phillip B. Messersmith, who was one of the study's leaders. He is Professor of Biomedical Engineering at Northwestern's McCormick School of Engineering and Applied Science.

The findings were published online by the *American Journal of Obstetrics & Gynecology*.

The fetal membrane is the structure that surrounds the developing fetus. Defects in the membrane result either from incisions during endoscopic fetal surgeries used in the treatment of some birth defects or premature and spontaneous ruptures in the fetal sac.

Messersmith and colleagues from Belgium, Switzerland and Canada punched holes three millimeters wide into human fetal tissue in vitro to replicate the tiny holes found in fetal membrane defects. They then applied their sealant as well as other sealant candidates (such as medical-grade superglues) to the holes and analyzed fetal tissue cell death for each sealant. The mussel-inspired sealant had the best results in both bonding and toxicity.

The injectable sealant is a mixture of two different solutions that, when combined, form a sealant or gel in 10 to 20 seconds. One solution is a simple synthetic polymer containing DOPA, a key amino acid found in the sophisticated proteins that are essential to mussels' ability to adhere to wet surfaces, and the other is a catalyst. (Messersmith first developed the polymer in 2002.)

The foot of the common mussel (*Mytilus edulis*) produces a sticky glue that keeps the shelled organism anchored to rocks and other objects, allowing them to withstand the extreme pounding of waves. Chemical analysis of this natural, waterproof glue showed that the key to its adhesiveness is a family of unique proteins called mussel adhesive proteins, which contain a high concentration of DOPA (dihydroxyphenylalanine).

Messersmith and his colleagues currently are testing the mechanical qualities of the mussel-inspired sealant and plan to conduct in vivo experiments in animal models.

Do you or your colleagues have interesting research results, observations, human interest stories, reports of meetings, etc. that you would like to share with the neonatology community?

Submit a brief summary of your proposed article to: Article@Neonate.biz

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